UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 20-F

(Mark One)

☐ **REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR (g) OF THE SECURITIES EXCHANGE ACT OF 1934**

OR

☒ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2021

OR

☐ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from to

OR

☐ SHELL COMPANY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Date of event requiring this shell company report
For the transition period from to

Commission file number 001-39670

PURETECH HEALTH PLC

(Exact name of registrant as specified in its charter)

N/A
(Translation of Registrant's name into English)

England and Wales
(Jurisdiction of incorporation or organization)
6 Tide Street, Suite 400
Boston, Massachusetts 02210
United States
(Address of principal executive offices)
Daphne Zohar
Chief Executive Officer Tel: (617) 482-2333
E-mail: ir@puretechhealth.com

c/o PureTech Health LLC
6 Tide Street, Suite 400
Boston, Massachusetts 02210
United States
(Name, telephone, e-mail and/or facsimile number and address of company contact person)

Securities registered or to be registered pursuant to Section 12(b) of the Act:

Title of each class:	Trading Symbol(s)	Name of each exchange on which registered:
American Depositary Shares, each representing 10 ordinary shares, par value £0.01 per share	PRTC	The Nasdaq Global Market
Ordinary shares, par value £0.01 per share*	*	The Nasdaq Global Market*

* Listed not for trading, but only in connection with the registration of the American Depositary Shares on The Nasdaq Global Market.

Securities registered or to be registered pursuant to Section 12(g) of the Act: None.
Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act: None.

Indicate the number of outstanding shares of each of the issuer's classes of capital or common stock as of the close of the period covered by the annual report: Ordinary Shares: 287,796,585 outstanding as of December 31, 2021.

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days: Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files): Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☒	Accelerated filer	☐	Non-accelerated filer	☐	Emerging growth company	☐

If an emerging growth company that prepares its financial statements in accordance with U.S. GAAP, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

† The term "new or revised financial accounting standard" refers to any update issued by the Financial Accounting Standards Board to its Accounting Standards Codification after April 5, 2012.

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

Indicate by check mark which basis of accounting the registrant has used to prepare the financial statements included in this filing:

U.S. GAAP ☐	International Financial Reporting Standards as issued by the International Accounting Standards Board ☒	Other ☐

If "Other" has been checked in response to the previous question, indicate by check mark which financial statement item the registrant has elected to follow. Item 17 ☐ Item 18 ☐

If this is an annual report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

TABLE OF CONTENTS

Special Note Regarding Forward-Looking Statements

This annual report on Form 20-F contains forward-looking statements that involve substantial risks and uncertainties. All statements contained in this report, other than statements of historical fact, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “target,” “potential,” “would,” “could,” “should,” “continue” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. The forward-looking statements in this annual report on Form 20-F include, among other things, statements about:

- our ability to realize value from our Founded Entities, which may be impacted if we reduce our ownership to a minority interest or otherwise cede control to other investors through contractual agreements or otherwise;
- the success, cost and timing of our clinical development of our Wholly Owned Programs, including the progress of, and results from, our preclinical and clinical trials of LYT-100, LYT-200, LYT-210, LYT-300, LYT-510, LYT-500, LYT-503/IMB-150, our discovery programs (Glyph, Orasome and our meningeal lymphatics discovery research program) and other potential product candidates within our Wholly Owned Programs;
- our ability to obtain and maintain regulatory approval of the therapeutic candidates in our Wholly Owned Pipeline, and any related restrictions, limitations or warnings in the label of any of the therapeutic candidates in our Wholly Owned Pipeline, if approved;
- our ability to compete with companies currently marketing or engaged in the development of treatments for indications that the therapeutic candidates in our Wholly Owned Pipeline or those of our Founded Entities are designed to target;
- our plans to pursue research and development of other future product candidates;
- the potential advantages of our Wholly Owned Programs and the therapeutic candidates being developed by our Founded Entities;
- the rate and degree of market acceptance and clinical utility of our therapeutic candidates;
- the success of our collaborations and partnerships with third parties;
- our estimates regarding the potential market opportunity for our Wholly Owned Programs and the therapeutic candidates being developed by our Founded Entities;
- our sales, marketing and distribution capabilities and strategy;
- our ability to establish and maintain arrangements for manufacture of the therapeutic candidates in our Wholly Owned Pipeline and those being developed by our Founded Entities;
- our intellectual property position;
- our expectations related to the use of capital;
- the effect of the COVID-19 pandemic, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations, including but not limited to our preclinical studies and future clinical trials;
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- the impact of government laws and regulations; and
- our competitive position.

SUMMARY OF RISK FACTORS

The risk factors described below are a summary of the principal risk factors associated with our business. These are not the only risks we face. You should carefully consider these risk factors, together with the risk factors incorporated by reference into Item 3D. of this annual report on Form 20-F and the other reports and documents filed by us with the SEC.

- As of December 31, 2021, we had never generated revenue from the therapeutic candidates within our Wholly Owned Pipeline, and we may never be operationally profitable.
- We may require substantial additional funding to achieve our business goals. If we are unable to obtain this funding when needed and on acceptable terms, we could be forced to delay, limit or terminate certain of our therapeutic development efforts. Certain of our Founded Entities will similarly require substantial additional funding to achieve their business goals.
- Our ability to realize value from our Founded Entities may be impacted if we reduce our ownership or otherwise cede control to other investors through contractual agreements or otherwise.
- We have limited information about and limited control or influence over our Non-Controlled Founded Entities.
- The therapeutic candidates within our Wholly Owned Pipeline and most of our Founded Entities' therapeutic candidates are in preclinical or clinical development, which is a lengthy and expensive process with uncertain outcomes and the potential for substantial delays. We cannot give any assurance that any of our and our Founded Entities' therapeutic candidates will receive regulatory approval, which is necessary before they can be commercialized.
- Preclinical development is uncertain. Our preclinical programs may experience delays or may never advance to clinical trials, which would adversely affect our ability to obtain regulatory approvals or commercialize these programs on a timely basis or at all, which would have an adverse effect on our business.
- Clinical trials of our or our Founded Entities' therapeutic candidates may be delayed, and certain programs may never advance in the clinic or may be more costly to conduct than we anticipate, any of which can affect our ability to fund our company and would have a material adverse impact on our platform or our business.
- If we encounter difficulties enrolling patients in clinical trials, our clinical development activities could be delayed or otherwise adversely affected.
- Use of the therapeutic candidates within our Wholly Owned Pipeline or the therapeutic candidates being developed by our Founded Entities could be associated with side effects, AEs or other properties or safety risks, which could delay or halt their clinical development, prevent their regulatory clearance or approval, cause us to suspend or discontinue clinical trials, abandon a therapeutic candidate, limit their commercial potential, if cleared or approved, or result in other significant negative consequences that could severely harm our business, prospects, operating results and financial condition.
- Our clinical trials may fail to demonstrate substantial evidence of the safety and effectiveness of therapeutic candidates that we may identify and pursue for their intended uses, which would prevent, delay or limit the scope of regulatory approval and potential commercialization.
- Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the potential commercialization of therapeutic candidates.
- If we are unable to obtain regulatory clearance or approval in one or more jurisdictions for any therapeutic candidates that we may identify and develop, our business could be substantially harmed.
- Certain of the therapeutic candidates being developed by us or our Founded Entities are novel, complex and difficult to manufacture. We could experience manufacturing problems that result in delays in our development or commercialization programs or otherwise harm our business.
- If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any therapeutic candidates we may develop, we may not be successful in commercializing those therapeutic candidates if and when they are approved.
- If we fail to comply with healthcare laws, we could face substantial penalties and our business, operations and financial conditions could be adversely affected.
- We face significant competition in an environment of rapid technological and scientific change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer, more advanced or more effective than ours, which may negatively impact our ability to successfully market or commercialize any therapeutic candidates we may develop and ultimately harm our financial condition.
- We are currently party to and may seek to enter into additional collaborations, licenses and other similar arrangements and may not be successful in maintaining existing arrangements or entering into new ones, and even if we are, we may not realize the benefits of such relationships.
- We rely on third parties to assist in conducting our clinical trials and some aspects of our research and preclinical testing, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research, or testing.
- If we or our Founded Entities are unable to obtain and maintain sufficient intellectual property protection for our or our Founded Entities' existing therapeutic candidates or any other therapeutic candidates that we or they may identify, or if the scope of the intellectual property protection we or they currently have or obtain in the future is not sufficiently broad, our competitors could develop and commercialize therapeutic candidates similar or identical to ours, and our ability to successfully commercialize our existing therapeutic candidates and any other therapeutic candidates that we or they may pursue may be impaired.
- We may not be able to protect our intellectual property rights throughout the world.
- Our or our Founded Entities' proprietary rights may not adequately protect our technologies and therapeutic candidates, and do not necessarily address all potential threats to our competitive advantage.
- The failure to maintain our licenses and realize their benefits may harm our business.

- If we or our Founded Entities fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or these agreements are terminated or we or our Founded Entities otherwise experience disruptions to our business relationships with our licensors, we could lose intellectual property rights that are important to our business.
- Patent terms may be inadequate to protect our competitive position on therapeutic candidates for an adequate amount of time.
- Issued patents covering our Wholly Owned Programs or our Founded Entities' therapeutic candidates could be found invalid or unenforceable if challenged in courts or patent offices.
- If we are unable to protect the confidentiality of our trade secrets, the value of our technology could be materially adversely affected and our business would be harmed.
- We and our Founded Entities may be subject to claims challenging the inventorship of our patents and other intellectual property.
- The COVID-19 pandemic has impacted, and will likely continue to impact, our business, including our clinical trials and preclinical studies, and may materially and adversely affect our business in the future.
- We may not be successful in our efforts to develop LYT-100 for the treatment of Long COVID respiratory complications and related sequelae.
- Failures in one or more of our programs could adversely impact other programs and have a material adverse impact on our business, results of operations and ability to fund our business.
- Our business is highly dependent on the clinical advancement of our programs and our success in identifying potential therapeutic candidates across the brain, immune and gastrointestinal therapeutic areas. Delay or failure to advance our programs could adversely impact our business.
- Our future success depends on our ability to retain key employees, directors, consultants and advisors and to attract, retain and motivate qualified personnel.
- The market price of our ADSs has been and will likely continue to be highly volatile, and you could lose all or part of your investment.
- Holders of ADSs are not treated as holders of our ordinary shares.
- As a foreign private issuer, we are permitted to adopt certain home country practices in relation to corporate governance matters that differ significantly from Nasdaq corporate governance listing standards. These practices may afford less protection to shareholders than they would enjoy if we complied fully with corporate governance listing standards.
- If we are unable to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, shareholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our ADSs.
- In connection with the audit of our consolidated financial statements in accordance with the standards of the PCAOB and U.S. securities laws, a material weakness in our internal control over financial reporting was found to exist. If we fail to implement and maintain effective internal control over financial reporting, we may be unable to accurately report our results of operations, meet our reporting obligations or prevent fraud.

EXPLANATORY NOTE

Pursuant to Rule 12b-23(a) of the Securities Exchange Act of 1934, as amended, the information for the 2021 Form 20-F of PureTech Health plc (the "Company") set out below is being incorporated by reference from PureTech's "Annual Report and Accounts 2021", portions of which are included as exhibit 15.1 to this annual report on Form 20-F. Only the information set out below with specific reference to items and pages of PureTech's "Annual Report and Accounts 2021" is deemed to be filed as part of this annual report on Form 20-F. Other information contained within PureTech's "Annual Report and Accounts 2021" that is not specified, including graphs and tabular data, is not included in this annual report on Form 20-F and is not deemed to be filed as part of this annual report on Form 20-F. Photographs are also not included. References herein to PureTech's websites are textual references only and information on or accessible through such websites does not form part of and is not incorporated into this annual report on Form 20-F.

References below to major headings include all information under such major headings, including subheadings, unless such reference is a reference to a subheading, in which case such reference includes only the information contained under such subheading. Unless the context otherwise requires, "PureTech" and "PureTech Health" refer to the Company, which is comprised of PureTech and its Founded Entities (together, the "Group"). "Founded Entities" are comprised of "Controlled Founded Entities" and "Non-Controlled Founded Entities." References in this annual report on Form 20-F to "Controlled Founded Entities" refer to Follica, Incorporated, Vedanta Biosciences, Inc., Sonde Health, Inc. Alivio Therapeutics, Inc. and Entrega, Inc. References to "Non-Controlled Founded Entities" refer to Gelesis, Inc., and for periods after January 13, 2022, Gelesis Holdings, Inc. as its successor, Akili Interactive Labs, Inc., Karuna Therapeutics, Inc. and Vor Biopharma Inc., and, for all periods prior to December 18, 2019, resTORbio, Inc. PureTech formed each of its Founded Entities and has been involved in development efforts in varying degrees. In the case of each of the Company's Controlled Founded Entities, the Company continues to maintain majority voting control. With respect to Non-Controlled Founded Entities, the Company may benefit from appreciation in its investment as a shareholder of such companies.

PART I

ITEM 1. IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISERS.

Not applicable.

ITEM 2. OFFER STATISTICS AND EXPECTED TIMETABLE

Not applicable.

ITEM 3. KEY INFORMATION

A. [Reserved]

B. CAPITALIZATION AND INDEBTEDNESS

Not applicable.

C. REASONS FOR THE OFFER AND USE OF PROCEEDS

Not applicable.

D. RISK FACTORS

The information (including tabular data) set forth or referenced under the heading “Risk Factor Annex" on pages 217 to 251 of PureTech’s “Annual Report and Accounts 2021” included as exhibit 15.1 to this annual report on Form 20-F is incorporated by reference.

ITEM 4. INFORMATION ON THE COMPANY

A. HISTORY AND DEVELOPMENT OF THE COMPANY

The information set forth under the heading "History and Development of the Company" on page 216 of PureTech's "Annual Report and Accounts 2021" included as exhibit 15.1 to this annual report on Form 20-F is incorporated by reference.

For a description of our principal capital expenditures and divestitures for the three years ended December 31, 2021 and for those currently in progress, see Item 5. "Operating and Financial Review and Prospects—A. Operating Results".

The United States Securities and Exchange Commission (the "SEC") maintains an internet website that contains reports, proxy and information statements, and other information regarding issuers, like us, that file electronically with the SEC. The address of that website is www.sec.gov. We also maintain an Internet website at www.puretechhealth.com. The information contained on, or that may be accessed through, our website is not part of, and is not incorporated into, annual report on Form 20-F.

B. BUSINESS OVERVIEW

The information (including graphs and tabular data) set forth under the following headings is incorporated by reference herein: "Highlights of the Year—2021" (for the years of 2019, 2020 and 2021) on pages 2 to 9, "Components of Value" on pages 10 to 11, "How PureTech is building value for investors" on pages 23 to 27, "PureTech's Wholly Owned Programs" on pages 35 to 56, "ESG Report—Patients" on page 75, "Risk Management—Risks related to regulatory approval" on page 91 and "Risk Management—Risks related to intellectual property protection" on page 92, "Financial Review—Revenue" on page 100, in each case of PureTech's "Annual Report and Accounts 2021" included as exhibit 15.1 to this annual report on Form 20-F, "Consolidated Statements of Comprehensive Income/(Loss)," "Notes to the Consolidated Financial Statements—Note 3.—Revenue" and "Notes to the Consolidated Financial Statements—Note 4.—Segment information," in each case of our audited consolidated financial statements included elsewhere in this annual report on Form 20-F. Seasonality does not materially impact the Company's main business.

Competition

The biotechnology and pharmaceutical industries utilize rapidly advancing technologies and are characterized by intense competition. There is also a strong emphasis on intellectual property and proprietary products. Our pipeline around brain, immune and gastrointestinal therapeutic areas with a particular focus on immunological disorders builds on validated biology of known therapeutics while applying unique inventive steps that improve the clinical pharmacology. We further de-risk programs with key experiments at an early stage to validate the underlying value proposition. We believe that our technology, drug discovery and development expertise and capabilities enable such strong pipeline creation and provide us with a competitive advantage. However, we will continue to face competition from different sources including major pharmaceutical companies, biotechnology companies, academic institutions, government agencies, and public and private research institutions. In addition, there are companies that are working on potential medicines targeting the brain, immune and gastrointestinal systems and many companies that have approved therapeutics for some of our target indications. For any products that we eventually commercialize, we will not only compete with existing therapies but also compete with new therapies that may become available in the future.

In addition to the competition we will face from the parties described above, we face competition for certain of the product candidates we are developing internally.

LYT-100

We are aware of two current drug product candidates in development for secondary lymphedema. Celltaxis is studying acebilustat, a leukotriene A4 hydrolase inhibitor, in an investigator-sponsored study, and Theralymph is developing a preclinical gene therapy.

The other current treatments for lymphedema include durable medical goods, such as compression sleeves and garments, and surgical options, including liposuction and debulking. A novel investigational surgery, lymph node transfer, is also being tested.

In the field of IPF, there are two approved drugs, pirfenidone (Esbriet), marketed by Roche, and nintedanib (Ofev), marketed by Boehringer Ingelheim. These drugs have unfavorable tolerability profiles, leading to sustained unmet need for novel therapies. Other potential competitive product candidates in various stages of development include, but are not limited to: Fibrogen's pamrevlumab in Phase 3 clinical trials, Roche/Promedior, Inc.'s PRM-151 in Phase 3 clinical trials, treprostinil in Phase 3 clincial trials, Avalyn's AP01 which is expected to enter a Phase 3 trial in 2022, Horizon Therapeutics' HZN-825 in Phase 2 clinical development, Pliant Therapeutics' PLN-74809 in Phase 2 clinical development, Boehringer Ingelheim's BI1015550 in Phase 2 development, BMS' BMS-986278 in Phase 2 clinical development, BMS/Celgene's CC-90001 in Phase 2 clinical development, and Galecto's GB0139 in Phase 2 clinical development.

In the field of COVID-19, there are numerous clinical trials for prevention of COVID-19 using vaccines, or for acute treatment of COVID-19 using anti-viral and anti-inflammatory agents. Few trials are underway targeting respiratory complications of post-acute COVID-19 syndrome. The other potential competitive product candidates in development include: an investigator-sponsored study of pirfenidone in post-acute COVID-19 syndrome, an investigator-sponsored study of nintedanib collaborating with Boehringer Ingelheim, and a pilot study of Treamid sponsored by PHARMENTERPRISES. Several pulmonary rehabilitation studies are also underway.

LYT-200

We are aware of one current drug product candidate targeting galectin-9 - HiFiBio Therapeutics' HFB-200902 which was licensed by FibroGen in June 2021 and expects to enter clinical development in 2023. Additionally, if we are successful in developing LYT-200 as an immuno-oncology treatment we would expect to compete with currently approved IO therapies and those that may

be developed in the future. Current marketed IO products include CTLA-4, such as BMS' Yervoy, and PD-1/PD-L1, such as BMS' Opdivo, Merck's Keytruda and Genentech's Tecentriq, and T cell engager immunotherapies, such as Amgen's Blincyto. In addition, there are other academic groups and/or companies that may be involved in pre-clinical research centered around galectin-9 as a therapeutic target.

LYT-210

To the best of our knowledge, there are no competitors in the space of immunosuppressive γδ T cells. However, there are other academic groups and/or companies that are involved in pre-clinical and clinical research and development centered around cytotoxic gamma delta T cells.

LYT-300

In the field of GABAA positive allosteric modulators, there are two approved drugs, allopregnanolone (Zulresso), marketed by Sage Therapeutics, and ganaxolone (Ztalmy), marketed by Marinus Pharmaceuticals. Other potential competitive product candidates in various stages of development include, but are not limited to, Sage Therapeutics's SAGE-217 (Zuranolone) in Phase 3 clinical development, Praxis's PRAX-114 in Phase 2/3 clinical development and Eliem Therapeutics' ETX-155 in Phase 1b clinical development.

LYT-510, 500 and 503/IMB-150

In the field of inflammatory bowel disease (IBD), there are many approved treatments and numerous clinical trials ongoing for induction and maintenance of IBD. If we are successful in developing LYT-510 for IBD, we would expect to compete with currently approved IBD therapies and those that may be developed in the future. Current marketed IBD products include anti-TNF agents like AbbVie's Humira and JnJ's Simponi, anti-integrin agents like Takeda's Entyvio, anti-IL-12/IL-23 agents like JnJ's Stelara and JAK-inhibitors like Pfizer's Xeljanz.

LYT-510: There are no FDA-approved therapies are available for chronic pouchitis. Current chronic pouchitis agents in development include Applied Molecular Transport's AMT-101 in Phase 2 clinical development and investigator sponsored clinical trials with Pfizer's Xeljanz, Aviva Pharmaceutical's metronidazole and Reponex Pharmaceutical's molgramostim.

LYT-500: There are no FDA approved therapies in the field of interleukin-22 therapeutics. Competitive IL-22 product candidates in various stages of development include, but are not limited to, Genentech's efmarodocokin alfa in Phase 2 clinical development, Evive Biotech's F-652 in Phase 2 clinical development, Applied Molecular Transport's AMT-126 in Phase 1 clinical development, AbbVie's ABBV-022 in Phase 1 clinical development.

LYT-503/IMB-150

In the field of interstitial cystitis/bladder pain syndrome, there are a few FDA approved agents including JnJ's Elmiron, , and Mylan Pharmaceutical's Rimso-50. There are also numerous clinical trials ongoing for interstitial cystitis. If LYT-503 is successful in interstitial cystitis, we would expect to compete with currently approved therapies and those that may be developed in the future. Current interstitial cystitis products in development include, but are not limited to, Urigen Pharmaceutical's URG-101, Vaneltix Pharma's Alenura, Trigone Pharma's TRG-100, and Seikagaku Corp's SI-722 all in Phase 2 clinical development.

Other Programs

We are not aware of any direct competitors to our Glyph, Orasome and meningeal lymphatics platforms, but they may compete with new therapies that become available in the future to target the indications we are focused on. There are several exosome programs being developed but to the best of our knowledge none of them are targeting oral delivery or using milk, thus differentiating our approach. Competitors developing exosomes or engineered exosomes to deliver payloads include Inc AstraZeneca plc, Capricor Therapeutics, Evox Therapeutics Ltd, ArunA Biomedical Inc, ExoCoBio Inc, Codiak Biosciences, Inc. and Exopharm Ltd.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of drugs, biological products and medical devices. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations, require the expenditure of substantial time and financial resources.

U.S. Government Regulation of Drug and Biological Products

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations and biologics under the FDCA and the Public Health Service Act, or PHSA, and their implementing regulations. Both drugs and biologics also are subject to other federal, state and local statutes and regulations, such as those related to competition. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, and local statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or following approval may subject an applicant to administrative actions or judicial sanctions. These actions and sanctions could include, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval, license revocation, a clinical hold, untitled or warning letters, voluntary or mandatory product recalls or market withdrawals, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement and civil or criminal fines or penalties. Any agency or judicial enforcement action could have a material adverse effect on our business, the market acceptance of our products and our reputation.

Product candidates must be approved by the FDA through either a new drug application, or NDA, or a biologics license application, or BLA, process before they may be legally marketed in the United States. The process generally involves the following:

- completion of nonclinical, or preclinical, laboratory tests, animal studies and formulation studies in compliance with applicable good laboratory practice, or GLP, regulations;
- submission to the FDA of an investigational new drug application, or IND, which must take effect before human clinical trials may begin;
- approval by an independent IRB representing each clinical site before each clinical trial may be initiated at that site;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCPs, to establish the safety and efficacy, or with respect to biologics, the safety, purity and potency, of the proposed drug product for each indication;
- preparation and submission to the FDA of an NDA or BLA, and payment of user fees, if applicable;
- a determination by the FDA within 60 days of its receipt of an NDA or BLA to accept the application for substantive review;
- review of the product by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA pre-approval inspections of the manufacturing facility or facilities where the drug or biologic will be produced to assess compliance with Current Good Manufacturing Practices, or cGMP, requirements to assure that the facilities, methods and controls are adequate to preserve the drug or biologic's identity, strength, quality and purity;
- satisfactory completion of potential FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data; and
- FDA review and approval of the marketing application prior to any commercial marketing or sale of the drug or biologic in the United States.

Preclinical Studies

Before testing any drug or biological product candidate in humans, the product candidate must undergo rigorous preclinical testing. Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as in vitro and animal studies to assess safety and in some cases to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal and state regulations and requirements, including GLP regulations.

The IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved drug or biological product to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer such investigational drug or biological product to humans. Such authorization must be secured prior to interstate shipment and administration of the investigational drug or biological product. In an IND, applicants must submit a protocol for each clinical trial proposed to be initiated and any subsequent protocol amendments. In addition, the results of the preclinical tests, manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events, or AEs, and carcinogenicity, may continue after the IND is submitted.

The FDA requires a 30-day waiting period after the submission of each IND before clinical trials may begin. At any time during this 30-day period, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial due to safety concerns or non-compliance with specific FDA requirements. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the proposed or ongoing clinical investigation. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all FDA IND requirements must be met unless waived. When the foreign clinical study is not conducted under an IND, the FDA may accept data from such study if the sponsor ensures that the study is conducted in accordance with GCP, including review and approval by an independent ethics committee, or IEC, and informed consent from subjects. The FDA must also be able to validate the data from the study through an on-site inspection if necessary.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review of the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, often known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the subjects or patients are being exposed to an unacceptable health risk.

Information about certain clinical trials must be submitted within specific timeframes to the NIH for public dissemination on its ClinicalTrials.gov website. Information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Although sponsors are obligated to disclose the results of their clinical trials after completion, disclosure of the results can be delayed in some cases for up to two years after the date of completion of the trial. Failure to timely register a covered clinical study or to submit study results as provided for in the law can give rise to civil monetary penalties and also prevent the non-compliant party from receiving future grant funds from the federal government.

Clinical Trials

The clinical stage of development involves the administration of the investigational product to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, the parameters to be used to monitor subject safety and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

- Phase 1. The drug is initially introduced into healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.
- Phase 2. The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- Phase 3. The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.

In most cases, the FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the safety and efficacy of the drug or biologic. In certain instances, a single Phase 3 trial may be sufficient when, for example, the trial is a large, multicenter trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible, or) the single trial is supported by other confirmatory evidence. Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication and are commonly intended to generate additional safety data regarding use of the product in a clinical setting. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA or BLA.
Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators 15 days after the trial sponsor determines the information qualifies for reporting for serious and unexpected suspected AEs, findings from other studies or animal or in vitro testing that suggest a significant risk for human subjects and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must also notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction as soon as possible but in no case later than seven calendar days after the sponsor's initial receipt of the information.

The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug or biologic has been associated with unexpected serious harm to patients. Concurrent with clinical trials, companies usually complete additional animal studies and also must develop additional information about the chemistry and physical characteristics of the drug or biologic as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product and, among other things, companies must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidates do not undergo unacceptable deterioration over their shelf life.

FDA Review Process

Following completion of the clinical trials, data are analyzed to assess whether the investigational product is safe and effective for the proposed indicated use or uses. The results of preclinical studies and clinical trials are then submitted to the FDA as part of an NDA or BLA, along with proposed labeling, chemistry and manufacturing information to ensure product quality and other relevant data. The NDA or BLA is a request for approval to market the drug or biologic for one or more specified indications and must contain proof of safety and efficacy for a drug or safety, purity and potency for a biologic. The application may include both negative and ambiguous results of preclinical studies and clinical trials, as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the satisfaction of FDA. FDA approval of an NDA or BLA must be obtained before a drug or biologic may be marketed in the United States.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each NDA or BLA must be accompanied by a user fee. FDA adjusts the PDUFA user fees on an annual basis. Fee waivers or reductions are available in certain circumstances, including a waiver

of the application fee for the first application submitted by a small business. Additionally, no user fees are assessed on NDAs or BLAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA reviews all submitted NDAs and BLAs before it files them, and may request additional information rather than filing the NDA or BLA. The FDA must make a decision on filing an NDA or BLA within 60 days of receipt, and such decision could include a refusal to file by the FDA. In this event, the NDA or BLA must be resubmitted with the additional information requested by FDA. The resubmitted application also is subject to review before the FDA files it. Once the submission is filed, the FDA begins an in-depth review of the NDA or BLA. Under the goals and policies agreed to by the FDA under PDUFA, the FDA targets ten months, from the filing date, in which to complete its initial review of a new molecular entity NDA or original BLA and respond to the applicant, and six months from the filing date of a new molecular entity NDA or original BLA designated for priority review. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs or BLAs, and the review process is often extended by FDA requests for additional information or clarification.

Before approving an NDA or BLA, the FDA will generally conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether the facilities comply with cGMP requirements. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The FDA also may audit data from clinical trials to ensure compliance with GCP requirements. Additionally, the FDA may refer applications for novel products or products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions, if any. The FDA is not bound by recommendations of an advisory committee, but it considers such recommendations when making decisions on approval. The FDA may reanalyze the clinical trial data provided by the sponsor, including in connection with an advisory committee meeting, which could result in extensive discussions between the FDA and the applicant during the review process. After the FDA evaluates an NDA or BLA, it will issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug or biologic with specific prescribing information for specific indications. A Complete Response Letter states that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes all of the specific deficiencies in the NDA or BLA identified by the FDA. The Complete Response Letter may require the applicant to obtain additional clinical data, including the potential requirement to conduct additional clinical trial(s) and/or to complete other significant and time-consuming requirements related to clinical trials, or to conduct additional preclinical studies or manufacturing activities. If a Complete Response Letter is issued, the applicant may appeal the decision through the FDA's administrative dispute resolution process, resubmit the NDA or BLA addressing all of the deficiencies identified in the letter, withdraw the application or request an opportunity for a hearing. Even if the data and information requested in a Complete Response letter are submitted by the sponsor, the FDA may decide that the NDA or BLA does not satisfy the criteria for approval.

Expedited Development and Review Programs

A sponsor may seek to develop and obtain approval of its product candidates under programs designed to accelerate the development, FDA review and approval of new drugs and biologics that meet certain criteria. For example, the FDA has a fast track program that is intended to expedite or facilitate the process for reviewing new drugs and biologics that are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the condition. Fast track designation applies to both the product and the specific indication for which it is being studied. For a fast track-designated product candidate, the FDA may consider sections of the NDA or BLA for review on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable and the sponsor pays any required user fees upon submission of the first section of the application. The sponsor can request the FDA to designate the product candidate for fast track status any time before receiving NDA or BLA approval, but ideally no later than the pre-NDA or pre-BLA meeting.

A product candidate submitted to the FDA for marketing, including under a fast track program, may be eligible for other types of FDA programs intended to expedite development or review, such as priority review and accelerated approval. Priority review means that, for a new molecular entity or original BLA, the FDA sets a target date for FDA action on the marketing application at six months after accepting the application for filing as opposed to ten months. An NDA or BLA is eligible for priority review if the product candidate designed to treat a serious or life-threatening disease condition and, if applicable and if approved, would provide a significant improvement in safety and effectiveness compared to available therapies. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug or biologic designated for priority review in an effort to facilitate the review. If criteria are not met for priority review, the application for a new molecular entity or original BLA is subject to the standard FDA review period of ten months after FDA accepts the application for filing. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

A product candidate may also be eligible for accelerated approval if it is designed to treat a serious or life-threatening disease or condition upon a determination that the product candidate an effect on either a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the disease or condition and the availability or lack of alternative treatments. As a condition of approval, the FDA generally requires that a sponsor of a drug or biologic receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials to confirm the product's clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval that promotional materials be submitted for review prior to dissemination, which could adversely impact the timing of the commercial launch of the product. FDA may withdraw approval of a drug or indication approved under accelerated approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product.

Additionally, a drug or biologic may be eligible for designation as a breakthrough therapy if the product is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. If the FDA designates a breakthrough therapy, it may take actions appropriate to expedite the development and review of the application, which may include holding meetings with the sponsor and the review team throughout the development of the therapy; providing timely advice to, and interactive communication with, the sponsor regarding the development of the drug to ensure that the development program to gather the nonclinical and clinical data necessary for approval is as efficient as practicable; involving senior managers and experienced review staff, as appropriate, in a collaborative, cross-disciplinary review; assigning a cross-disciplinary project lead for the FDA review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor; and considering alternative clinical trial designs when scientifically appropriate, which may result in smaller trials or more efficient trials that require less time to complete and may minimize the number of patients exposed to a potentially less efficacious treatment. Breakthrough therapy designation comes with all of the benefits of fast track designation.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or the time period for FDA review or approval may not be shortened. Furthermore, fast track designation, priority review, accelerated approval and breakthrough therapy designation do not change the standards for approval.

Post-Marketing Requirements

Following approval of a new product, the manufacturer and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and record-keeping activities, reporting of adverse experiences, complying with promotion and advertising requirements, which include restrictions on promoting products for unapproved uses or patient populations (known as “off-label use”) and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe legally available products for off-label uses, manufacturers may not market or promote such uses. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including investigation by federal and state authorities. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use or first publication. Further, if there are any modifications to the drug or biologic, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA/BLA or NDA/BLA supplement, which may require the development of additional data or preclinical studies and clinical trials.

The FDA may also place other conditions on approvals including the requirement for a Risk Evaluation and Mitigation Strategy, or REMS, to assure the safe use of the product. If the FDA concludes a REMS is needed, the sponsor of the NDA or BLA must submit a proposed REMS. The FDA will not approve the NDA or BLA without an approved REMS, if required. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following initial marketing.

FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMP regulations. Manufacturers must comply with cGMP regulations that require, among other things, quality control and quality assurance, the maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Manufacturers and other entities involved in the manufacture and distribution of approved drugs or biologics are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP requirements and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. The discovery of violative conditions, including failure to conform to cGMP regulations, could result in enforcement actions, and the discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved NDA or BLA, including recall or withdrawal of approval.

Once an approval is granted, the FDA may issue enforcement letters or withdraw the approval of the product if compliance with regulatory requirements and standards is not maintained or if problems occur after the drug or biologic reaches the market. Corrective action could delay drug or biologic distribution and require significant time and financial expenditures. Later discovery of previously unknown problems with a drug or biologic, including AEs of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or voluntary product recalls;
- fines, warning or untitled letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs and biologics may be promoted only for the approved indications and in accordance with the provisions of the approved label. However, companies may share truthful and not misleading information that is otherwise consistent with a product’s FDA approved

labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Hatch-Waxman Amendments

Section 505 of the FDCA describes three types of marketing applications that may be submitted to the FDA to request marketing authorization for a new drug. A Section 505(b)(1) NDA is an application that contains full reports of investigations of safety and efficacy. A 505(b)(2) NDA is an application that contains full reports of investigations of safety and efficacy but where at least some of the information required for approval comes from investigations that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. This regulatory pathway enables the applicant to rely, in part, on the FDA's prior findings of safety and efficacy for an existing product, or published literature, in support of its application. Section 505(j) establishes an abbreviated approval process for a generic version of approved drug products through the submission of an abbreviated new drug application, or ANDA. An ANDA provides for marketing of a generic drug product that has the same active ingredients, dosage form, strength, route of administration, labeling, performance characteristics and intended use, among other things, to a previously approved product, known as a reference listed drug, or RLD. ANDAs are termed “abbreviated” because they are generally not required to include preclinical (animal) and clinical (human) data to establish safety and efficacy. Instead, generic applicants must scientifically demonstrate that their product is bioequivalent to, or performs in the same manner as, the innovator drug through in vitro, in vivo, or other testing. The generic version must deliver the same amount of active ingredients into a subject’s bloodstream in the same amount of time as the innovator drug and can often be substituted by pharmacists under prescriptions written for the reference listed drug.

Non-Patent Exclusivity

Under the Hatch-Waxman Amendments, the FDA may not approve (or in some cases accept) an ANDA or 505(b)(2) application until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity, or NCE. For the purposes of this provision, an NCE is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, non 505(b)(2) NDA referencing the approved product or ANDA may be submitted to FDA for review until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, which states the proposed 505(b)(2) or generic drug will not infringe one or more of the already approved product’s listed patents or that such patents are invalid or unenforceable, in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity for non-NCE drugs if the NDA or a supplement to the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application or supplement. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication, but it generally would not protect the original, unmodified product from generic competition. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from filing and reviewing 505(b)(2) NDAs referencing the approved drug product or ANDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product; it only prevents FDA from approving such 505(b)(2) NDAs or ANDAs.

Hatch-Waxman Patent Certification and the 30-Month Stay

In seeking approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant’s product or an approved method of using the product. Upon approval, each of the patents listed by the NDA sponsor is published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Upon submission of an ANDA or 505(b)(2) NDA, an applicant is required to certify to the FDA concerning any patents listed for the RLD in the Orange Book that:

- no patent information on the drug product that is the subject of the application has been submitted to the FDA;
- such patent has expired;
- the date on which such patent expires; or
- such patent is invalid, unenforceable or will not be infringed upon by the manufacture, use, or sale of the drug product for which the application is submitted.

Generally, the ANDA or 505(b)(2) NDA cannot be approved until all listed patents have expired, except where the ANDA or 505(b)(2) NDA applicant challenges a listed patent through the last type of certification, also known as a paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the ANDA or 505(b)(2) NDA application will not be approved until all of the listed patents claiming the referenced product have expired. The ANDA or 505(b)(2) NDA applicant may also elect to submit a section viii statement certifying that its proposed label does not contain (or carves out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent.. If the ANDA or 505(b)(2) NDA applicant has provided a paragraph IV certification the applicant must send notice of the paragraph IV certification to the NDA and patent holders once the application has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the paragraph IV certification. If the paragraph IV certification is challenged by an NDA holder or the patent owner(s) asserts a patent challenge to the paragraph IV certification, the FDA may not approve that application until the earlier of 30 months from the receipt of the notice of the paragraph IV certification, the expiration of the patent, when the infringement case concerning each such patent was favorably

decided in the applicant's favor or settled, or such shorter or longer period as may be ordered by a court. This prohibition is generally referred to as the 30-month stay. In instances where an ANDA or 505(b)(2) NDA applicant files a paragraph IV certification, the NDA holder or patent owner(s) regularly take action to trigger the 30-month stay, recognizing that the related patent litigation may take many months or years to resolve. Thus, approval of an ANDA or 505(b)(2) NDA could be delayed for a significant period of time depending on the patent certification the applicant makes and the reference drug sponsor's decision to initiate patent litigation. If the drug has NCE exclusivity and the ANDA or 505(b)(2) NDA is submitted four years after approval, the 30-month stay is extended so that it expires seven and a half years after approval of the innovator drug, unless the patent expires or there is a decision in the infringement case that is favorable to the ANDA or 505(b)(2) NDA applicant before then.

Patent Term Restoration and Extension

Depending upon the timing, duration and specifics of FDA approval of our future product candidates, if any, some of our U.S. patents may be eligible for limited patent term extension. A patent term of up to five years as compensation for patent term lost during the FDA regulatory review process. Patent-term restoration, however, cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. The patent-term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA or BLA plus the time between the submission date of an NDA or BLA and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA or BLA.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or 200,000 or more individuals in the United States and for which there is no reasonable expectation that the cost of developing and making the product available in the United States for this type of disease or condition will be recovered from sales of the product.

Orphan drug designation must be requested before submitting an NDA or BLA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same disease or condition for seven years from the date of such approval, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity by means of greater effectiveness, greater safety or providing a major contribution to patient care or in instances of drug supply issues. Competitors, however, may receive approval of either a different product for the same indication or the same product for a different disease or condition but that could be used off-label in the orphan indication. If an orphan designated product receives marketing approval for an disease or condition broader than what is designated, it may not be entitled to orphan exclusivity.

Pediatric Information and Pediatric Exclusivity

Under the Pediatric Research Equity Act, or PREA, certain NDAs and BLAs and certain supplements to an NDA or BLA must contain data to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of pediatric data or full or partial waivers. A sponsor who is planning to submit a marketing application for a drug that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, within 60 days of an end-of-Phase 2 meeting or, if there is no such meeting, as early as practicable before the initiation of the Phase 3 or Phase 2/3 study. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach an agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from preclinical studies, early phase clinical trials and/or other clinical development programs.

A drug or biologic product can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms in the case of drugs and exclusivity periods in the case of biologics.. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

Biosimilars and Exclusivity

Certain of our product candidates are regulated as biologics. An abbreviated approval pathway for biological products shown to be similar to, or interchangeable with, an FDA-licensed reference biological product was created by the Biologics Price Competition and Innovation Act of 2009, or BPCI Act, as part of the Affordable Care Act, or the ACA. This amendment to the PHSA, in part, attempts to minimize duplicative testing. Biosimilarity, which requires that the biological product be highly similar to a biologic already licensed by the FDA pursuant to a BLA notwithstanding minor differences in clinically inactive components and that there be no clinically meaningful differences between the product and the reference product in terms of safety, purity and potency, can be shown through analytical studies, animal studies and a clinical trial or trials. Interchangeability requires that a biological product

be biosimilar to the reference product and that the product can be expected to produce the same clinical results as the reference product in any given patient and, for products administered multiple times to an individual, that the product and the reference product may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biological product without such alternation or switch.

A reference biological product is granted four and twelve year exclusivity periods from the time of first licensure of the product. FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product, and FDA will not approve an application for a biosimilar or interchangeable product based on the reference biological product until twelve years after the date of first licensure of the reference product. "First licensure" typically means the initial date the particular product at issue was licensed in the United States. Date of first licensure does not include the date of licensure of (and a new period of exclusivity is not available for) a biological product if the licensure is for a supplement for the biological product or for a subsequent application by the same sponsor or manufacturer of the biological product (or licensor, predecessor in interest, or other related entity) for a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength, or for a modification to the structure of the biological product that does not result in a change in safety, purity, or potency. Therefore, one must determine whether a new product includes a modification to the structure of a previously licensed product that results in a change in safety, purity, or potency to assess whether the licensure of the new product is a first licensure that triggers its own period of exclusivity. Whether a subsequent application, if approved, warrants exclusivity as the "first licensure" of a biological product is determined on a case-by-case basis with data submitted by the sponsor.

U.S. Government Regulation of Medical Devices

General Requirements

Under the FDCA, a medical device is an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component part, or accessory which is: (i) recognized in the official National Formulary, or the U.S. Pharmacopoeia, or any supplement to them; (ii) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals; or (iii) intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.

In the United States, medical devices are subject to extensive regulation by the FDA under the FDCA, and its implementing regulations, and certain other federal and state statutes and regulations. The laws and regulations govern, among other things, the research and development, design, testing, manufacture, packaging, storage, recordkeeping, approval, labeling, promotion, post-approval monitoring and reporting, distribution and import and export of medical devices. Failure to comply with applicable requirements may subject a device and/or its manufacturer to a variety of administrative sanctions, such as FDA refusal to approve pending premarket applications, issuance of warning letters, mandatory product recalls, import detentions, civil monetary penalties, and/or judicial sanctions, such as product seizures, injunctions, and criminal prosecution. Unless an exemption applies, medical devices require marketing clearance or approval from the FDA prior to commercial distribution. The two primary types of FDA marketing authorization applicable to a medical device are premarket notification, also called 510(k) clearance, and premarket approval, or PMA approval; however, some devices may be commercialized after the FDA grants marketing authorization under other premarket submission types, including a de novo request.

The FDCA classifies medical devices into one of three categories based on the risks associated with the device and the level of control necessary to provide reasonable assurance of safety and effectiveness. Class I devices are deemed to be low risk and are subject only to the general regulatory controls. Class II devices are moderate risk. They are subject to general controls and may also be subject to special controls. Class III devices are generally the highest risk devices. They are required to obtain premarket approval and comply with postmarket conditions of approval in addition to general regulatory controls.

Pre-Market Authorization and Notification

While most Class I and some Class II devices may be marketed without prior FDA authorization, most other medical devices can be legally sold within the U.S. only if the FDA has: (i) approved a pre-market approval, or PMA, application prior to marketing, generally applicable to most Class III devices; (ii) cleared the device in response to a premarket notification, or 510(k) submission, generally applicable to Class I and II devices; or (iii) authorized the device to be marketed through the de novo classification process, generally applicable for novel Class I or II devices. PMA applications, 510(k) premarket notifications, and de novo requests require payment of substantial user fees that are generally increased each fiscal year.

The 510(k) Process

Product marketing in the U.S. for most Class II and a limited number of Class I devices typically follows the 510(k) premarket notification pathway. Under the 510(k) process, the manufacturer must submit to the FDA a premarket notification, demonstrating that the device is "substantially equivalent," as defined in the statute, to either

- a device that was legally marketed prior to May 28, 1976, the date upon which the Medical Device Amendments of 1976 were enacted, or
- another commercially available, similar device that was cleared through the 510(k) process.

To be "substantially equivalent," the proposed device must have the same intended use as the predicate device, and either have the same technological characteristics as the predicate device or have different technological characteristics and not raise different questions of safety or effectiveness than the predicate device. Clinical data are sometimes required to support substantial equivalence.

After a 510(k) notification is submitted, the FDA determines whether to accept it for substantive review. If it lacks necessary information for substantive review, the FDA will refuse to accept the 510(k) notification. The applicant has 180 days to respond to the identified deficiencies. If it is accepted for filing, the FDA begins a substantive review. If the FDA agrees that the device is substantially equivalent, it will grant clearance to commercially market the device.

After a device receives 510(k) clearance, any modification that could significantly affect its safety or effectiveness, or that would constitute a major change in its intended use, requires a new 510(k) clearance or could require a PMA approval or de novo classification. The FDA requires each manufacturer to make this determination in the first instance, but the FDA can review any such decision. If the FDA disagrees with a manufacturer's decision not to seek a new 510(k) clearance for the modified device, the agency may retroactively require the manufacturer to seek 510(k) clearance, de novo classification, or PMA approval. The FDA also can require the manufacturer to cease marketing and/or recall the modified device until 510(k) clearance or PMA approval is obtained.

The De Novo Process

Devices of a new type that the FDA has not previously classified based on risk are automatically classified into Class III regardless of the level of risk they pose. To avoid requiring PMA review of novel low- to moderate-risk devices classified in Class III by operation of law, Congress enacted a provision that allows the FDA to classify a novel low- to moderate-risk device into Class I or II in the absence of a predicate device that would support 510(k) clearance. The FDA evaluates the safety and effectiveness of devices submitted for review under the de novo pathway and devices determined to be Class II through this pathway oftenserve as predicate devices for future 510(k) applicants. The de novo pathway can requires the submission of clinical data.

The PMA Process

A Class III product not eligible for either 510(k) clearance or de novo classification must follow the PMA approval pathway.
Class III devices include devices deemed by the FDA to pose the greatest risk such as life-supporting or life-sustaining devices, or implantable devices, in addition to those deemed not substantially equivalent following the 510(k) process. The safety and effectiveness of Class III devices cannot be reasonably assured solely by the FDA's General Controls and Special Controls for medical devices. Therefore, these devices are subject to the PMA application process, which is generally more costly, rigorous, time consuming, and uncertain than the 510(k) and de novo processes. Through the PMA application process, the applicant must submit data and information demonstrating reasonable assurance of the safety and effectiveness of the device for its intended use to the FDA's satisfaction. Accordingly, a PMA application typically includes, but is not limited to, extensive technical information regarding device design and development, preclinical and clinical study data, manufacturing information, labeling and financial disclosure information for the clinical investigators in device studies. The PMA application must provide valid scientific evidence that demonstrates to the FDA's satisfaction reasonable assurance of the safety and effectiveness of the device for its intended use. Overall, the FDA review of a PMA application generally takes between one and three years, but may take significantly longer.

As part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with Quality System Regulation, or QSR, requirements, which impose elaborate testing, control, documentation and other quality assurance procedures.

If the FDA's evaluation of the PMA application is favorable, the FDA will issue a PMA for the approved indications, which can be more limited than those originally sought by the manufacturer. The PMA can include post-approval conditions that the FDA believes necessary to ensure the safety and effectiveness of the device including, among other things, restrictions on labeling, promotion, sale and distribution. Failure to comply with the conditions of approval can result in material adverse enforcement action, including the loss or withdrawal of the approval and/or placement of restrictions on the sale of the device until the conditions are satisfied.

Even after approval of a PMA, a new PMA or PMA supplement may be required in the event of a modification to the device, its labeling or its manufacturing process. Supplements to a PMA often require the submission of the same type of information required for an original PMA, except that the supplement is generally limited to that information needed to support the proposed change from the product covered by the original PMA.

Exempt Devices

If a manufacturer's device falls into a generic category of Class I or Class II devices that FDA has exempted by regulation, a premarket notification is not required before marketing the device in the United States. Manufacturers of such devices are required to register their establishments and list their devices. Some 510(k)-exempt devices are also exempt from QSR requirements, except for the QSR's complaint handling and recordkeeping requirements.

Pre-Submission Meetings

The FDA has mechanisms to provide companies with guidance prior to formal submission of either a 510(k), de novo request or PMA. One such mechanism is the pre-submission program in which a company has a "pre-submission" meeting as outlined in the FDA guidance document "Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program" that was issued in January 2021. The main purpose of the pre-submission meeting is to provide companies with guidance from the FDA on matters of significance to product development, including verification and validation testing, and/or submission preparation. Prior to the pre-submission meeting, the company provides a briefing document to the FDA that poses specific questions on which the company is seeking FDA feedback.

Clinical Trials

A clinical trial is almost always required to support a PMA application or de novo request and is sometimes required for a 510(k) premarket notification. Clinical trials may also be required to be conducted or continued to satisfy post-approval requirements for devices with PMAs. For significant risk devices, the FDA regulations require that human clinical investigations conducted in the United States be approved via an investigational device exemption, or IDE, which must become effective before clinical testing may commence. A significant risk device is one that presents a potential for serious risk to the health, safety or welfare of a subject

and either is implanted, used in supporting or sustaining human life, substantially important in diagnosing, curing, mitigating or treating disease or otherwise preventing impairment of human health, or otherwise presents a potential for serious risk to a subject. A nonsignificant risk device does not require FDA approval of an IDE; however, the clinical trial must still be conducted in compliance with abbreviated IDE regulations, such as those relating to trial monitoring, informed consent, and labeling and record-keeping. In some cases, one or more smaller studies may precede a pivotal clinical trial intended to demonstrate the safety and effectiveness of the investigational device. A 30-day waiting period after the submission of each IDE is required prior to the commencement of clinical testing in humans. If the FDA determines that there are deficiencies or other concerns with an IDE that require modification, the FDA may permit a clinical trial to proceed under a conditional approval. If the FDA disapproves the IDE within this 30-day period, the clinical trial proposed in the IDE may not begin.

An IDE application must be supported by appropriate data, such as animal and laboratory test results, showing that it is safe to test the device in humans and that the testing protocol is scientifically sound. The IDE application must also include a description of product manufacturing and controls, and a proposed clinical trial protocol. FDA typically grants IDE approval for a specified number of patients to be treated at specified study centers. During the study, the sponsor must comply with the FDA's IDE requirements for investigator selection, trial monitoring, reporting, and record keeping. The investigators must obtain patient informed consent, rigorously follow the investigational plan and study protocol, control the disposition of investigational devices, and comply with all reporting and record keeping requirements. Certain IDE requirements apply to all investigational devices, whether such devices are considered significant or nonsignificant risks. Prior to granting PMA approval, the FDA typically inspects the records relating to the conduct of the study and the clinical data supporting the PMA application for compliance with IDE requirements.

Clinical trials must be conducted: (i) in compliance with federal regulations; (ii) GCPs, which are intended to protect the rights and health of patients and to define the roles of clinical trial sponsors, investigators, and monitors; and (iii) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Clinical trials are typically conducted at geographically diverse clinical trial sites, and are designed to permit FDA to evaluate the overall benefit-risk relationship of the device and to provide adequate information for the labeling of the device. Clinical trials for both significant and nonsignificant risk devices, must be approved by an IRB.

The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial subjects. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions.

Although the QSR does not fully apply to investigational devices, the requirement for controls on design and development does apply. The sponsor also must manufacture the investigational device in conformity with the quality controls described in the IDE application and any conditions of IDE approval that FDA may impose with respect to manufacturing. Investigational devices may only be distributed for use in an investigation, and must bear a label with the statement: "CAUTION—Investigational device. Limited by Federal law to investigational use."

Information about certain clinical trials must be submitted within specific timeframes to the NIH for public dissemination on its ClinicalTrials.gov website.

Post-Marketing Requirements

After a device is placed on the market, numerous regulatory requirements apply. These include:

- annual establishment registration and device listing with the FDA;
- the QSR requirements, which require manufacturers, including specification developers and contract manufacturers, among others, to follow stringent design, testing, control, documentation, complaint handling and other quality assurance procedures during all aspects of the design, manufacturing, and distribution process;
- advertising and promotion requirements, which require that promotional materials are truthful, not misleading, and that all claims are substantiated, and also prohibit the promotion of products for unapproved or "off-label" uses and impose other restrictions on labeling;
- restrictions on sale, distribution or use of a device;
- labeling regulations, which include requirements that labelling is truthful, not misleading, and provides adequate directions;
- medical device reporting regulations, which require that a manufacturer report to the FDA if a device it markets may have caused or contributed to a death or serious injury, or has malfunctioned and the device or a similar device that it markets would be likely to cause or contribute to a death or serious injury, if the malfunction were to recur;
- correction, removal and recall reporting regulations, which require that manufacturers report to the FDA field corrections and product recalls or removals if undertaken to reduce a risk to health posed by the device or to remedy a violation of the FDCA that may present a risk to health; and
- complying with the federal law and regulations requiring Unique Device Identifiers on devices and also requiring the submission of certain information about each device to the FDA's Global Unique Device Identification Database.

The FDA also may require post-marketing testing, surveillance, or other measures to monitor the effects of an approved or cleared product. The FDA may place conditions on a PMA-approved device that could restrict the distribution or use of the product. In addition, quality-control, manufacture, packaging, and labeling procedures must continue to conform to the QSR after approval and clearance, and manufacturers are subject to periodic inspections by the FDA. Accordingly, manufacturers must continue to expend time, money, and effort in the areas of production and quality control to maintain compliance with the QSR. The FDA may withdraw product approvals or recommend or require product recalls if a company fails to comply with regulatory requirements.

FDA enforces these requirements by inspection and market surveillance. If the FDA finds a violation, it can institute a wide variety of enforcement actions, ranging from a public warning letter to more severe sanctions such as:

- warning letters, untitled letters, fines, injunctions, consent decrees, and civil penalties;
- recall, withdrawals, or administrative detention or seizure of products;
- operating restrictions, partial suspension or total shutdown of production;
- refusing or delaying requests for 510(k) clearance, de novo classification, or PMA approval of new products or modified products;
- withdrawing PMA approvals, de novo authorization, or 510(k) clearances already granted;
- refusal to grant export or import approvals for marketing products; and
- criminal prosecution.

Discovery of previously unknown problems with a product or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, warning letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties, among others. Newly discovered or developed safety or effectiveness data may require changes to a product's cleared, authorized, or approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent marketing authorization of products under development.

Regulation of Companion Diagnostics

If safe and effective use of a product depends on an in vitro diagnostic, the FDA generally will require approval, authorization or clearance of that diagnostic, known as a companion diagnostic, before or at the same time that the FDA approves the therapeutic product. If FDA determines that a companion diagnostic device is essential to the safe and effective use of a new therapeutic product or indication, FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic device is not approved, authorized or cleared for that indication. Approval, authorization or clearance of the companion diagnostic device will ensure that the device has been adequately evaluated and has adequate performance characteristics in the intended population. The review of in vitro companion diagnostics in conjunction with the review of our products will, therefore, likely involve coordination of review by the FDA's Center for Drug Evaluation and Research or the FDA's Center for Biologics Evaluation and Research and the FDA's Office of Health Technology 7: In Vitro Diagnostics and Radiological Health. Premarket review of a companion diagnostic is typically done in parallel with development of the therapeutic product. However, it is possible that FDA may permit clearance, authorization or approval of the companion diagnostic for a therapeutic product as a post-marketing commitment following a potential regulatory approval. Under the FDCA, in vitro diagnostics, including companion diagnostics, are regulated as medical devices. The vast majority of companion diagnostics require PMA approval.

US Government Regulation of Combination Products

A combination product is a product comprised of (i) two or more regulated components, i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity; (ii) two or more separate products packaged together in a single package or as a unit and comprised of drug and device products, device and biological products, or biological and drug products; (iii) a drug, device, or biological product packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug, device, or biological product where both are required to achieve the intended use, indication, or effect and where, upon approval of the proposed product, the labeling of the approved product would need to be changed, e.g., to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose; or (iv) any investigational drug, device, or biological product packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect.

The FDA is divided into various Centers by product type. Different Centers typically review drug, biologic, or device applications. In order to review an application for a combination product, FDA must decide which Center should be responsible for the review. FDA regulations require that FDA determine the combination product's primary mode of action, or PMOA, which is the single mode of a combination product that provides the most important therapeutic action of the combination product. The Center that regulates that portion of the product that generates the PMOA becomes the lead evaluator. If there are two independent modes of action, neither of which is subordinate to the other, the FDA makes a determination as to which Center to assign the product based on consistency with other combination products raising similar types of safety and effectiveness questions or to the Center with the most expertise in evaluating the most significant safety and effectiveness questions raised by the combination product. When evaluating an application, a lead Center may consult other Centers but still retain complete reviewing authority, or it may collaborate with another Center, by which the Center assigns review of a specific section of the application to another Center, delegating its review authority for that section. Typically, the FDA requires a single marketing application submitted to the Center selected to be the lead evaluator, although the agency has the discretion to require separate applications to more than one Center. One reason to submit multiple evaluations is if the applicant wishes to receive some benefit that accrues only from approval under a particular type of application, like new drug product exclusivity. If multiple applications are submitted, each may be evaluated by a different lead Center.

European Union Drug Development

In the European Union, or EU, our future products and product candidates also may be subject to extensive regulatory requirements. As in the United States, medicinal products can be marketed only if a marketing authorization from the competent regulatory agencies has been obtained.

Similar to the United States, the various phases of preclinical and clinical research in the EU are subject to significant regulatory controls.

Non-clinical studies are performed to demonstrate the health or environmental safety of new chemical or biological substances. Non-clinical studies must be conducted in compliance with the principles of GLP, as set forth in EU Directive 2004/10/EC. In particular, non-clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical trials of medicinal products in the EU must be conducted in accordance with EU and national regulations and the International Conference on Harmonization, or ICH, guidelines on Good Clinical Practices, or GCP, as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If the sponsor of the clinical trial is not established within the EU, it must appoint an EU entity to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU countries, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

While the Clinical Trials Directive required a separate clinical trial application, or CTA, to be submitted in each member state, to both the competent national health authority and an independent ethics committee, much like the FDA and IRB respectively, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The CTA must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed.

The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. For clinical trials whose CTA was made under the Clinical Trials Directive before January 31, 2022, the Clinical Trials Directive will continue to apply on a transitional basis for three years. Additionally, sponsors may still choose to submit a CTA under either the Clinical Trials Directive or the CTR until January 31, 2023 and, if authorized, those will be governed by the Clinical Trials Directive until January 31, 2025. By that date, all ongoing trials will become subject to the provisions of the CTR.

Medicines used in clinical trials must be manufactured in accordance with Good Manufacturing Practice, or GMP. Other national and EU-wide regulatory requirements may also apply.

European Union Drug Marketing

Much like the Anti-Kickback Statue prohibition in the United States, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU and in the UK. The provision of benefits or advantages to induce or reward improper performance generally is usually governed by national anti-bribery laws of the EU Member States. Infringement of these laws could result in substantial fines and imprisonment. EU Directive 2001/83/EC, which is the EU Directive governing medicinal products for human use, further provides that, where medicinal products are being promoted to persons qualified to prescribe or supply them, no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such persons unless they are inexpensive and relevant to the practice of medicine or pharmacy.

Payments made to physicians in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and/or approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

European Union Drug Review and Approval

In the EU, medicinal products can only be commercialized after obtaining a marketing authorization, or MA. There are two main types of MA.

- The centralized MA is issued by the European Commission through the centralized procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the EMA, and is valid throughout the entire territory of the EU. The centralized procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced-therapy medicinal products (i.e. gene-therapy, somatic cell-therapy or tissue-engineered medicines) and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, autoimmune and other immune dysfunctions and viral diseases. The centralized procedure is optional for products containing a new active substance not yet authorized in the EU, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health. Under the centralized procedure the maximum timeframe for the evaluation of a MA application by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Clock stops may extend the timeframe of evaluation of a MA application considerably beyond 210 days. Where the CHMP gives a positive opinion, the EMA provides the opinion together with supporting documentation to the European Commission, who make the final decision to grant an MA, which is issued within 67 days of receipt of the CHMP's opinion. Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of a MA application under the accelerated assessment procedure is of 150 days, excluding stop-clocks, but it is possible that the

CHMP may revert to the standard time limit for the centralized procedure if it determines that the application is no longer appropriate to conduct an accelerated assessment.

- National MAs are issued by the competent authorities of the EU Member States only cover their respective territory, and are available for products not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in an EU Member State, , this national MA can be recognized in other Member States through the mutual recognition procedure. If the product has not received a national MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the decentralized procedure. Under the decentralized procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State, or RMS. The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics, or SmPC, and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Concerned Member States, or CMSs) for their approval. If the CMSs raise no objections, based on a potential serious risk to public health, to the assessment, SmPC, labeling, or packaging proposed by the RMS, the product is subsequently granted a national MA in all the Member States (i.e., in the RMS and the CMSs).

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the EU Member States make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Now that the UK (which comprises Great Britain and Northern Ireland) has left the EU, Great Britain will no longer be covered by centralized MAs (under the Northern Irish Protocol, centralized MAs will continue to be recognized in Northern Ireland). All medicinal products with a current centralized MA were automatically converted to Great Britain MAs on January 1, 2021 unless the MA holder chose to opt out. For a period of two years from January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, the UK medicines regulator, may rely on a decision taken by the European Commission on the approval of a new MA in the centralized procedure, in order to more quickly grant a new Great Britain MA. A separate application will, however, still be required.

European Data and Marketing Exclusivity

In the EU, innovative medicinal products (including both small molecules and biological medicinal products) generally receive eight years of data exclusivity upon MA and an additional two years of market exclusivity. The data exclusivity, if granted, prevents generic or biosimilar applicants from referencing the innovator's pre-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA , for a period of eight years from the date on which the reference product was first authorized in the EU. During the additional two-year period of market exclusivity, a generic or biosimilar MA can be submitted, and the innovator's data may be referenced, but no generic or biosimilar product can be marketed until the expiration of the market exclusivity period. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are determined to bring a significant clinical benefit in comparison with currently approved therapies.

In the EU, there is a special regime for biosimilars, or biological medicinal products that are similar to a reference medicinal product but that do not meet the definition of a generic medicinal product, for example, because of differences in raw materials or manufacturing processes. For such products, the results of appropriate preclinical or clinical trials must be provided, and guidelines from the EMA detail the type of quantity of supplementary data to be provided for different types of biological product. There are no such guidelines for complex biological products, such as gene or cell therapy medicinal products, and so it is unlikely that biosimilars of those products will currently be approved in the EU. However, guidance from the EMA states that they will be considered in the future in light of the scientific knowledge and regulatory experience gained at the time.

European Orphan Designation and Exclusivity

The criteria for designating an "orphan medicinal product" in the EU are similar in principle to those in the United States. A medicinal product can be designated as an orphan if its sponsor can establish that: (1) the product is intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions, (2) either (a) such condition affects no more than 5 in 10,000 persons in the EU when the application is made, or (b) where it is unlikely that the marketing of the medicine would generate sufficient return in the EU to justify the necessary investment in its development, and (3) there exists no satisfactory method of diagnosis, prevention or treatment of the condition must have been authorized (or, if such a method exists, the product in question would be of significant benefit to those affected by the condition).

In the EU, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity is granted following marketing approval for the orphan product. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed pediatric investigation plan, or PIP. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications.

This period may be reduced to six years if, at the end of the fifth year the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, MA may only be granted to a "similar medicinal product" for the same indication at any time, if (i) the holder of the MA for the original orphan medicinal product consents to a second orphan medicinal product application, (ii) the holder of the MA for the original orphan medicinal product cannot supply sufficient quantities of the orphan medicinal product, or (iii) the second applicant can establish that the second medicinal product, although similar, is safer, more effective or otherwise clinically superior to the authorized orphan medicinal product. A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic

indication. Orphan drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

European Pediatric Investigation Plan

In the EEA, companies developing a new medicinal product must agree upon a pediatric investigation plan, or PIP, with the EMA's Pediatric Committee, or PDCO and must conduct pediatric clinical trials in accordance with that PIP, unless a waiver applies. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which marketing authorization is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when this data is not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Products that are granted a marketing authorization with the results of the pediatric clinical trials conducted in accordance with the PIP (even where such results are negative) are eligible for six months' supplementary protection certificate extension (if any is in effect at the time of approval). In the case of orphan medicinal products, a two year extension of the orphan market exclusivity may be available. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

The aforementioned EU rules are generally applicable in the European Economic Area, or EEA, which consists of the 27 EU member states plus Norway, Liechtenstein and Iceland.

European Union Device Development

In the EU, until May 25, 2021, medical devices were regulated by the Council Directive 93/42/EEC, or the EU Medical Devices Directive, and Active Implantable Medical Devices were regulated under Directive 90/385/EEC which both have been repealed and replaced by Regulation (EU) No 2017/745, or the EU Medical Devices Regulation. Unlike directives, regulations are directly applicable in all EU Member States without the need for member states to implement into national law. However, as of May 26, 2021, some of the EU Medical Devices Regulation requirements apply in place of the corresponding requirements of the EU Medical Devices Directive with regard to registration of economic operators and of devices, post-market surveillance and vigilance requirements.

Medical Devices Directive

Under the EU Medical Devices Directive, all medical devices placed on the market in the EU must meet the relevant essential requirements laid down in Annex I to the EU Medical Devices Directive, including the requirement that a medical device must be designed and manufactured in such a way that it will not compromise the clinical condition or safety of patients, or the safety and health of users and others. In addition, the device must achieve the performance intended by the manufacturer and be designed, manufactured, and packaged in a suitable manner.

To demonstrate compliance with the essential requirements laid down in Annex I to the EU Medical Devices Directive, medical device manufacturers must undergo a conformity assessment procedure, which varies according to the type of medical device and its (risk) classification. Except for low-risk medical devices (Class I non-sterile, non-measuring devices), where the manufacturer can self-assess the conformity of its products with the essential requirements (except for any parts which relate to sterility or metrology), a conformity assessment procedure requires the intervention of a notified body. Notified bodies are independent organizations designated by EU member states to assess the conformity of devices before being placed on the market. The conformity assessment usually involves an audit of the manufacturer's quality system (the notified body must presume that quality systems which implement the relevant harmonized standards – which is ISO 13485:2016 for Medical Devices Quality Management Systems – conform to these requirements) and a review of the technical documentation from the manufacturer on the safety and performance of the device. If the notified body considers that the device is in conformity with the regulatory requirements, it will issue a conformity assessment certificate which the manufacturer uses as a basis for its own declaration of conformity. The manufacturer may then apply the CE mark to the device, allowing it to be marketed in any EU Member State .Notified bodies also conduct periodic inspections to ensure applicable regulatory requirements are met.

Medical Devices Regulation

The EU Medical Devices Regulation became effective on May 26, 2021. Devices lawfully placed on the market pursuant to the EU Medical Devices Directive prior to May 26, 2021 may generally continue to be made available on the market or put into service until May 26, 2025, provided that the requirements of the transitional provisions are fulfilled. In particular, the certificate in question must still be valid. However, even in this case, manufacturers must comply with a number of new or reinforced requirements set forth in the EU Medical Devices Regulation, in particular the obligations described below.

The EU Medical Devices Regulation requires that before placing a device, other than a custom-made device, on the market, manufacturers (as well as other economic operators such as authorized representatives and importers) must register by submitting identification information to the electronic system (Eudamed), unless they have already registered. The information to be submitted by manufacturers (and authorized representatives) also includes the name, address and contact details of the person or persons responsible for regulatory compliance. The new Regulation also requires that before placing a device, other than a custom-made device, on the market, manufacturers must assign a unique identifier to the device and provide it along with other core data to the unique device identifier, or UDI, database. These new requirements aim at ensuring better identification and traceability of the devices. Each device – and as applicable, each package – will have a UDI composed of two parts: a device identifier, or UDI-DI, specific to a device, and a production identifier, or UDI-PI, to identify the unit producing the device. Manufacturers are also notably responsible for entering the necessary data on Eudamed, which includes the UDI database, and for keeping it up to date. The obligations for registration in Eudamed will become applicable at a later date (as Eudamed is not yet fully functional). Until Eudamed is fully functional, the corresponding provisions of the EU Medical Devices Directive continue to apply for the purpose of

meeting the obligations laid down in the provisions regarding exchange of information, including, and in particular, information regarding registration of devices and economic operators.

All manufacturers placing medical devices into the market in the EU must comply with the EU medical device vigilance system. Under this system, serious incidents and Field Safety Corrective Actions, or FSCAs, must be reported to the relevant authorities of the EU member states. Manufacturers are required to take FSCAs defined as any corrective action for technical or medical reasons to prevent or reduce a risk of a serious incident associated with the use of a medical device that is made available on the market. An FSCA may include the recall, modification, exchange, destruction or retrofitting of the device.

The aforementioned EU rules are generally applicable in the EEA.

In Vitro Diagnostic Medical Devices

The EU regulatory landscape concerning medical devices is evolving. On April 5, 2017 Regulation (EU) 2017/746 of the European Parliament and of the Council on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU, or the IVDR, was adopted to establish a modernized and more robust EU legislative framework, with the aim of ensuring better protection of public health and patient safety. This aims at reducing the risk of discrepancies in interpretation across the different European markets. On October 14, 2021, the European Commission proposed a “progressive” roll-out of the IVDR to prevent disruption in the supply of IVD MDs. The European Parliament and Council voted to adopt the proposed regulation on December 15, 2021 and the regulation entered into force on January 2022.

The IVDR will fully apply on May 26, 2022 but there will be a tiered system extending the grace period for many devices (depending on their risk classification) before they have to be fully compliant with the regulation. Once applicable, the IVDR will among other things:

- strengthen the rules on placing devices on the market and reinforce surveillance once they are available;
- establish explicit provisions on manufacturers’ responsibilities for the follow-up of the quality, performance and safety of devices placed on the market;
- establish explicit provisions on importers’ and distributors’ obligations and responsibilities;
- impose an obligation to identify a responsible person who is ultimately responsible for all aspects of compliance with the requirements of the new regulation;
- improve the traceability of medical devices throughout the supply chain to the end-user or patient through the introduction of a unique identification number, to increase the ability of manufacturers and regulatory authorities to trace specific devices through the supply chain and to facilitate the prompt and efficient recall of medical devices that have been found to present a safety risk;
- set up a central database (Eudamed) to provide patients, healthcare professionals and the public with comprehensive information on products available in the EU; and
- strengthen rules for the assessment of certain high-risk devices that may have to undergo an additional check by experts before they are placed on the market.

The aforementioned EU rules are generally applicable in the EEA.

Brexit and the Regulatory Framework in the United Kingdom

The United Kingdom, or UK, left the EU on January 31, 2020, following which existing EU medicinal product legislation continued to apply in the UK during the transition period under the terms of the EU-UK Withdrawal Agreement. The transition period, which ended on December 31, 2020, maintained access to the EU single market and to the global trade deals negotiated by the EU on behalf of its members. The transition period provided time for the UK and EU to negotiate a framework for partnership for the future, which was then crystallized in the Trade and Cooperation Agreement, or TCA, and became effective on the January 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations.

EU laws which have been transposed into UK law through secondary legislation continue to be applicable as “retained EU law”. However, new legislation such as the EU CTR will not be applicable. The UK government has passed a new Medicines and Medical Devices Act 2021, which introduces delegated powers in favor of the Secretary of State or an ‘appropriate authority’ to amend or supplement existing regulations in the area of medicinal products and medical devices. This allows new rules to be introduced in the future by way of secondary legislation, which aims to allow flexibility in addressing regulatory gaps and future changes in the fields of human medicines, clinical trials and medical devices.

As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, is the UK’s standalone medicines and medical devices regulator. As a result of the Northern Ireland protocol, different rules will apply in Northern Ireland than in England, Wales, and Scotland, together, Great Britain, or GB. Broadly, Northern Ireland will continue to follow the EU regulatory regime, but its national competent authority will remain the MHRA. The MHRA has published a guidance on how various aspects of the UK regulatory regime for medicines will operate in GB and in Northern Ireland following the expiry of the Brexit transition period on December 31, 2020. The guidance includes clinical trials, importing, exporting, and pharmacovigilance and is relevant to any business involved in the research, development, or commercialization of medicines in the UK. The new guidance was given effect via the Human Medicines Regulations (Amendment etc.) (EU Exit) Regulations 2019, or the Exit Regulations.

The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, including a 150-day assessment and a rolling review procedure. All existing EU MAs for centrally authorized products were automatically converted or grandfathered into UK MAs, effective in GB (only), free of charge on January 1, 2021, unless the MA holder chooses to opt-out. In order to use the centralized procedure to obtain a MA that will be valid throughout the EEA, companies must be established in the EEA. Therefore after Brexit, companies established in the UK can no longer use the EU centralized procedure and instead an EEA entity must hold any centralized MAs. In order to obtain a UK MA to commercialize products in the UK, an applicant must be established in the UK and must follow one of the UK national authorization procedures or one of the remaining post-Brexit international cooperation procedures to obtain an MA to commercialize products in the UK. The MHRA may rely on a decision taken by the European Commission on the approval of a new (centralized procedure) MA when determining an application for a GB authorization; or use the MHRA’s decentralized or mutual recognition procedures which enable MAs approved in EU member states (or Iceland, Liechtenstein, Norway) to be granted in GB.

European and United Kingdom Data Collection Regulation

In the event we decide to conduct clinical trials in the European Union and/or the United Kingdom, we may be subject to additional data protection requirements. The collection and use of personal data (which includes health information) in the European Union is governed by the provisions of the General Data Protection Regulation 2016/679, or GDPR. The GDPR applies to any company established in the EEA and to companies established outside the EEA that process personal data in connection with the offering of goods or services to data subjects in the EU or the monitoring of the behavior of data subjects in the European Union. The GDPR enhances data protection obligations for controllers of personal data, including requiring controllers to: ensure legal bases they rely on to process personal data are aligned to the legal bases prescribed under the GDPR; individuals are informed as to what personal data is collected from them, how it is used and how they can exercise certain rights in line with the increased disclosures; conduct data protection impact assessments for “high risk” processing; only retain personal data for as long as it is needed in line with the purpose it was obtained; ensure an appropriate level of security in line with the nature and scope of the personal data being processed, and where there has been a personal data breach (i.e. a breach to security which had led to personal data being compromised), notify the relevant supervisory authority and/or individuals affected; embed “privacy by design” practices into new technologies which involve the processing of personal data; enter into data processing terms and carry out appropriate due diligence on any service provider which processes personal data on behalf of the controller (and therefore qualifying as a processor). The GDPR also imposes strict rules on the transfer of personal data outside of the EEA to countries that do not ensure an adequate level of protection, like the U.S. Failure to comply with the requirements of the GDPR and the related national data protection laws of the EEA Member States may result in fines up to 20 million Euros or 4 percent of a company’s global annual revenues for the preceding financial year, whichever is higher. Moreover, the GDPR grants data subjects the right to claim for material and non-material damages resulting from infringement of the GDPR. In addition, further to the United Kingdom's exit from the EU on January 31, 2020, the GDPR ceased to apply in the United Kingdom at the end of the transition period on December 31, 2020. However, as of January 1, 2021, the UK’s European Union (Withdrawal) Act 2018 incorporated the GDPR (as it existed on December 31, 2020 but subject to certain UK specific amendments) into UK law (referred to as the 'UK GDPR'). The UK GDPR and the UK Data Protection Act 2018 set out the UK’s data protection regime, which is independent from but aligned to the EU’s data protection regime. Non-compliance with the UK GDPR may result in monetary penalties of up to £17.5 million or 4% of worldwide revenue, whichever is higher. The UK, however, is now regarded as a third country under the EU’s GDPR which means that transfers of personal data from the EEA to the UK will be restricted unless an appropriate safeguard, as recognized by the EU’s GDPR, has been put in place. Although, under the EU-UK Trade Cooperation Agreement it is lawful to transfer personal data between the UK and the EEA for a 6 month period following the end of the transition period, with a view to achieving an adequacy decision from the European Commission during that period. Like the EU GDPR, the UK GDPR restricts personal data transfers outside the UK to

countries not regarded by the UK as providing adequate protection (this means that personal data transfers from the UK to the EEA remain free flowing).

Given the breadth and depth of these data protection obligations, maintaining compliance with the GDPR and UK GDPR will require significant time, resources and expense, and as an ongoing compliance measure we may be required to put in place additional mechanisms which help to ensure our compliance with the data protection rules. This may be onerous and adversely affect our business, financial condition, results of operations and prospects.

Rest of the World Regulation

For other countries outside of the European Union and the United States, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. Additionally, the clinical trials must be conducted in accordance with GCP requirements and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Additional Laws and Regulations Governing International Operations

If we further expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

Healthcare and Data Privacy and Security Laws and Regulation

Manufacturing, sales, promotion and other activities following product approval are also subject to regulation by numerous regulatory authorities in the United States in addition to the FDA, including the Centers for Medicare & Medicaid Services, or CMS, the Office of Inspector General and Office for Civil Rights, other divisions of the Department of Health and Human Services, or HHS, the Department of Justice, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments.

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of drug products and other medical items and services. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians and teaching hospitals and patient privacy laws and regulations and other healthcare laws and regulations that may constrain our business and/or financial arrangements. Restrictions under applicable federal and state healthcare and data privacy and security laws and regulations, include the following:

- the federal Anti-Kickback Statute, which makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf), to knowingly and willfully solicit, receive, offer or pay any remuneration (including any kickback, bribe or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, or in return for, that is intended to induce or reward referrals, including the purchase, recommendation, order or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. A person or entity need not have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation.
- the federal civil and criminal false claims laws, including the civil False Claims Act, or FCA, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false, fictitious or fraudulent; knowingly making, using or causing to be made or used, a false statement or record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. The FCA also permits a private individual

acting as a “whistleblower” to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery.

- the federal civil monetary penalties laws, which impose civil fines for, among other things, the offering or transfer or remuneration to a Medicare or state healthcare program beneficiary if the person knows or should know it is likely to influence the beneficiary’s selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state health care program, unless an exception applies;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes civil and criminal liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys’ fees and costs associated with pursuing federal civil actions;
- the federal transparency requirements known as the federal Physician Payments Sunshine Act,which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to CMS information related to payments and other transfers of value made by that entity to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician practitioners such as physician assistants and nurse practitioners, and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members.
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- federal price reporting laws, which require manufacturers to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on approved products;
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers;
- many state laws govern the privacy of personal information in specified circumstances, for example, in California the California Consumer Privacy Act, or CCPA, which went into effect on January 1, 2020, establishes a new privacy framework for covered businesses by creating an expanded definition of personal information, establishing new data privacy rights for consumers in the State of California, imposing special rules on the collection of consumer data from minors, and creating a new and potentially severe statutory damages framework for violations of the CCPA and for businesses that fail to implement reasonable security procedures and practices to prevent data breaches. While clinical trial data and information governed by HIPAA are currently exempt from the current version of the CCPA, other personal information may be applicable and possible changes to the CCPA may broaden its scope. Further, the California Privacy Rights Act, or CPRA, recently passed in California, which significantly amends the CCPA and will impose additional data protection obligations on covered businesses, and will create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. Similar laws have passed in Virginia and Colorado, and have been proposed in other states and at the federal level, reflecting a trend toward more stringent privacy legislation in the United States. Foreign laws, including, for example, the European Union General Data Protection Regulation, also govern the privacy and security of personal data, including health information, in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and
- some state laws require pharmaceutical companies to comply with the industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring manufacturers to report information related to payments to physicians and other healthcare providers, marketing expenditures, and pricing information. Certain state and local laws require the registration of pharmaceutical sales and medical representatives.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, in the event we obtain regulatory approval for any one of our products, it is possible that some of our business activities could be subject to challenge and may not comply under one or more of such laws, regulations, and guidance. Law enforcement authorities are increasingly focused on enforcing fraud and abuse laws, and it is possible that some of our practices may be challenged under these laws. Violations of these laws can subject us to administrative, civil and criminal penalties, damages, fines, disgorgement, the exclusion from participation in federal and state healthcare programs, individual imprisonment, reputational harm, and the curtailment or restructuring of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws. Efforts to ensure that our current and future business arrangements with third parties, and our business generally, will comply with applicable healthcare laws and regulations will involve substantial costs.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Coverage and Reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, the product. In the United States, no uniform policy of coverage and reimbursement for drug and other medical products exists among third-party payors. Although CMS determines whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree, coverage and reimbursement for drug and other medical products can differ significantly from payor to payor. The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic or other studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. Additionally, companies may also need to provide discounts to purchasers, private health plans or government healthcare programs. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, our operations and financial condition. Additionally, a third-party payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor. Factors payors consider in determining reimbursement are based on whether the product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price, or ASP, and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of products have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party payor reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Healthcare Reform

In the United States and some foreign jurisdictions, there have been, and likely will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system directed at broadening the availability of healthcare, improving the quality of healthcare, and containing or lowering the cost of healthcare. For example, in March 2010, the U.S. Congress enacted the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA which, among other things, included changes to the coverage and payment for products under government health care programs. The ACA included provisions of importance to our potential product candidates that:

- created an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic products, apportioned among these entities according to their market share in certain government healthcare programs;
- expanded eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133 percent of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices;

- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50 percent point-of-sale-discount (increased to 70% as of January 1, 2019 pursuant to subsequent legislation) off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D; and
- created a Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA.

On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other healthcare reform measures of the Biden administration, if any, will impact our business. Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2 percent per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030 unless additional Congressional action is taken. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. More recently, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, beginning January 1, 2024.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their commercial products, which has resulted in several Congressional inquiries and proposed and enacted state and federal legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical products. Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. Furthermore, there has been increased interest by third party payors and governmental authorities in reference pricing systems and publication of discounts and list prices. It is difficult to predict the future legislative landscape in healthcare and the effect on our business, results of operations, financial condition and prospects. However, we expect that additional state and federal healthcare reform measures will be adopted in the future.

On May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act. Drug manufacturers who provide their investigational product under the Right to Try Act are required to submit to FDA an annual summary of the use of their drug.

Outside the United States, ensuring coverage and adequate payment for a product also involves challenges. Pricing of prescription pharmaceuticals is subject to government control in many countries. Pricing negotiations with government authorities can extend well beyond the receipt of regulatory approval for a product and may require a clinical trial that compares the cost-effectiveness of a product to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in commercialization.

In the European Union, or EU, pricing and reimbursement schemes vary widely from country to country Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the EU provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the EU have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the EU. The downward pressure on

healthcare costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states, and parallel trade, i.e., arbitrage between low-priced and high-priced member states, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

In December 2021, Regulation No 2021/2282 on health technology assessment, or HTA, amending Directive 2011/24/EU, was adopted. This regulation which entered into force in January 2022 intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas. The regulation foresees a three-year transitional period and will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technologies, and making decisions on pricing and reimbursement.

Foreign Private Issuer Status

We report under the Securities Exchange Act of 1934, as amended, or the Exchange Act, as a non-U.S. company with foreign private issuer status. As long as we qualify as a foreign private issuer under the Exchange Act, we will be exempt from certain provisions of the Exchange Act that are applicable to U.S. domestic public companies, including:

- the sections of the Exchange Act regulating the solicitation of proxies, consents or authorizations in respect of a security registered under the Exchange Act;
- sections of the Exchange Act requiring insiders to file public reports of their stock ownership and trading activities and liability for insiders who profit from trades made in a short period of time;
- the rules under the Exchange Act requiring the filing with the SEC of quarterly reports on Form 10-Q containing unaudited financial and other specified information, or current reports on Form 8-K, upon the occurrence of specified significant events; and
- Regulation FD, which regulates selective disclosures of material information by issuers.

C. ORGANIZATIONAL STRUCTURE

The information (including tabular data) set forth or referenced under the heading “Highlights of the Year—Founded Entities” on pages 5 to 9, of PureTech’s “Annual Report and Accounts 2021” included as exhibit 15.1 to this annual report on Form 20-F is incorporated by reference.

D. PROPERTY, PLANTS AND EQUIPMENT

The information (including tabular data) set forth or referenced under the headings “Notes to the Consolidated Financial Statements—Note 11. Property and Equipment” and “Notes to the Consolidated Financial Statements—Note 21. Leases” in each case of our audited consolidated financial statements included elsewhere in this annual report on Form 20-F.

ITEM 4A. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 5. OPERATING AND FINANCIAL REVIEW AND PROSPECTS

You should read the following discussion and analysis, including those portions incorporated herein by reference, together with our consolidated financial statements, including the notes thereto, included elsewhere in this annual report on Form 20-F. Some of the information contained in this discussion and analysis or incorporated herein, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section incorporated herein by reference, our actual results could differ materially from the results described in or implied by these forward-looking statements.

Our audited consolidated financial statements as of and for the years ended December 31, 2021, 2020 and 2019 have been prepared in accordance with UK-adopted International Financial Reporting Standards (IFRSs). The audited consolidated financial statements also comply fully with IFRSs as issued by the International Accounting Standards Board ("IASB").

The following discussion contains references to the consolidated financial statements of PureTech Health plc and its consolidated subsidiaries, or the Company. These financial statements consolidate the Company's subsidiaries and include the Company's interest in associates and investments held at fair value. Subsidiaries are those entities over which the Company maintains control. Associates are those entities in which the Company does not have control for financial accounting purposes but maintains significant influence over the financial and operating policies. Where we have neither control nor significant influence for financial accounting purposes, we recognize our holding in such entity as an investment at fair value. For purposes of our consolidated financial statements, each of our Founded Entities are considered to be either a "subsidiary" or an "associate" depending on whether PureTech Health plc controls or maintains significant influence over the financial and operating policies of the respective entity at the respective period end date. For additional information regarding the accounting treatment of these entities, see Note 1 of our consolidated financial statements included elsewhere in this annual report on Form 20-F.

A. OPERATING RESULTS

The information (including tabular data) set forth or referenced under the heading "Key Performance Indicators—2021" on page 95 of PureTech's "Annual Report and Accounts 2021" included as exhibit 15.1 to this annual report on Form 20-F is incorporated by reference.

2021 Compared with 2020

The information (including tabular data) set forth or referenced under the heading "Financial Review" on pages 96 to 110 of PureTech's "Annual Report and Accounts 2021" included as exhibit 15.1 to this annual report on Form 20-F is incorporated by reference.

2020 Compared with 2019

The information (including tabular data) set forth or referenced under the heading "Financial Review" on pages 96 to 110 of PureTech's "Annual Report and Accounts 2021" included as exhibit 15.1 to this annual report on Form 20-F is incorporated by reference.

The information (including tabular data) set forth or referenced under the headings "Risk Management—Brexit" on page 93 and "Risk Management" on pages 90 to 93 of PureTech's "Annual Report and Accounts 2021" included as exhibit 15.1 to this annual report on Form 20-F is incorporated by reference.

B. LIQUIDITY AND CAPITAL RESOURCES

The information (including tabular data) set forth or referenced under the following headings is incorporated by reference herein: "Viability" on page 94 and "Financial Review—Cash Flow and Liquidity" on pages 106 to 108 of PureTech's "Annual Report and Accounts 2021" included as exhibit 15.1 to this annual report on Form 20-F and "Notes to the Consolidated Financial Statements—Note 17.—Subsidiary Notes Payable", "Notes to the Consolidated Financial Statements—Note 20.—Long-term Loan", "Notes to the Consolidated Financial Statements—Note 21.—Leases", "Notes to the Consolidated Financial Statements—Note 22.—Capital and Financial Risk Management" and "Notes to the Consolidated Financial Statements—Note 23.—Commitments and Contingencies", in each case of our consolidated financial statements included elsewhere in this annual report on Form 20-F.

Under various license and collaboration agreements we are required to make milestone payments upon successful completion and achievement of certain intellectual property, clinical, regulatory and sales milestones. We will also be required to make royalty payments in connection with the sale of products developed under these agreements, if and when such sales occur. As of December 31, 2021, these milestone events have not yet occurred and therefore the Company does not have a present obligation to make the related payments in respect of the licenses. We believe that the occurrence of many of these milestones is remote at this time. As of December 31, 2021 payments in respect of contingent developmental milestones that are dependent on events that are outside the control of the Company but are reasonably possible to occur amounted to approximately $10.3 million. These milestone amounts represent an aggregate of multiple milestone payments depending on different milestone events in multiple agreements. The probability that all such milestone events will occur in the aggregate is remote. We are not able to predict when and if such milestone events will occur. Payments made to license IP represent the acquisition cost of intangible assets. For more information, see "Note 12 - Intangible Assets" to our audited consolidated financial statements included elsewhere in this annual report on Form 20-F.

We present the preferred shares issued by our subsidiaries to third parties as liabilities. Such preferred shares are redeemable only upon liquidation or deemed liquidation (as defined in the subsidiaries' incorporation documents) of the respective subsidiaries. We

are unable to predict when and if such liquidation or deemed liquidation events will occur, and therefore when and if such shares will be redeemed, if at all.

As of December 31, 2021, our off-balance sheet arrangements consist of outstanding standby letters of credit. We have no other off-balance sheet arrangements that have had, or are reasonably likely to have, a material current or future effect on our consolidated financial statements or changes in financial condition, revenues or expenses, results of operations, liquidity, capital expenditures or capital resources. See “Notes to the Consolidated Financial Statements—Note 13.—Other Financial Assets” included in our audited consolidated financial statements included elsewhere in this annual report on Form 20-F.

We consider the Group's working capital to be sufficient for its present requirements.

C. RESEARCH AND DEVELOPMENT, PATENTS AND LICENSES, ETC.

See "Notes to the Consolidated Financial Statements - Note 3-12" of our consolidated financial statements included elsewhere in this annual report on Form 20-F.

D. TREND INFORMATION

Other than as disclosed elsewhere in this annual report on Form 20-F, we are not aware of any trends, uncertainties, demands, commitments or events for the period from January 1, 2021 to the present time that are reasonably likely to have a material adverse effect on our net revenue, income, profitability, liquidity or capital resources, or that would cause the disclosed financial information to be not necessarily indicative of future operating results or financial condition.

E. CRITICAL ACCOUNTING ESTIMATES

Not applicable.

ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

A. DIRECTORS AND SENIOR MANAGEMENT

The information (including tabular data) set forth under the heading “Board of Directors” on pages 112 to 114, “Management team” on pages 115 to 116 and "Directors' Report for the year ended December 31, 2021” on pages 123 to 126 in each case of PureTech’s “Annual Report and Accounts 2021" included as exhibit 15.1 to this annual report on Form 20-F is incorporated by reference.

Board Diversity

The table below provides certain information regarding the diversity of our Board and Directors as of the date of this annual report.

Board Diversity Matrix

Country of Principal Executive Offices	United States
Foreign Private Issuer	Yes
Disclosure Prohibited Under Home Country Law	No
Total Number of Directors	9

	Female	Male	Non-Binary	Did Not Disclose Gender
Part I: Gender Identity				
Directors	4	5	0	0
Part II: Demographic Background				
Underrepresented Individual in Home Country Jurisdiction		0		
LGBTQ+		0		
Did Not Disclose Demographic Background		0		

B. COMPENSATION

The information (including graphs and tabular data) set forth under the following headings is incorporated by reference herein: “Directors’ Report for the year ended December 31, 2021” on pages 123 to126, “Directors’ Remuneration Report for the year ended December 31, 2021” on pages 131 to 132, “Directors’ Remuneration Policy” on pages 133 to 137, “Annual Report on Remuneration” on pages 138 to 146, in each case of PureTech’s “Annual Report and Accounts 2021” included as exhibit 15.1 to this annual report on Form 20-F and “Notes to the Consolidated Financial Statements—Note 8.—Share-Based Payments” of our audited consolidated financial statements included elsewhere in this annual report.

C. BOARD PRACTICES

The information (including graphs and tabular data) set forth under the headings "Board of Directors" on pages 112 to 114 “The Board” on pages 117 to 120,“Report of the Nomination Committee” on page 127, “Report of the Audit Committee” on pages 128 to 130, and "Directors' Remuneration Report for the year ended December 31, 2021" on pages 131 to 132 in each case of PureTech’s “Annual Report and Accounts 2021” included as exhibit 15.1 to this annual report on Form 20-F is incorporated by reference.

D. EMPLOYEES

The information (including tabular data) set forth under the heading “ESG Report—People” on pages 76 to 79 of PureTech’s “Annual Report and Accounts 2021” included as exhibit 15.1 to this annual report on Form 20-F is incorporated by reference.

E. SHARE OWNERSHIP

The information (including graphs and tabular data) set forth under the headings “Directors’ Report for the year ended December 31, 2021” on pages 123 to 126 and “Annual Report on Remuneration” on pages 138 to 146, in each case of PureTech’s “Annual Report and Accounts 2021” included as exhibit 15.1 to this annual report on Form 20-F 1 is incorporated by reference. For information regarding the share ownership of our directors and executive officers, see Item 7.A - "Major Shareholders".

ITEM 7. MAJOR SHAREHOLDERS AND RELATED PARTY TRANSACTIONS

A. MAJOR SHAREHOLDERS

The following table sets forth information with respect to the beneficial ownership of our ordinary shares as of by:

- each of our directors;
- each of our executive officers; and
- each person, or group of affiliated persons, who is known by us to beneficially own more than 3 percent of our outstanding ordinary shares.

The column entitled "Percentage of Shares Beneficially Owned" is based on a total of 287,841,508 ordinary shares outstanding as of March 31, 2022.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our ordinary shares. Ordinary shares subject to options that are currently exercisable or exercisable within 60 days after March 31, 2022 are considered outstanding and beneficially owned by the person holding the options for the purpose of calculating the percentage ownership of that person but not for the purpose of calculating the percentage ownership of any other person. Except as otherwise noted, the persons and entities in this table have sole voting and investment power with respect to all of the ordinary shares beneficially owned by them, subject to community property laws, where applicable. Except as otherwise set forth below, the address of the beneficial owner is c/o PureTech Health, 6 Tide Street, Suite 400, Boston, Massachusetts 02210. The information in the table below is based on information known to us or ascertained by us from public filings made by the shareholders. We have also set forth below information known to us regarding any significant change in the percentage ownership of our ordinary shares by any major shareholders during the past three years. The major shareholders listed below do not have voting rights with respect to their ordinary shares that are different from the voting rights of other holders of our ordinary shares.

NAME OF BENEFICIAL OWNER	PERCENTAGE OF SHARES BENEFICIALLY OWNED
3 Percent Shareholders	
Invesco Asset Management Limited[1]	22.5 %
Baillie Gifford & Co[2]	10.8 %
Lansdowne Partners Limited[3]	8.7 %
M&G Investment Management, LTD[4]	4.2 %
Miller Value Partners[5]	3.7 %
Recordati S.p.A.[6]	3.3 %
Executive Officers and Directors	
Daphne Zohar[7]	4.3 %
Bharatt Chowrira, Ph.D., J.D.	*
Sharon Barber-Lui	*
Raju Kucherlapati, Ph.D.	*
John LaMattina, Ph.D.	*
Robert Langer, Sc.D.[8]	1.0 %
Kiran Mazumdar-Shaw	*
Dame Marjorie Scardino	*
Christopher Viehbacher	*

* Represents beneficial ownership of less than 1 percent of our outstanding ordinary shares.

1 Consists of 64,796,214 shares beneficially held. The address for Invesco Asset Management Limited is c/o 43-45 Portman Square, London W1H GLY, United Kingdom.

2 Consists of 29,594,224 shares beneficially held. The address for Baillie Gifford & Co. is c/o Calton Square, 1 Greenside Row, Edinburgh EH1 3AN, United Kingdom.

3 Consists of 24,918,760 shares beneficially held. The address for Lansdowne Partners Limited is c/o 15 Davies Street, London W1K 3AG, United Kingdom.

4 Consists of 12,102,590 shares beneficially held. The address for M&G Investment Management, LTD is c/o 10 Fenchurch Avenue London EC3M 5BM, United Kingdom.The address for Miller Value Partners is c/o 1 South Street #2550, Baltimore, MD 21202.

5 Consists of 10,538,400 shares beneficially held. The address for Miller Value Partners is c/o 1 South Street #2550, Baltimore, MD 21202.

6 Consists of 9,544,140 shares beneficially held. The address for Recordati S.p.A. is c/o Via Civitali, 1, 20148 Milano, Italy.

7 Consists of an aggregate of 12,197,307 shares held by (i) the Zohar Family Trust I, a U.S. established trust of which Ms. Zohar is a beneficiary and trustee (ii) the Zohar Family Trust II, a U.S. established trust of which Ms. Zohar is a beneficiary (in the event of her spouse's death) and trustee; (iii) Zohar LLC, a U.S. established limited liability company and (iv) Ms. Zohar directly. Ms. Zohar owns or has a beneficial interest in 100 percent of the share capital of Zohar LLC.

8 Consists of an aggregate of 2,944,134 shares held by (i) Langer Family 2020 Trust and (ii) Dr. Langer directly.

We are not aware that the Company is directly owned or controlled by another corporation, any foreign government or any other natural or legal person(s) severally or jointly. We are not aware of any arrangement, the operation of which may result in a change of control of the Company.

The number of record holders in the United States is not representative of the number of beneficial holders nor is it representative of where such beneficial holders are resident since many of these ordinary shares were held by brokers or other nominees. As of March 31, 2022, assuming that all of our ordinary shares represented by ADSs are held by residents of the United States, we estimate that approximately 27% of our outstanding ordinary shares were held in the United States by approximately 102 holders of record.

The information (including graphs and tabular data) set forth under the headings “Directors’ Report for the year ended December 31, 2021—Substantial Shareholders” on page 123 and “Annual Report on Remuneration” on page 138 to 146, in each case of PureTech’s “Annual Report and Accounts 2021” included as exhibit 15.1 to this annual report on Form 20-F is incorporated by reference.

Change in Ownership of Major Shareholders

The following ownership changes are based upon the reported ownership of the respective shareholders in each of our annual reports and accounts for the years 2019, 2020 and 2021.

From 2020 to 2021, changes in ownership of major shareholders were approximately as follows: Invesco Asset Management Limited's ownership decreased from 23.7% to 22.5%. Baillie Gifford & Co.’s ownership decreased from 10.8% to 10.3%, Landsdowne Partners International Limited's ownership increased from 7.2% to 8.7%, M&G Investment Management, LTD's ownership increased from 3.4% to 4.2%, and Miller Value Partners' ownership increased from 3.5% to 3.7%.

From 2019 to 2020, changes in ownership of major shareholders were approximately as follows: Invesco Asset Management Limited’s decreased from 31.6% to 23.7%, Baillie Gifford & Co.’s ownership increased from 9.1% to 10.8%, Landsdowne Partners International Limited decreased from 8.3% to 7.2%, Jupiter Asset Management Ltd. decreased from 8.2% to less than 3% and Miller Value Partners increased to 3.5%.

B. RELATED PARTY TRANSACTIONS

The information (including graphs and tabular data) set forth under the following headings is incorporated reference herein: headings “Directors’ Report for the year ended December 31, 2021—Related party transactions” on page 124, “Highlights of the Year – 2021” on pages 1 to 9, and "Highlights of the Year—Founded Entities" on pages 5 to 9, in each case of PureTech’s “Annual Report and Accounts 2021” included as exhibit 15.1 to this annual report on Form 20-F and “Notes to the Consolidated Financial Statements—Note 24—Related Parties Transactions” of our audited consolidated financial statements included elsewhere in this annual report. For information regarding transactions with our Founded Entities, see Item 10.C - "Material Contracts."

C. INTERESTS OF EXPERTS AND COUNSEL

Not applicable.

ITEM 8. FINANCIAL INFORMATION

A. CONSOLIDATED STATEMENTS AND OTHER FINANCIAL INFORMATION

Consolidated Financial Statements

Please see the information below under the heading Item 18—"Financial Statements."

Dividend Distribution Policy

We have never declared or paid any dividends on our ordinary shares, though we may consider doing so in the future depending on the progression of our business. Under English law, we may only pay dividends if our accumulated realized profits, which have not been previously distributed or capitalized, exceed our accumulated realized losses, so far as such losses have not been previously written off in a reduction or reorganization of capital. Therefore, we must have sufficient distributable profits before issuing a dividend. Distributable profits are determined at the holding company level and not on a consolidated basis. Subject to such restrictions and to any restrictions set out in the Articles of Association, declaration and payment of cash dividends in the future, if any, will be at the discretion of our Board of Directors (the "Board") (and in the case of final dividends, must be approved by our shareholders), and will depend upon such factors as results of operations, capital requirements, contractual restrictions, our overall financial condition or applicable laws and any other factors deemed relevant by the Board.

Legal Proceedings

As of the date of this annual report, we were not party to any material legal matters or claims. In the future, we may become party to legal matters and claims arising in the ordinary course of business, the resolution of which we do not anticipate would have a material adverse impact on our financial position, results of operations or cash flows.

B. SIGNIFICANT CHANGES

Except as otherwise disclosed in this annual report on Form 20-F, no significant change has occurred since the date of the most recent financial statements included elsewhere in this annual report on Form 20-F.

ITEM 9. THE OFFER AND LISTING

A. OFFER AND LISTING DETAILS

Our American Depositary Shares ("ADSs") have been listed on The Nasdaq Global Market under the symbol “PRTC” since November 16, 2020. Prior to that date, there was no public trading market for our ADSs. Our ordinary shares have been trading on the main market of the London Stock Exchange since June 2015 under the ticker code “PRTC.” Prior to that date, there was no public trading market for our ordinary shares.

B. PLAN OF DISTRIBUTION

Not applicable.

C. MARKETS

Our ADSs have been listed on the Nasdaq Global Market under the symbol “PRTC” since November 16, 2020 and our ordinary shares have been listed on the main market of the London Stock Exchange since June 2015.

D. SELLING SHAREHOLDERS

Not applicable.

E. DILUTION

Not applicable.

F. EXPENSES OF THE ISSUE

Not applicable.

ITEM 10. ADDITIONAL INFORMATION

A. SHARE CAPITAL

Not applicable.

B. MEMORANDUM AND ARTICLES OF ASSOCIATION

Objects

Section 31 of the Companies Act 2006 provides that the objects of a company are unrestricted unless any restrictions are set out in the articles. There are no such restrictions in our Articles of Association ("Articles") and our objects are therefore unrestricted.

A copy of our Articles is attached as Exhibit 1.1 to this annual report on Form 20-F. The information called for by this Item is set forth in Exhibit 2.3 to this annual report on Form 20-F for the year ended December 31, 2021.

C. MATERIAL CONTRACTS

Except as otherwise set forth below or as otherwise disclosed in this report, we are not currently, and have not been in the last two years, party to any material contract, other than contracts entered into in the ordinary course of business.

The PureTech Health plc Performance Share Plan, or PSP, and forms of award agreements thereunder were approved on June 18, 2015. Under the PSP and subsequent amendments, awards of ordinary shares may be made to the Directors, senior managers and employees of, and other individuals providing services to the Company and its subsidiaries up to a maximum authorized amount of 10.0 percent of the total ordinary shares outstanding. The shares have various vesting terms over a period of service between two and four years, provided the recipient remains continuously engaged as a service provider.

On August 10, 2018, we entered into a Lease Agreement with RBK I Tenant, LLC for certain premises of approximately 50,858 rentable square feet of space at 6 Tide Street, Boston, MA 02210. The lease commenced on April 26, 2019 for an initial term consisting of ten years and three months and there is an option to extend for two consecutive periods of five years each.

We have executed agreements with the members of the Board substantially in the form of our Form of Deed of Indemnity.

We entered into an Asset Purchase Agreement by and between Auspex Pharmaceuticals, Inc. and PureTech Health LLC, dated July 15, 2019, pursuant to which Auspex assigned and transferred all patent claims, inventory, technology, contracts and related rights relating to LYT-100 to us. As consideration, we paid an upfront payment, which we do not deem material. In addition, Auspex is eligible to receive milestone payments of approximately $84 million in the aggregate depending upon specified developmental, regulatory and commercial achievements. In addition, for ten years following the first commercial sale of any commercialized product containing LYT-100, Auspex is eligible to receive low to middle single-digit royalties on the worldwide net sales of such product.

We entered into a Royalty Agreement with Follica, Incorporated, dated July 23, 2013, pursuant to which Follica agreed to pay us a two percent royalty on net sales by Follica or its sublicensees of (i) products involving skin disruption using any mechanical, energy or chemical based approaches, applying compounds to the skin, or any other approaches to the treatment of hair follicles or other dermatological disorders commercialized by Follica, (ii) processes involving such products, or (iii) services which use or incorporate any such product or process. In the event that Follica sublicenses the rights to any of these products, processes or services, Follica will be obligated to pay us low teen royalties on any income received from the sublicensee. Either party may terminate this agreement upon an uncured material breach by the other party. To date, we have not received any royalty payments pursuant to this agreement. We do not direct or control the development and commercialization of the intellectual property licensed pursuant to this agreement.

We entered into a Royalty and Sublicense Income Agreement with Gelesis, dated December 18, 2009, pursuant to which we are required to provide certain funding, management services and services relating to intellectual property. In exchange, Gelesis is required to pay us a royalty equal to 2 percent of all net product sales and 10 percent of gross sublicense income received on certain food products as a result of developing hydrogel-based products that are covered by a licensed patent that has issued and has not been revoked or abandoned. The royalty rate is subject to customary downward adjustments in the event Gelesis is required to pay third parties to obtain a license to intellectual property rights that are necessary for Gelesis to develop or commercialize our products. There are no milestone payment obligations under this agreement. Management services provided by us include advisory services on corporate strategy, general and administrative support including office space, supplies and administrative support, payroll services and website development and support. Gelesis' obligation to pay royalties to us will terminate on a country-by-country basis upon termination or expiration of the underlying patents. To date, we have not received any royalty payments pursuant to this agreement. We do not direct or control the development and commercialization of the intellectual property sublicensed pursuant to this agreement.

We entered into an Exclusive Patent License Agreement with Karuna, dated March 4, 2011, pursuant to which we granted Karuna an exclusive license to patent rights relating to combinations of a muscarinic activator with a muscarinic inhibitor for the treatment of central nervous system disorders. Karuna agreed to make milestone payments to us of up to an aggregate of $10 million upon the achievement of specified development and regulatory milestones. In addition, for the term of this agreement Karuna is obligated to pay us low single-digit running royalties on the worldwide net sales of any commercialized product covered by the licenses granted under this agreement. In the event that Karuna sublicenses any of the patent rights granted under this agreement, Karuna will be obligated to pay us royalties within the range of 15 percent to 25 percent on any income received from the sublicensee, excluding royalties. Karuna may terminate this agreement for any reason with proper prior notice to us, provided that it would lose its rights to the underlying patents as a result. Either party may terminate this agreement upon an uncured material

breach by the other party. To date, we have not received any royalty payments pursuant to this agreement. We do not direct or control the development and commercialization of the intellectual property licensed pursuant to this agreement.

We entered into a Research and License Agreement with New York University, or NYU, on March 6, 2017, pursuant to which NYU granted to us an exclusive worldwide license to patents relating to LYT-200 and LYT-210. In connection with this agreement, we are required to pay an annual license fee in addition to milestone payments upon the achievement of certain clinical and commercial milestones, both of which we deem immaterial. Additionally, for the term of this agreement, we are obligated to make low single digit royalty payments on the net sales of any commercialized product covered by the license granted under the agreement. In the event that we sublicense any of the patent rights granted under the Research and License Agreement, we will be obligated to pay NYU a low teen percentage of any royalties received by such sublicensee, provided that such payments are capped at a low single digit of net sales of any commercialized product by such sublicensee.

On January 13, 2022, Gelesis, Capstar Special Acquisition Corp., a Delaware corporation ("CPSR"), and CPSR Gelesis Merger Sub, Inc., a Delaware corporation, and wholly-owned subsidiary of CPSR ("Merger Sub"), consummated a business combination ("Gelesis Merger") pursuant to the business combination agreement, dated July 19, 2021, as amended on November 8, 2021 (the "Gelesis Business Combination Agreement"). Pursuant to the terms of the Gelesis Business Combination Agreement, Merger Sub merged with and into Gelesis, with Gelesis surviving the merger as a wholly-owned subsidiary of CPSR. In connection with the consummation of the Merger on the Closing Date, CPSR changed its name to Gelesis Holdings, Inc ("GLS"). As a result of the Gelesis Merger, among other things, each common share of Gelesis that was issued and outstanding immediately prior to the effective time of the Merger, after giving effect to the conversion of all preferred shares of Gelesis into common shares of Gelesis immediately prior to the effective time, was canceled and converted into the right to receive a number of shares of GLS Common Stock equal to an exchange ratio of approximately 2.59 multiplied by the number of common shares of Gelesis held by such holder immediately prior to the effective time. In addition, (a) all vested and unvested stock options of Gelesis were assumed by GLS and (b) each warrant of Old Gelesis was cancelled in exchange for a warrant to purchase shares of GLS, in each case based on an implied equity value of $675,000,000 as of the Closing.

Concurrently with the execution of the Gelesis Business Combination Agreement, on July 19, 2021, CPSR entered into subscription agreements (the "Subscription Agreements") with certain investors, including us, pursuant to which we purchased 1.5 million shares of GLS common stock at a price of $10.00 per share, for an aggregate purchase price of $15.0 million (the "PIPE Financing"). The PIPE Financing was consummated concurrently with the closing of the Gelesis Merger.

On December 30, 2021, CPSR entered into a Backstop Agreement (the "Backstop Agreement") with us and SSD2, LLC ("SSD2" and together with us, the "Backstop Purchasers"), pursuant to which the Backstop Purchasers agreed to purchase an aggregate of up to 1,500,000 shares of GLS common stock immediately prior to the closing at a cash purchase price of $10.00 per share (the "Backstop Purchase Shares"), resulting in aggregate proceeds of up to $15.0 million, which amount, when added to the proceeds from the PIPE Financing, would ensure that the minimum cash condition would be satisfied. Based on the number of redemptions at closing, we purchased 496,145 shares for an aggregate price of $5.0 million. In addition, at the closing of the sale of the Backstop Purchase Shares, GLS issued an additional 1,322,500 shares of common stock to us.

On the Closing January 13,2022, Gelesis, CPSR, certain former directors of CPSR (the "Director Holders") and certain former stockholders of Gelesis (collectively with Sponsor and the Director Holders, the "Holders"), including us, entered into an Amended and Restated Registration and Stockholder Rights Agreement, pursuant to which, among other things, the Holders agreed not to effect any sale or distribution of any equity securities of GLS held by any of them during a lock-up period (180 days after closing of the Gelesis Merger in the case of PureTech Health LLC), and GLS agreed to register for resale, pursuant to Rule 415 of the Securities Act of 1933, as amended, certain shares of common stock and other equity securities of GLS that are held by the parties thereto from time to time.

On January 26, 2022, Akili entered into an Agreement and Plan of Merger (the "Akili Merger Agreement"), by and among Akili, Social Capital Suvretta Holdings Corp. I ("SCS"), and Karibu Merger Sub, Inc., a Delaware corporation and a direct wholly owned subsidiary of SCS ("Merger Sub"). Pursuant to the Akili Merger Agreement, among other things: (i) prior to the closing of the transactions contemplated by the Akili Merger Agreement, SCS will domesticate as a Delaware corporation in accordance with the DGCL, and the Cayman Islands Companies Act (As Revised), (ii) at the closing, upon the terms and subject to the conditions of the Merger Agreement, in accordance with the DGCL, Merger Sub will merge with and into Akili, with Akili continuing as the surviving corporation and a wholly owned subsidiary of SCS (the "Merger"), (iii) at the closing, all of the outstanding capital stock of Akili and all options and warrants to acquire capital stock of Akili will be converted into the right to receive shares of common stock, par value $0.0001 per share, of SCS (after its domestication) ("SCS Common Stock") or comparable equity awards that are settled or are exercisable for shares of SCS Common Stock, representing an aggregate of 60 million shares of SCS Common Stock, (iv) at the closing, SCS will be renamed "Akili, Inc." and (v) at the closing, SCS will deposit into an escrow account for the benefit of the pre-Closing Akili stockholders, optionholders and warrantholders an aggregate number of shares of SCS Common Stock equal to 7.5% of the fully diluted shares of SCS Common Stock (including shares reserved under the equity incentive plan to be adopted by the combined company in connection with the Closing), determined as of immediately following the Closing (collectively, the "Earnout Shares"), which Earnout Shares will be subject to release from escrow to the pre-Closing Akili stockholders, optionholders and warrantholders in three equal tranches upon the daily volume weighted average price of a share of SCS Common Stock reaching $15.00/share, $20.00/share and $30.00/share, respectively, over any 20 trading days within any 30 consecutive trading day period following the closing and prior to the fifth anniversary of the closing, in each case, on the terms set forth in the Akili Merger Agreement.The Closing is subject to the satisfaction or waiver of certain closing conditions contained in the Merger Agreement, including the approval of SCS's shareholders.

Voting and Investors' Rights Agreements

We are party to voting and investors' rights agreements with certain of our Founded Entities as described below:

- Pursuant to an Amended and Restated Investors' Rights Agreement, as amended, between Vedanta and certain of its investors, dated July 15, 2021, we are entitled to designate a total of four directors to Vedanta's board of directors, including (i) two directors for so long as PureTech Health LLC continues to hold a majority of Vedanta's Series A-1 preferred stock, and (ii) two directors for so long as PureTech Health LLC continues to hold a majority of Vedanta's Series B preferred stock. The execution of this agreement replaced and terminated the previous Amended and Restated Investors' Rights Agreement dated December 21, 2018, which had provided us with equivalent rights.
- Pursuant to a Voting Agreement between Sonde and certain of its investors, dated April 9, 2019, we are entitled to designate one director to Sonde's board of directors for so long as PureTech Health LLC and its affiliates continue to hold at least 1,000,000 shares of Sonde's Series A-2 preferred stock.
- Pursuant to a Voting Agreement between Entrega and certain of its investors, dated December 18, 2017, we are entitled to designate four directors to Entrega's board of directors.
- Pursuant to the Fifth Amended and Restated Voting Agreement between Follica and certain of its investors, dated July 19, 2019, we are entitled to designate one director to Follica's board of directors for so long as PureTech Health LLC and its affiliates continue to own at least 1,000,000 shares of Follica's common stock.

Agreements with Founded Entities Restricting Sale of Shares in Connection with an Initial Public Offering

We are party to agreements containing market stand-off provisions with certain of our Founded Entities that restrict our ability to sell shares of such Founded Entities for 180 days after their initial public offerings or initial public listing through a business combination as follows:

- Third Amended and Restated Investors' Rights Agreement between Akili and the investor parties named therein, dated May 25, 2021, the execution of which replaced and terminated the Second Amended and Restated Investors' Rights Agreement dated May 8, 2018, which had contained an equivalent restriction;
- Fifth Amended and Restated Investors' Rights Agreement between Follica and the investor parties named therein, dated July 19, 2019;
- Amended and Restated Investors' Rights Agreement between Vedanta, as amended, and the investor parties named therein, dated July 15, 2021,the execution of which replaced and terminated the previous Amended and Restated Investors' Rights Agreement dated December 21, 2018, which had contained an equivalent restriction;
- Investors' Rights Agreement between Entrega and the investor parties named therein, dated December 18, 2017;
- Investors' Rights Agreement between Sonde and the investor parties named therein, dated April 9, 2019;
- Amended and Restated Investors' Rights Agreement between Vor and the investor parties named therein, dated June 30, 2020, which terminated as of Vor's initial public offering, except for the registration rights granted thereunder;
- Amended and Restated Registration and Stockholders Rights Agreement dated January 13, 2022 between CPSR and the stockholder parties named therein, the execution of which terminated the Ninth Amended and Restated Stockholders Agreement between Gelesis and the stockholder parties named therein, dated December 5, 2019, which had contained an equivalent restriction; and
- The Backstop Agreement between CPSR and us, among others, dated December 30, 2021, which provides that certain shares acquired thereunder are subject to a 180-day market stand off provision.

Other Shareholder Rights Agreements

We have certain registration rights provisions in agreements with our Founded Entities as follows:

- Third Amended and Restated Investors' Rights Agreement between Akili and the investor parties named therein, dated May 25, 2021, the execution of which replaced and terminated the Second Amended and Restated Investors' Rights Agreement dated May 8, 2018, which had provided us with similar rights;
- Fifth Amended and Restated Investors' Rights Agreement between Follica and the investor parties named therein, dated July 19, 2019;
- Amended and Restated Investors' Rights Agreement between Vedanta, as amended, and the investor parties named therein, dated July 15, 2021,the execution of which replaced and terminated the previous Amended and Restated Investors' Rights Agreement dated December 21, 2018, which had provided us with similar rights;
- Investors' Rights Agreement between Entrega and the investor parties named therein, dated December 18, 2017;
- Investors' Rights Agreement between Sonde and the investor parties named therein, dated April 9, 2019;
- Amended and Restated Registration and Stockholders Rights Agreement dated January 13, 2022 between CPSR and the stockholder parties named therein, the execution of which terminated the Ninth Amended and Restated Stockholders Agreement between Gelesis and the stockholder parties named therein, dated December 5, 2019, which had contained an equivalent restriction, which had provided us with similar rights;
- The Backstop Agreement between CPSR and us, among others, dated December 30, 2021;
- Subscription Agreement between CPSR and the investor parties thereto dated July 19, 2021; and
- Amended and Restated Investors' Rights Agreement between Vor and the investor parties named therein, dated June 30, 2020.

We have certain preemptive rights of first refusal with respect to transfers of shares by other holders pursuant to the following agreements:

- Fifth Amended and Restated Right of First Refusal and Co-Sale Agreement, dated July 19, 2019, by and among Follica, Incorporated and the investors and key holders party thereto;
- Right of First Refusal and Co-Sale Agreement, dated April 9, 2019, by and between Sonde Health, Inc. and the investors and key holders party thereto; and

- Right of First Refusal and Co-Sale Agreement, dated December 18, 2017, by and between Entrega, Inc. and the investors and key holders party thereto.

D. EXCHANGE CONTROLS

Other than certain economic sanctions which may be in place from time to time, there are currently no UK laws, decrees or other regulations restricting the import or export of capital or affecting the remittance of dividends or other payment to holders of ordinary shares who are non-residents of the United Kingdom. Similarly, other than certain economic sanctions which may be in force from time to time, there are no limitations relating only to nonresidents of the United Kingdom under English law or the Company's articles of association on the right to be a holder of, and to vote in respect of, the ordinary shares.

E. TAXATION

Certain United Kingdom Tax Considerations

The following is a general summary of certain U.K. tax considerations relating to the ownership and disposal of an ordinary share or ADS and does not address all possible tax consequences relating to an investment in an ordinary share or ADS. It is based on U.K. tax law and generally published HM Revenue & Customs, or HMRC, practice (which may not be binding on HMRC) as of the date of this annual report on Form 20-F, both of which are subject to change, possibly with retrospective effect.

Save as provided otherwise, this summary applies only to a person who is the absolute beneficial owner of an ordinary share or ADS and who is resident (and, in the case of an individual, domiciled) in the United Kingdom for tax purposes and who is not resident for tax purposes in any other jurisdiction and does not have a permanent establishment or fixed base in any other jurisdiction with which the holding of an ordinary share or ADS is connected ("U.K. Holders"). A person (a) who is not resident (or, if resident, is not domiciled) in the United Kingdom for tax purposes, including an individual and company who trades in the United Kingdom through a branch, agency or permanent establishment in the United Kingdom to which an ordinary share or ADS is attributable, or (b) who is resident or otherwise subject to tax in a jurisdiction outside the United Kingdom, is recommended to seek the advice of professional advisors in relation to their taxation obligations.

This summary is for general information only and is not intended to be, nor should it be considered to be, legal or tax advice to any particular investor. It does not address all of the tax considerations that may be relevant to specific investors in light of their particular circumstances or to investors subject to special treatment under U.K. tax law. In particular:

- this summary only applies to an absolute beneficial owner of an ordinary share or ADS and any dividend paid in respect of the ordinary share where the dividend is regarded for U.K. tax purposes as that person's own income (and not the income of some other person);
- this summary: (a) only addresses the principal U.K. tax consequences for an investor who holds an ordinary share or ADS as a capital asset, (b) does not address the tax consequences that may be relevant to certain special classes of investor such as a dealer, broker or trader in shares or securities and any other person who holds an ordinary share or ADS otherwise than as an investment, (c) does not address the tax consequences for a holder that is a financial institution, insurance company, collective investment scheme, pension scheme, charity or tax-exempt organization, (d) assumes that a holder is not an officer or employee of the company (nor of any related company) and has not (and is not deemed to have) acquired the an ordinary share or ADS by virtue of an office or employment, and (e) assumes that a holder does not control or hold (and is not deemed to control or hold), either alone or together with one or more associated or connected persons, directly or indirectly (including through the holding of an ordinary share or ADS), an interest of 10 percent or more in the issued share capital (or in any class thereof), voting power, rights to profits or capital of the company, and is not otherwise connected with the company.

This summary further assumes that a holder of an ordinary share or ADS is the beneficial owner of the underlying ordinary share for U.K. direct tax purposes.

POTENTIAL INVESTORS IN THE ORDINARY SHARES OR ADSs SHOULD SATISFY THEMSELVES PRIOR TO INVESTING AS TO THE OVERALL TAX CONSEQUENCES, INCLUDING, SPECIFICALLY, THE CONSEQUENCES UNDER U.K. TAX LAW AND HMRC PRACTICE OF THE ACQUISITION, OWNERSHIP AND DISPOSAL OF THE ORDINARY SHARES OR ADSs, IN THEIR OWN PARTICULAR CIRCUMSTANCES BY CONSULTING THEIR TAX ADVISERS.

Taxation of Dividends

Withholding Tax

A dividend payment in respect of an ordinary share may be made without withholding or deduction for or on account of U.K. tax.

Income Tax

A dividend received by individual U.K. Holders may, depending on his or her particular circumstances, be subject to U.K. income tax on the gross amount of the dividend paid.

An individual holder of an ordinary share or ADS who is not a U.K. Holder will not be chargeable to U.K. income tax on a dividend paid by the company, unless such holder carries on (whether solely or in partnership) a trade, profession or vocation in the United Kingdom through a permanent establishment in the United Kingdom to which the ordinary share or ADS is attributable. In these circumstances, such holder may, depending on his or her individual circumstances, be chargeable to U.K. income tax on a dividend received from the company.

All dividends received by a UK Holder from the Company or from other sources will form part of the UK Holder's total income for UK income tax purposes and will constitute the top slice of that income. The rate of U.K. income tax that is chargeable on dividends received in the tax year 2020/2021 by (i) an additional rate taxpayer is 38.1 percent, (ii) a higher rate taxpayer is 32.5 percent, and (iii) a basic rate taxpayer is 7.5 percent. A nil rate of income tax will apply to the first £2,000 of taxable dividend income received by an individual U.K. Holder in a tax year.

Corporation Tax

A U.K. Holder within the charge to U.K. corporation tax may be entitled to exemption from U.K. corporation tax in respect of dividend payments, provided the dividends qualify for exemption (which is likely) and certain conditions are met (including anti-avoidance conditions). If the conditions for the exemption are not satisfied, or such U.K. Holder elects for an otherwise exempt dividend to be taxable, U.K. corporation tax will be chargeable on the gross amount of a dividend. If potential investors are in any doubt as to their position, they should consult their own professional advisers.

A corporate holder of an ordinary share or ADS that is not a U.K. Holder will not be subject to U.K. corporation tax on a dividend received from the company, unless it carries on a trade in the United Kingdom through a permanent establishment to which the ordinary share or ADS is attributable. In these circumstances, such holder may, depending on its individual circumstances and if the exemption from U.K. corporation tax discussed above does not apply, be chargeable to U.K. corporation tax on dividends received from the company.

Taxation of Disposals

U.K. Holders

A disposal or deemed disposal of an ordinary share or ADS by an individual U.K. Holder may, depending on his or her individual circumstances, give rise to a chargeable gain or to an allowable loss for the purpose of U.K. capital gains tax. The principal factors that will determine the capital gains tax position on a disposal of an ordinary share or ADS are the extent to which the holder realizes any other capital gains in the tax year in which the disposal is made, the extent to which the holder has incurred capital losses in that or any earlier tax year and the level of the annual exemption for tax-free gains in that tax year (the "annual exemption"). The annual exemption for the 2020/2021 tax year is £12,500. If, after all allowable deductions, an individual U.K. Holder's total taxable income for the year exceeds the basic rate income tax limit, a taxable capital gain accruing on a disposal of an ordinary share or an ADS is taxed at the rate of 20 percent. In other cases, a taxable capital gain accruing on a disposal of an ordinary share or ADS may be taxed at the rate of 10 percent save to the extent that any capital gains exceed the unused basic rate tax band. In that case, the rate currently applicable to the excess would be 20 percent.

An individual U.K. Holder who ceases to be resident in the United Kingdom (or who fails to be regarded as resident in a territory outside the United Kingdom for the purposes of double taxation relief) for a period of five tax years or less than five years and who disposes of an ordinary share or ADS during that period of temporary non-residence may be liable to U.K. capital gains tax on a chargeable gain accruing on such disposal on his or her return to the United Kingdom (or upon ceasing to be regarded as resident outside the United Kingdom for the purposes of double taxation relief) (subject to available exemptions or reliefs).

A disposal (or deemed disposal) of an ordinary share or ADS by a corporate U.K. Holder may give rise to a chargeable gain or an allowable loss for the purpose of U.K. corporation tax. Any gain or loss in respect of currency fluctuations over the period of holding an ordinary share or an ADS are also brought into account on a disposal.

Non-U.K. Holders

An individual holder who is not a U.K. Holder should not normally be liable to U.K. capital gains tax on capital gains realized on the disposal of an ordinary share or ADS unless such holder carries on (whether solely or in partnership) a trade, profession or vocation in the United Kingdom through a permanent establishment in the United Kingdom to which the ordinary share or ADS is attributable. In these circumstances, such holder may, depending on his or her individual circumstances, be chargeable to U.K. capital gains tax on chargeable gains arising from a disposal of his or her ordinary share or ADS.

A corporate holder of an ordinary share or ADS that is not a U.K. Holder will not be liable for U.K. corporation tax on chargeable gains realized on the disposal of an ordinary share or ADS unless: (i) it carries on a trade in the United Kingdom through a permanent establishment to which the ordinary share or ADS is attributable; or (ii) the corporate holder is disposing of an interest in a company and that disposal is of an asset that derives 75 percent or more of its gross asset value from UK land and that holder has a substantial indirect interest in UK land (broadly at least 25 percent at any time during the previous two years). In these circumstances, a disposal (or deemed disposal) of an ordinary share or ADS by such holder may give rise to a chargeable gain or an allowable loss for the purposes of U.K. corporation tax.

Inheritance Tax

If, for the purposes of the Double Taxation Relief (Taxes on Estates of Deceased Persons and on Gifts) Treaty United States of America Order 1979 (S1 1979/1454) between the United States and the United Kingdom, an individual holder is domiciled at the time of their death or at the time of a transfer made during their lifetime in the United States and is not a national of the United Kingdom, any ordinary share or ADS beneficially owned by that holder should not generally be subject to U.K. inheritance tax, provided that any applicable U.S. federal gift or estate tax liability is paid, except where (i) the ordinary share or ADS is part of the business property of a U.K. permanent establishment or pertain to a U.K. fixed base used for the performance of independent personal services; or (ii) the ordinary share or ADS is comprised in a settlement unless, at the time the settlement was made, the settlor was domiciled in the United States and not a national of the U.K. (in which case no charge to U.K. inheritance tax should apply).

Stamp Duty and Stamp Duty Reserve Tax

The stamp duty and stamp duty reserve tax, or SDRT, treatment of the issue, transfer and agreement to transfer an ordinary share outside a depositary receipt system or a clearance service are discussed in the paragraphs under "General" below. The stamp duty and SDRT treatment of such transactions in relation to such systems are discussed in the paragraphs under "Depositary Receipt Systems and Clearance Services" below. The discussion below relates to the holders of our ordinary shares or ADSs wherever resident, however it should be noted that special rules may apply to certain persons such as market makers, brokers, dealers or intermediaries.

General

Issue of Ordinary Shares or ADSs

The issue of an ordinary share or ADS does not give rise to a SDRT liability, according to the HM Revenue & Customs practice and recent case law and is not subject to stamp duty.

Transfer of Ordinary Shares

A transfer of an ordinary share will generally be subject to stamp duty at the rate of 0.5 percent of the consideration given for the transfer (rounded up to the next £5). An exemption from stamp duty is available on an instrument transferring an ordinary share where the amount or value of the consideration is £1,000 or less, and it is certified on the instrument that the transaction effected does not form part of a larger transaction or series of transactions in respect of which the aggregate amount or value of the consideration exceeds £1,000. The purchaser normally pays the stamp duty.

An unconditional agreement to transfer an ordinary share will normally give rise to a charge to SDRT at the rate of 0.5 percent of the amount or value of the consideration payable for the transfer. SDRT is, in general, payable by the purchaser. If a duly stamped transfer completing an agreement to transfer is produced within six years of the date on which the agreement is made (or, if the agreement is conditional, the date on which the agreement becomes unconditional) any SDRT already paid is generally repayable, normally with interest, and any SDRT charge yet to be paid is cancelled.

Transfer of ADSs

No stamp duty will, in practice, be payable on a written instrument transferring an ADS or on an unconditional agreement to transfer an ADS provided the instrument of transfer or the unconditional agreement to transfer is executed and remains at all times outside the UK. Where these conditions are not met, the transfer of, or agreement to transfer, an ADS could, depending on the circumstances, attract a charge to U.K. stamp duty at the rate of 0.5 percent of the value of the consideration. No SDRT will be payable in respect of an agreement to transfer an ADS.

Depositary Receipt Systems and Clearance Services

Based on current HM Revenue & Customs practice and recent case law in respect of the European Council Directives 69/335/EC and 2009/7/EC, or the Capital Duties Directives, no SDRT is generally payable when shares are issued or transferred to a clearance service or depositary receipt system as an integral part of a raising of capital. HM Revenue & Customs has confirmed that it will continue not to apply the 1.5 percent stamp duty and SDRT charge on the issue of shares (and transfers integral to the raising of capital) into overseas clearance systems and depository receipt issuers once the U.K. leaves the European Union. In addition, a recent Court of Justice of the European Union judgment (Air Berlin plc v HM Revenue & Customs (2017)) held on the relevant facts that the Capital Duties Directives preclude the taxation of a transfer of legal title to shares for the sole purpose of listing those shares on a stock exchange which does not impact the beneficial ownership of the shares, but, as yet, the U.K. domestic law and HM Revenue & Customs' published practice remain unchanged and, accordingly, we anticipate that amounts on account of SDRT will continue to be collected by the depositary receipt issuer or clearance service. Holders of ordinary shares should consult their own independent professional advisers before incurring or reimbursing the costs of such a 1.5 percent SDRT charge.

Where an ordinary share or ADS is otherwise transferred (i) to, or to a nominee or an agent for, a person whose business is or includes the provision of clearance services or (ii) to, or to a nominee or an agent for a person whose business is or includes issuing depositary receipts, stamp duty or SDRT will generally be payable at the higher rate of 1.5 percent of the amount or value of the consideration given or, in certain circumstances, the value of the shares.

There is an exception from the 1.5 percent charge on the transfer to, or to a nominee or agent for, a clearance service where the clearance service has made and maintained an election under section 97A(1) of the Finance Act 1986, which has been approved by HM Revenue & Customs. It is understood that HM Revenue & Customs regards the facilities of DTC as a clearance service for these purposes and we are not aware of any section 97A election having been made by the DTC.

Any liability for stamp duty or SDRT in respect of a transfer into a clearance service or depositary receipt system, or in respect of a transfer within such a service, which does arise will strictly be accountable by the clearance service or depositary receipt system operator or their nominee, as the case may be, but will, in practice, be borne by the participants in the clearance service or depositary receipt system.

Repurchase of Ordinary Shares

U.K. stamp duty will generally be due at a rate of 0.5% of the consideration paid (rounded up to the next £5.00) on a repurchase by the company of its ordinary shares.

Taxation in the United States

The following summary of the material U.S. federal income tax consequences of the acquisition, ownership and disposition of our ordinary shares or ADSs is based upon current law and does not purport to be a comprehensive discussion of all the tax considerations that may be relevant to a decision to purchase our ordinary shares or ADSs. This summary is based on current provisions of the Internal Revenue Code of 1986, as amended, or the Code, existing, final, temporary and proposed U.S. Treasury Regulations, administrative rulings and judicial decisions, in each case as available on the date of this annual report on Form 20-F. All of the foregoing are subject to change, which change could apply retroactively and could affect the tax consequences described below.

This section summarizes the material U.S. federal income tax consequences to U.S. holders and certain non-U.S. holders, each as defined below, of our ordinary shares or ADSs. This summary addresses only the U.S. federal income tax considerations for holders that acquire our ordinary shares or ADSs at their original issuance and hold our ordinary shares or ADSs as capital assets. This summary does not address all U.S. federal income tax matters that may be relevant to a particular holder. Each prospective investor should consult a professional tax advisor with respect to the tax consequences of the acquisition, ownership or disposition of our

ordinary shares or ADSs. This summary does not address tax considerations applicable to a holder of our ordinary shares or ADSs that may be subject to special tax rules including, without limitation, the following:

- banks or other financial institutions;
- insurance companies;
- dealers or traders in securities, currencies, or notional principal contracts;
- tax-exempt entities, including an "individual retirement account" or "Roth IRA" retirement plan;
- regulated investment companies or real estate investment trusts;
- "qualified foreign pension funds," or entities wholly owned by a "qualified foreign pension fund"; persons who have elected to mark securities to market
- persons that hold the ordinary shares as part of a hedge, straddle, conversion, constructive sale or similar transaction involving more than one position;
- holders (whether individuals, corporations or partnerships) that are treated as expatriates for some or all U.S. federal income tax purposes;
- persons who acquired the ADSs as compensation for the performance of services;
- persons holding the ADSs in connection with a trade or business conducted outside of the United States;
- holders that own (or are deemed to own) 10 percent or more of our ordinary shares or ADSs, by vote or value; and
- holders that have a "functional currency" other than the U.S. dollar.

Further, this summary does not address any aspects of any U.S. state, local or non-U.S. tax law, alternative minimum tax, gift or estate consequences, the rules regarding qualified small business stock within the meaning of Section 1202 of the Code, any election to apply Section 1400Z-2 of the Code to gains recognized with respect to our ordinary shares, any other U.S. federal tax other than the income tax or the indirect effects on the holders of equity interests in entities that own our ordinary shares or ADSs.

For the purposes of this summary, a "U.S. holder" is a beneficial owner of ordinary shares or ADSs that is (or is treated as), for U.S. federal income tax purposes:

- an individual who is either a citizen or resident of the United States;
- a corporation, or other entity that is treated as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States or any state of the United States or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust, if a court within the United States is able to exercise primary supervision over its administration and one or more U.S. persons have the authority to control all of the substantial decisions of such trust or has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a U.S. person.

If a partnership holds ordinary shares or ADSs, the tax treatment of a partner will generally depend upon the status of the partner and upon the activities of the partnership. This discussion does not address the tax treatment of partnerships or other entities that are pass-through entities for U.S. federal income tax purposes or persons that hold their ordinary shares or ADSs through partnerships or other pass-through entities. A partner in a partnership or other pass-through entity that will hold our ordinary shares or ADSs should consult his, her or its tax advisor regarding the tax consequences of acquiring, holding and disposing of our ordinary shares or ADSs through a partnership or other pass-through entity, as applicable.

We will not seek a ruling from the U.S. Internal Revenue Service, or IRS, with regard to the U.S. federal income tax treatment of an investment in our ordinary shares or ADSs, and we cannot assure you that the IRS will agree with the conclusions set forth below.

PERSONS CONSIDERING AN INVESTMENT IN ORDINARY SHARES OR ADSs SHOULD CONSULT THEIR TAX ADVISORS AS TO THE PARTICULAR TAX CONSEQUENCES APPLICABLE TO THEM RELATING TO THE ACQUISITION, OWNERSHIP AND DISPOSITION OF THE ORDINARY SHARES OR ADSs, INCLUDING THE APPLICABILITY OF U.S. FEDERAL, STATE AND LOCAL TAX LAWS.

Ownership of ADSs

For U.S. federal income tax purposes, a holder of ADSs generally will be treated as the owner of the ordinary shares represented by such ADSs. Gain or loss will generally not be recognized on account of exchanges of ordinary shares for ADSs, or of ADSs for ordinary shares. References to ordinary shares in the discussion below are deemed to include ADSs, unless context otherwise requires.

F. DIVIDENDS AND PAYING AGENTS

Not applicable.

G. STATEMENT BY EXPERTS

Not applicable.

H. DOCUMENTS ON DISPLAY

We are required to make certain filings with the SEC. The SEC maintains a website at http://www.sec.gov from which filings may be accessed.

We also make available on our website, free of charge, our annual reports on Form 20-F and the text of our reports on Form 6-K, including any amendments to these reports, as well as certain other SEC filings, as soon as reasonably practicable after they are electronically filed with or furnished to the SEC. Our website address is www.puretechhealth.com. The information contained on our website is not incorporated by reference into this annual report on Form 20-F.

I. SUBSIDIARY INFORMATION

Not applicable.

ITEM 11. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

The information (including graphs and tabular data) set forth under the following headings is incorporated by reference herein: “Quantitative and Qualitative Disclosures about Financial Risks” on pages 109 to 110 of PureTech’s “Annual Report and Accounts 2021” included as exhibit 15.1 to this annual report on Form 20-F and in “Financial Statements—Notes to the Consolidated Financial Statements—Note 22.—Capital and Financial Risk Management” in the audited consolidated financial statements included elsewhere in this annual report on Form 20-F.

ITEM 12. DESCRIPTION OF SECURITIES OTHER THAN EQUITY SECURITIES

A. DEBT SECURITIES

Not applicable.

B. WARRANTS AND RIGHTS

Not applicable.

C. OTHER SECURITIES

Not applicable.

D. AMERICAN DEPOSITARY SHARES

Our ADSs are registered with Citibank, N.A., as depositary . Each ADS represents ten ordinary shares (or a right to receive ten ordinary shares) deposited with Citibank, N.A. (London), as custodian for the depositary in the United Kingdom. Citibank's depositary offices are located at 388 Greenwich Street, New York, New York, 10013. ADSs represent ownership interests in securities that are on deposit with the depositary bank. ADSs may be represented by certificates that are commonly known as "American Depositary Receipts" or "ADRs." The depositary bank typically appoints a custodian to safekeep the securities on deposit. In this case, the custodian is Citibank, N.A.—London Branch, located at Citigroup Centre Canary Wharf, London E14 5LB D.

A deposit agreement among us, the depositary, ADS holders and beneficial owners of ADSs issued thereunder sets out ADS holder rights as well as the rights and obligations of the depositary. New York law governs the deposit agreement and the ADSs. A copy of the deposit agreement is incorporated by reference as an exhibit to this annual report on Form 20-F.

Fees and Charges

As an ADS holder, you will be required to pay the following fees under the terms of the deposit agreement:

SERVICE	FEES
• Issuance of ADSs (e.g., an issuance of ADS upon a deposit of ordinary shares, upon a change in the ADS(s)-to-ordinary share(s) ratio, or for any other reason), excluding ADS issuances as a result of distributions of ordinary shares)	Up to U.S.$0.05 per ADS issued
• Cancellation of ADSs (e.g., a cancellation of ADSs for delivery of deposited property, upon a change in the ADS(s)-to-ordinary share(s) ratio, or for any other reason)	Up to U.S.$0.05 per ADS cancelled
• Distribution of cash dividends or other cash distributions (e.g., upon a sale of rights and other entitlements)	Up to U.S.$0.05 per ADS held
• Distribution of ADSs pursuant to (i) share dividends or other free share distributions, or (ii) exercise of rights to purchase additional ADSs	Up to U.S.$0.05 per ADS held
• Distribution of securities other than ADSs or rights to purchase additional ADSs (e.g., upon a spin-off)	Up to U.S.$0.05 per ADS held
• ADS Services	Up to U.S.$0.05 per ADS held on the applicable record date(s) established by the depositary bank
• Registration of ADS transfers (e.g., upon a registration of the transfer of registered ownership of ADSs, upon a transfer of ADSs into DTC and vice versa, or for any other reason)	Up to U.S.$0.05 per ADS (or fraction thereof) transferred
• Conversion of ADSs of one series for ADSs of another series (e.g., upon conversion of partial entitlement ADSs for full entitlement ADSs, or upon conversion of restricted ADSs (each as defined in the deposit agreement) into freely transferable ADSs, and vice versa).	Up to U.S.$0.05 per ADS (or fraction thereof) converted

As an ADS holder you will also be responsible to pay certain charges such as:

- taxes (including applicable interest and penalties) and other governmental charges;
- the registration fees as may from time to time be in effect for the registration of ordinary shares on the share register and applicable to transfers of ordinary shares to or from the name of the custodian, the depositary bank or any nominees upon the making of deposits and withdrawals, respectively;
- certain cable, telex and facsimile transmission and delivery expenses;
- the fees, expenses, spreads, taxes and other charges of the depositary bank and/or service providers (which may be a division, branch or affiliate of the depositary bank) in the conversion of foreign currency;
- the reasonable and customary out-of-pocket expenses incurred by the depositary bank in connection with compliance with exchange control regulations and other regulatory requirements applicable to ordinary shares, ADSs and ADRs; and
- the fees, charges, costs and expenses incurred by the depositary bank, the custodian, or any nominee in connection with the ADR program.

ADS fees and charges for (i) the issuance of ADSs, and (ii) the cancellation of ADSs are charged to the person for whom the ADSs are issued (in the case of ADS issuances) and to the person for whom ADSs are cancelled (in the case of ADS cancellations). In the case of ADSs issued by the depositary bank into DTC, the ADS issuance and cancellation fees and charges may be deducted from distributions made through DTC, and may be charged to the DTC participant(s) receiving the ADSs being issued or the DTC participant(s) holding the ADSs being cancelled, as the case may be, on behalf of the beneficial owner(s) and will be charged by the DTC participant(s) to the account of the applicable beneficial owner(s) in accordance with the procedures and practices of the DTC participants as in effect at the time. ADS fees and charges in respect of distributions and the ADS service fee are charged to the holders as of the applicable ADS record date. In the case of distributions of cash, the amount of the applicable ADS fees and charges is deducted from the funds being distributed. In the case of (i) distributions other than cash and (ii) the ADS service fee, holders as of the ADS record date will be invoiced for the amount of the ADS fees and charges and such ADS fees and charges may be deducted from distributions made to holders of ADSs. For ADSs held through DTC, the ADS fees and charges for distributions other than cash and the ADS service fee may be deducted from distributions made through DTC, and may be charged to the DTC participants in accordance with the procedures and practices prescribed by DTC and the DTC participants in turn charge the amount of such ADS fees and charges to the beneficial owners for whom they hold ADSs. In the case of (i) registration of ADS transfers, the ADS transfer fee will be payable by the ADS Holder whose ADSs are being transferred or by the person to whom the ADSs are transferred, and (ii) conversion of ADSs of one series for ADSs of another series, the ADS conversion fee will be payable by the Holder whose ADSs are converted or by the person to whom the converted ADSs are delivered.

In the event of refusal to pay the depositary bank fees, the depositary bank may, under the terms of the deposit agreement, refuse the requested service until payment is received or may set off the amount of the depositary bank fees from any distribution to be made to the ADS holder. Certain depositary fees and charges (such as the ADS services fee) may become payable shortly after the purchase of ADSs. Note that the fees and charges you may be required to pay may vary over time and may be changed by us and by the depositary bank. You will receive prior notice of such changes. The depositary bank may reimburse us for certain expenses incurred by us in respect of the ADR program, by making available a portion of the ADS fees charged in respect of the ADR program or otherwise, upon such terms and conditions as we and the depositary bank agree from time to time.

PART II

ITEM 13. DEFAULTS, DIVIDEND ARREARAGES AND DELINQUENCIES

Not applicable.

ITEM 14. MATERIAL MODIFICATIONS TO THE RIGHTS OF SECURITY HOLDERS AND USE OF PROCEEDS

Not applicable.

ITEM 15. CONTROLS AND PROCEDURES

A. Disclosure Controls and Procedures

We maintain "disclosure controls and procedures" as defined in Rule 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, that are designed to ensure that information required to be disclosed by us in the reports that are filed or submitted under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms, and is accumulated and communicated to the management of our company, including our Chief Executive Officer and Chief Financial Officer, as appropriately to allow timely decisions regarding required disclosure. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance of achieving their control objectives. Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of the design and operation of our disclosure controls and procedures pursuant to Exchange Act Rule 13a-15(b) as of December 31, 2021. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of December 31, 2021, our disclosure controls and procedures were not effective at the reasonable assurance level due to the material weakness described below.

B. Management's annual report on internal control over financial reporting.

In accordance with the requirements of section 404 of Sarbanes-Oxley, the following report is provided by management in respect of the Company's internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)):

- Management is responsible for establishing and maintaining adequate internal control over financial reporting for the Group. Internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with UK-adopted International Financial Reporting Standards, which audited consolidated financial statements also fully comply with International Financial Reporting Standards as issued by the International Accounting Standards Board;
- Management, including our Chief Executive Officer and Chief Financial Officer, conducted an evaluation of the effectiveness of internal control over financial reporting based on the framework in Internal Control – Integrated Framework (2013 Framework) issued by the Committee of Sponsoring Organizations of the Treadway Commission;
- Management has evaluated the effectiveness of internal control over financial reporting, as at 31 December 2021 and has concluded that such internal control over financial reporting was ineffective due to the material weakness described below. A material weakness is a significant deficiency, or a combination of significant deficiencies, in internal control over financial reporting such that it is reasonably possible that a material misstatement of the annual or interim consolidated financial statements will not be prevented or detected on a timely basis.

In connection with the preparation of our consolidated financial statements of the Group presented as of December 31, 2021 and 2020 and for the years ended December 31, 2021, 2020 and 2019, we concluded that there was a material weakness related to our risk assessment process over the design and implementation of our management review controls over the valuation of financial instruments, the completeness and accuracy of related sensitivity disclosures, the valuation of share based payment liabilities and completeness and the accuracy of the tax provision. There was insufficient precision in and documentation of the performance of such review controls resulting in controls not being designed in a way to sufficiently address the level of aggregation and criteria for investigation. Additionally, management did not completely identify the information used in the control and did not design sufficient controls to address the relevance and reliability of such information. We concluded that a material weakness related to insufficient precision and documentation of management review controls over the valuation of financial instruments and the accuracy of the tax provision existed as of December 31, 2020, which material weakness formed a part of the material weakness described above and continued to exist at December 31, 2021. This material weakness resulted in immaterial misstatements in the valuation of financial instruments that were corrected prior to the issuance of the Company's financial statements. Furthermore, a reasonable possibility exists that material misstatements in the Company's financial statements will not be prevented or detected on a timely basis.

C. Attestation Report of the Registered Public Accounting Firm

KPMG, LLP, the independent registered public accounting firm who audited the consolidated financial statements of the Group as of December 31, 2021 and 2020 and for the years ended December 31, 2021, 2020 and 2019, has issued an attestation report expressing an adverse opinion on the Group's internal control over financial reporting as stated in their report below.

Attestation Report of the Independent Registered Public Accounting Firm

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and Board of Directors

PureTech Health PLC:

Opinion on Internal Control Over Financial Reporting

We have audited PureTech Health PLC's and subsidiaries' (the Group) internal control over financial reporting as of December 31, 2021, based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. In our opinion, because of the effect of the material weakness, described below, on the achievement of the objectives of the control criteria, the Group has not maintained effective internal control over financial

reporting as of December 31, 2021, based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated statements of financial position of the Group as of December 31, 2021 and 2020, the related consolidated statements of comprehensive income / (loss), changes in equity, and cash flows for each of the years in the three-year period ended December 31, 2021 and the related notes (collectively, the consolidated financial statements) and our report dated 25 April 2022 expressed an unqualified opinion on those consolidated financial statements.

A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the group's annual or interim financial statements will not be prevented or detected on a timely basis. A material weakness related to the risk assessment process over the design and implementation of management review controls over the valuation of financial instruments, completeness and accuracy of related sensitivity disclosures, the valuation of share based payment liabilities and the completeness and accuracy of the tax provision, as well as the complete identification of information used in the control and the design of sufficient controls to address the relevance and reliability of such information. The material weakness was considered in determining the nature, timing, and extent of audit tests applied in our audit of the 2021 consolidated financial statements, and this report does not affect our report on those consolidated financial statements.

Basis for Opinion

The Group's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's annual report on internal control over financial reporting. Our responsibility is to express an opinion on the Group's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Group in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audit also included performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ KPMG LLP
KPMG LLP

London, United Kingdom

25 April, 2022

D. Changes in Internal Control Over Financial Reporting

Other than the ongoing remediation plan for a material weakness discussed below, and the remediation of a previously disclosed material weaknesses as discussed below, there were no changes in our internal control over financial reporting (as defined in Exchange Act Rule 13a-15(f)) that occurred during the period covered by this annual report on Form 20-F that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Ongoing Remediation Plan

Throughout 2021 and the beginning of 2022, management, under the oversight of the Audit Committee, has been actively engaged in the implementation of measures designed to address the material weaknesses in management review controls described in Part B above. During the year ended December 31, 2021, the Company took certain steps in its remediation plan, including (i) designing and documenting management review controls to address the level of aggregation and criteria for investigation, and (ii) implementing more robust procedures over the documentation of the performance of these management review controls. The Company has made progress toward remediation and will continue to implement its remediation plan for the ongoing material weaknesses in internal control over financial reporting described in Part B above. The material weaknesses will not

be considered remediated until the applicable controls operate for a sufficient period of time and management has concluded, through testing, that the controls are operating effectively. As we continue to work to improve our internal control over financial reporting, we may determine that additional measures to address control deficiencies or modifications to the remediation plan are necessary. It cannot be assured, however, when we will remediate such material weaknesses, nor can we be certain whether additional actions will be required. Moreover, it cannot be assured that additional material weaknesses will not arise in the future.

Remediation of Prior Material Weakness

In connection with the audit of our consolidated financial statements as of and for the year ended December 31, 2020, we identified a material weakness related to a lack of segregation of duties with regard to uploading and posting journal entries in our previous ERP system. We deployed a new ERP system that went live on January 1, 2021, and implemented automated internal controls, a self-assessment and further strengthening of our system of internal controls based on the COSO framework to address the risks associated with the new ERP system. As of December 31, 2021, we have concluded that this material weakness has been remediated.

ITEM 16. RESERVED

ITEM 16A. AUDIT COMMITTEE FINANCIAL EXPERT

Our board of directors has determined that Christopher Viehbacher, an independent director (under the standards set forth in Nasdaq Stock Market Rule 5605(a)(2) and Rule 10A-3 under the Exchange Act) and member of our audit committee, is an audit committee financial expert.

ITEM 16B. CODE OF ETHICS

Our Board of Directors has adopted a written Code of Business Conduct and Ethics. The Code of Business Conduct and Ethics applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. A current copy of the code is posted on the investor relations section of our website, which is located at www.puretechhealth.com.The information contained on, or that can be accessed through, our website is not and shall not be deemed to be part of this annual report on Form 20-F. Our Code of Business Conduct and Ethics is intended to meet the definition of "code of ethics" under Item 16B of Form 20-F under the Exchange Act. We will disclose on our website any amendment to, or waiver from, a provision of our Code of Business Conduct and Ethics that applies to our directors or executive officers to the extent required under the rules of the SEC or Nasdaq.

ITEM 16C. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The following table sets forth the aggregate fees for professional services rendered by KPMG LLP in 2021 and 2020.

For the years ending December 31,	**2021 $000s**	2020 $000s
Audit fees	**3,434**	**1,926**
Audit-related fees	**—**	—
Tax fees	**—**	—
All other fees*	**—**	173
Total	**3,434**	2,099

* 2020 - $173.2 thousand relates to capital market services in the UK with regard to obtaining shareholder approval for the sale of Karuna shares

The information set forth or referenced under the heading "Report of the Audit Committee" on pages 128 to 130 of PureTech's "Annual Report and Accounts 2021" included as exhibit 15.1 to this annual report on Form 20-F is incorporated by reference.

The Audit Committee evaluates the qualifications, independence and performance of the independent auditor as well as pre-approves and reviews the audit and non-audit services to be performed by the independent auditor. In accordance with this policy, all services performed by and fees paid to KPMG LLP were approved by the Audit Committee.

ITEM 16D. EXEMPTIONS FROM THE LISTING STANDARDS FOR AUDIT COMMITTEES

Not applicable.

ITEM 16E. PURCHASES OF EQUITY SECURITIES BY THE ISSUER AND AFFILIATED PURCHASERS

Not applicable.

ITEM 16F. CHANGE IN REGISTRANT'S CERTIFYING ACCOUNTANT

Not applicable.

ITEM 16G. CORPORATE GOVERNANCE

We qualify as a foreign private issuer. The Listing Rules of the Nasdaq Stock Market include certain accommodations in the corporate governance requirements that allow foreign private issuers to follow "home country" corporate governance practices in lieu of the otherwise applicable corporate governance standards of the Nasdaq Stock Market. We rely on the certain exemptions for foreign private issuers and follow United Kingdom corporate governance practices in lieu of the Nasdaq corporate governance rules.

A summary of the significant ways in which the Company's corporate governance practices differ from those followed by U.S. domestic companies under the Nasdaq corporate governance rules is set forth below.

The information (including tabular data) set forth or referenced under the headings "Directors' Report for the year ended 31 December 2021—Compliance with the UK Corporate Governance Code" (first paragraph only) on page 124 of PureTech's "Annual Report and Accounts 2021" included as exhibit 15.1 to this annual report on Form 20-F is incorporated by reference.

The Sarbanes-Oxley Act of 2002, as well as related rules subsequently implemented by the SEC, requires foreign private issuers, including our company, to comply with various corporate governance practices. In addition, Nasdaq rules provide that foreign private issuers may follow home country practice in lieu of the Nasdaq corporate governance standards, subject to certain exceptions and except to the extent that such exemptions would be contrary to U.S. federal securities laws. The home country practices followed by our company in lieu of Nasdaq rules are described below:

- We do not follow Nasdaq's quorum requirements applicable to meetings of shareholders. Such quorum requirements are not required under U.K. law. In accordance with generally accepted business practice, our articles of association provide alternative quorum requirements that are generally applicable to meetings of shareholders.
- We do not follow Nasdaq's requirements that independent directors have regularly scheduled meetings at which only independent directors are present. Under U.K. law the independent directors may choose to meet in executive session at their discretion.
- We do not follow Nasdaq's requirements to seek shareholder approval for the implementation of certain equity compensation plans, the issuances of ordinary shares under such plans, or in connection with certain private placements of equity securities. In accordance with U.K. law, we are not required to seek shareholder approval to allot ordinary shares in connection with applicable employee equity compensation plans. We will follow U.K. law with respect to any requirement to obtain shareholder approval prior to any private placements of equity securities

Other than as discussed above, we intend to comply with the rules generally applicable to U.S. domestic companies listed on Nasdaq. We may in the future, however, decide to use other foreign private issuer exemptions with respect to some or all of the other Nasdaq rules. Following our home country governance practices may provide less protection than is accorded to investors under Nasdaq rules applicable to domestic issuers.

We intend to take all actions necessary for us to maintain compliance as a foreign private issuer under the applicable corporate governance requirements of the Sarbanes-Oxley Act of 2002, the rules adopted by the SEC and Nasdaq's listing standards.

Because we are a foreign private issuer, our directors and senior management are not subject to short-swing profit and insider trading reporting obligations under Section 16 of the U.S. Securities Exchange Act of 1934, as amended, or Exchange Act. They are, however, subject to the obligations to report changes in share ownership under Section 13 of the Exchange Act and related SEC rules.

ITEM 16H. MINE SAFETY DISCLOSURE

Not applicable.

ITEM 16I. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

PART III

ITEM 17. FINANCIAL STATEMENTS

We have elected to furnish financial statements and related information specified in Item 18.

ITEM 18. FINANCIAL STATEMENTS

See pages F-1 through F-56 of this annual report.

Gelesis, Inc. was deemed a significant equity investee under Rule 3-09 of Regulation S-X for the fiscal year ended December 31, 2021. As such, the financial statements and related notes of Gelesis, Inc. required by Rule 3-09 of Regulation S-X are provided as Exhibit 99.1 to this annual report.

ITEM 19. EXHIBITS

The Exhibits listed in the Exhibit Index at the end of this annual report are filed as Exhibits to this annual report.

EXHIBIT NUMBER	DESCRIPTION OF EXHIBIT	INCORPORATION BY REFERENCE			
		Schedule/Form	File Number	Exhibit	File Date
1.1	Articles of Association of the Registrant	20FR12B	001-39670	3.1	10/27/2020
2.1	Deposit Agreement dated as of November 11, 2020, by and among the Registrant, Citibank N.A. and the holders of beneficial holders of American Depository Shares thereunder	20-F	001-39670	2.1	4/15/2021
2.2	Form of American Depository Receipt (included in Exhibit 2.1)				
2.3*	Description of Registrant's Securities				
4.1#	Performance Share Plan	20FR12B	001-39670	10.1	10/27/2020
4.2#	Form of Incentive Stock Option Deed of Agreement under the Performance Share Plan	20FR12B	001-39670	10.2	10/27/2020
4.3#	Form of Nonstatutory Stock Option Deed of Agreement under the Performance Share Plan	20FR12B	001-39670	10.3	10/27/2020
4.4#	Form of Restricted Share Units Agreement under the Performance Share Plan	20FR12B	001-39670	10.4	10/27/2020
4.5	Lease Agreement, dated as of August 10, 2018, by and between the Registrant and RBK I TENANT, LLC	20FR12B	001-39670	10.5	10/27/2020
4.6#	Form of Deed of Indemnity between the Registrant and each of its directors and executive officers	20FR12B	001-39670	10.6	10/27/2020
4.7†	Asset Purchase Agreement, dated July 15, 2019, by and between Auspex Pharmaceuticals, Inc. and PureTech Health LLC	20FR12B	001-39670	10.7	10/27/2020
4.8†	Royalty Agreement, dated as of July 23, 2013, by and between PureTech Ventures LLC and Follica, Incorporated	20FR12B	001-39670	10.8	10/27/2020
4.9	Royalty and Sublicense Income Agreement, dated as of December 18, 2009, as amended on June 28, 2012, by and between PureTech Ventures LLC, Gelesis, Inc. and Gelesis LP	20FR12B	001-39670	10.9	10/27/2020
4.10†	Exclusive Patent License Agreement, dated as of March 4, 2011, as amended on February 1, 2013 and February 25, 2015, by and between PureTech Ventures LLC and Karuna Pharmaceuticals, Inc.	20FR12B	001-39670	10.10	10/27/2020
4.11†	Ninth Amended and Restated Registration Rights Agreement, dated December 5, 2019, between Gelesis, Inc. and the stockholders party thereto	20FR12B	001-39670	10.12	10/27/2020
4.12†	Fifth Amended and Restated Investors' Rights Agreement, dated July 19, 2019, by and among Follica, Incorporated and the investors party thereto	20FR12B	001-39670	10.17	10/27/2020
4.13†	Fifth Amended and Restated Right of First Refusal and Co-Sale Agreement, dated July 19, 2019, by and among Follica, Incorporated and the investors and key holders party thereto	20FR12B	001-39670	10.18	10/27/2020
4.14†	Fifth Amended and Restated Voting Agreement, dated July 19, 2019, between Follica, Incorporated and the stockholders party thereto	20FR12B	001-39670	10.19	10/27/2020
4.15†	Amended and Restated Investors' Rights Agreement, dated June 30, 2020, by and between Vor Biopharma Inc. and the investors party thereto	20FR12B	001-39670	10.21	10/27/2020
4.16†	Voting Agreement, dated April 9, 2019, between Sonde Health, Inc. and the stockholders party thereto	20FR12B	001-39670	10.23	10/27/2020

EXHIBIT NUMBER	DESCRIPTION OF EXHIBIT	INCORPORATION BY REFERENCE			
		Schedule/Form	File Number	Exhibit	File Date
4.17†	Investors' Rights Agreement, dated April 9, 2019, by and between Sonde Health, Inc. and the investors party thereto	20FR12B	001-39670	10.24	10/27/2020
4.18†	Right of First Refusal and Co-Sale Agreement, dated April 9, 2019, by and between Sonde Health, Inc. and the investors and key holders party thereto	20FR12B	001-39670	10.25	10/27/2020
4.19†	Voting Agreement, dated December 18, 2017, between Entrega, Inc. and the stockholders party thereto	20FR12B	001-39670	10.26	10/27/2020
4.20†	Investors' Rights Agreement, dated December 18, 2017, by and between Entrega, Inc. and the investors party thereto	20FR12B	001-39670	10.27	10/27/2020
4.21†	Right of First Refusal and Co-Sale Agreement, dated December 18, 2017, by and between Entrega, Inc. and the investors and key holders party thereto	20FR12B	001-39670	10.28	10/27/2020
4.22†	Research and License Agreement, dated March 6, 2017, as amended on April 23, 2018, August 6, 2018, May 31, 2019, and July 22, 2020 between PureTech LYT, Inc. and New York University	20FR12B	001-39670	10.29	10/27/2020
4.23+	Amended and Restated Registration and Stockholder Rights Agreement, dated January 13, 2022, by and among Gelesis Holdings, Inc. and the stockholders party thereto	8-K	001-39362	10.2	1/20//2022
4.24*†	Third Amended and Restated Investors' Rights Agreement, dated May 25, 2021, by and among Akili Interactive Labs, Inc. and the investors party thereto				
4.25*†	Amended and Restated First Refusal and Co-Sale Agreement, dated May 25, 2021, by and among Akili Interactive Labs, Inc. and the investors party thereto				
4.26*†	Amended and Restated Investors' Rights Agreement, dated July 15, 2021, by and among Vedanta Biosciences, Inc. and the investors party thereto				
4.27+	Business Combination Agreement, dated as of July 19, 2021, by and among Gelesis, Inc., Capstar Special Purpose Acquisition Corp., and CPSR Gelesis Merger Sub, Inc.	S-4/A	333-258693	2.1	12/23/2021
4.28	Amendment to Business Combination Agreement, dated as of November 18, 2021, by and among Gelesis, Inc., Capstar Special Purpose Acquisition Corp., and CPSR Gelesis Merger Sub, Inc.	S-4/A	333-258693	2.2	12/23/2021
4.29	Second Amendment to Business Combination Agreement, dated as of December 30, 2021, by and among Gelesis, Inc., Capstar Special Purpose Acquisition Corp., and CPSR Gelesis Merger Sub, Inc.	8-K	001-39362	2.1	1/3/2022
4.30	Form of Subscription Agreement	S-4	333-258693	10.2	8/10/2021
4.31	Backstop Agreement, dated as of December 30, 2021, by and among Capstar Special Purpose Acquisition Corp. and the other parties listed as Purchasers party thereto	8-K	001-39362	10.1	1/3/2022

EXHIBIT NUMBER	DESCRIPTION OF EXHIBIT	INCORPORATION BY REFERENCE			
		Schedule/Form	File Number	Exhibit	File Date
4.32+	Agreement and Plan of Merger, dated January 26, 2022, between Akili Interative Labs, Inc., Social Capital Suvretta Holdings Corp. I, and Karibu Merger Sub, Inc.	8-K/A	001-40558	2.1	1/27/2022
8.1	Subsidiaries of PureTech Health plc	20FR12B	001-39670	21.1	10/27/2020
11.1	Code of Business Conduct and Ethics	20-F	001-39670	11.1	4/15/2021
12.1*	Certification by the Principal Executive Officer Pursuant to Securities Exchange Act Rules 13a-14(a) and 15d-14(a) as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				
12.2*	Certification of Principal Financial Officer Pursuant to Securities Exchange Act Rules 13a-14(a) and 15d-14(a) as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				
13.1***	Certification of Chief Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				
13.2***	Certification of Chief Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				
15.1**	Annual Report and Accounts 2021				
99.1*	Gelesis, Inc. and subsidiaries Consolidated Financial Statements as of and for the years ended December 31, 2021 and 2020				
101.INS*	XBRL Instance Document – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.				
101.SCH*	Inline XBRL Taxonomy Extension Schema Document				
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document				
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document				
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document				
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document				
104*	Cover Page Interactive Data File - the cover page interactive data file does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.				

* Filed herewith.
** Certain of the information included within Exhibit 15.1, which is provided pursuant to Rule 12b-23(a) of the Securities Exchange Act of 1934, as amended, is incorporated by reference in this annual report on Form 20-F, as specified elsewhere in this annual report on Form 20-F. With the exception of the items and pages so specified, the "Annual Report and Accounts 2021" is not deemed to be filed as part of this annual report on Form 20-F.
*** Furnished herewith.
# Indicates a management contract or any compensatory plan, contract or arrangement.
† Portions of this exhibit (indicated by asterisks) have been omitted because either (A) they are both (i) not material and (ii) would likely cause competitive harm if publicly disclosed., or (B) they are both (i) not material and (ii) the type of information that the Registrant customarily and actually treats as private or confidential, as applicable. The Registrant agrees to furnish an unredacted copy of this exhibit to the Securities and Exchange Commission upon request.
+ Schedules and exhibits to this exhibit omitted. The Registrant agrees to furnish supplementally a copy of any omitted schedule or exhibit to the SEC upon request.

SIGNATURES

The registrant hereby certifies that it meets all of the requirements for filing on Form 20-F and that it has duly caused and authorized the undersigned to sign this annual report on its behalf.

Date: April 25, 2022

PURETECH HEALTH PLC

By: /s/ Daphne Zohar
Name: Daphne Zohar
Title: Chief Executive Officer

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Shareholders and Board of Directors

PureTech Health PLC

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated statements of financial position of PureTech Health PLC and subsidiaries (the Group) as of December 31, 2021 and 2020, the related consolidated statements of comprehensive income / (loss), changes in equity, and cash flows for each of the years in the three-year period ended December 31, 2021 and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Group as of December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2021, in conformity with International Financial Reporting Standards (IFRSs) as issued by the International Accounting Standards Board and international accounting standards in conformity with the requirements of the UK-adopted IFRSs.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Group's internal control over financial reporting as of December 31, 2021 based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission , and our report dated 25 April 2022 expressed an adverse opinion on the effectiveness of the Group's internal control over financial reporting.

Basis for Opinion

These consolidated financial statements are the responsibility of the Group's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Group in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

The critical audit matters communicated below are matters arising from the current period audit of the consolidated financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

Identification and classification of newly issued financial instruments

As discussed in Notes 15 and 17 to the consolidated financial statements, Vedanta issued $68.4 million preferred shares and Sonde Health issued $4.3 million convertible notes during the year. Upon issuance, the Group assesses the terms of the instruments to determine if they meet the criteria to be liability of equity classified.

We identified the classification of the Vedanta preferred shares and Sonde Health convertible notes and the identification and classification of embedded derivatives within those financial instruments as a critical audit matter. Significant auditor judgement was required to assess whether the financial instruments meet the criteria to be liability or equity classified, including assessing if the agreement contains embedded derivatives and the classification of those embedded derivatives.

The following are the primary procedures we performed to address this critical audit matter:

We evaluated the design of a certain internal control related to the identification and classification for each new financial instrument and any embedded derivatives.

We inspected the terms of the agreements and features of the instruments and assessed these against the requirements of the relevant accounting standards to identify:

- whether the financial instruments should be classified as liability or equity
- whether the financial instruments contained embedded derivatives
- whether any embedded derivatives should be classified as equity or liability

Valuation of certain Level 3 financial assets and liabilities

As discussed in Notes 1 and 16 to the consolidated financial statements, the Group's Level 3 financial assets and liabilities were recorded at fair values of $254.7 million and $184.7 million respectively at December 31, 2021. The Group estimates the fair values of the Level 3 financial assets and liabilities by utilising various valuation techniques with one or more significant unobservable inputs

We identified the assessment of the fair value of certain Level 3 financial assets and liabilities as a critical audit matter. Subjective and complex auditor judgement, including specialized skills and knowledge, was required to assess the enterprise value which includes significant assumptions, including the likelihood of projected regulatory approval or probability of success, term to exit, probability of exit scenarios and discount rate.

The following are the primary procedures we performed to address this critical audit matter:

We evaluated the reasonableness of the likelihood of projected regulatory approval or probability of success used by comparing them to publicly available industry data.

We evaluated the reasonableness of the probability of exit scenarios and term to exit by inspecting strategic plans and public announcements and comparing against previous year assumptions and assessing if any changes were reasonable in the context of recent developments at the company.

We involved valuation professionals with specialized skills and knowledge who assisted us in:

-
- assessing the enterprise value, where derived from a market approach by comparing changes in the enterprise value to changes in the market value of comparable listed companies
- evaluating the reasonableness of the discount rates when an income approach is used by comparing the key inputs of the discount rates to publicly available market data information and assessing business changes in the company in the current year.

/s/ KPMG LLP
KPMG LLP
London, United Kingdom
25 April, 2022

We have served as the Group's auditor since 2015.

Consolidated Statements of Comprehensive Income/(Loss)

For the years ended December 31

	Note	**2021 $000s**	2020 $000s	2019 $000s
Contract revenue	3	**9,979**	8,341	8,688
Grant revenue	3	**7,409**	3,427	1,119
Total revenue		**17,388**	11,768	9,807
Operating expenses:				
General and administrative expenses	7	**(57,199)**	(49,440)	(59,358)
Research and development expenses	7	**(110,471)**	(81,859)	(85,848)
Operating income/(loss)		**(150,282)**	(119,531)	(135,399)
Other income/(expense):				
Gain on deconsolidation	5	**—**	—	264,409
Gain/(loss) on investments held at fair value	5	**179,316**	232,674	(37,863)
Loss realized on sale of investments	5	**(20,925)**	(54,976)	—
Gain on loss of significant influence	6	**—**	—	445,582
Other income/(expense)	6, 21	**1,592**	1,035	39
Other income/(expense)		**159,983**	178,732	672,167
Finance income/(costs):				
Finance income	9	**214**	1,183	4,362
Finance costs – contractual	9	**(4,771)**	(2,946)	(2,576)
Finance income/(costs) – fair value accounting	9	**9,606**	(4,351)	(46,475)
Finance income/(costs) – subsidiary preferred shares	9	**—**	—	(1,458)
Net finance income/(costs)		**5,050**	(6,115)	(46,147)
Share of net income/(loss) of associates accounted for using the equity method	6	**(73,703)**	(34,117)	30,791
Impairment of investment in associate	6	**—**	—	(42,938)
Income/(loss) before taxes		**(58,953)**	18,969	478,474
Taxation	25	**(3,756)**	(14,401)	(112,409)
Income/(Loss) for the year		**(62,709)**	4,568	366,065
Other comprehensive income/(loss):				
Items that are or may be reclassified as profit or loss				
Foreign currency translation differences		**—**	469	(10)
Total other comprehensive income/(loss)		**—**	469	(10)
Total comprehensive income/(loss) for the year		**(62,709)**	5,037	366,055
Income/(loss) attributable to:				
Owners of the Company		**(60,558)**	5,985	421,144
Non-controlling interests	18	**(2,151)**	(1,417)	(55,079)
		(62,709)	4,568	366,065
Comprehensive income/(loss) attributable to:				
Owners of the Company		**(60,558)**	6,454	421,134
Non-controlling interests	18	**(2,151)**	(1,417)	(55,079)
		(62,709)	5,037	366,055
		$	$	$
Earnings/(loss) per share:				
Basic earnings/(loss) per share	10	**(0.21)**	0.02	1.49
Diluted earnings/(loss) per share	10	**(0.21)**	0.02	1.44

The accompanying notes are an integral part of these financial statements.

Consolidated Statements of Financial Position

As of December 31,

	Note	**2021 $000s**	2020 $000s
Assets			
Non-current assets			
Property and equipment, net	11	**26,771**	22,777
Right of use asset, net	21	**17,166**	20,098
Intangible assets, net	12	**987**	899
Investments held at fair value	5, 16	**397,179**	530,161
Investments in associates	6	**—**	—
Lease receivable – long-term	21	**1,285**	1,700
Other non-current assets		**810**	11
Total non-current assets		**444,197**	575,645
Current assets			
Trade and other receivables	22	**3,174**	2,558
Income tax receivable	25	**4,514**	—
Prepaid expenses		**10,755**	5,405
Lease receivable – short-term	21	**415**	381
Other financial assets	13, 22	**2,124**	2,124
Short-term note from associate	16	**15,120**	—
Cash and cash equivalents	22	**465,708**	403,881
Total current assets		**501,809**	414,348
Total assets		**946,006**	989,994
Equity and liabilities			
Equity			
Share capital	14	**5,444**	5,417
Share premium	14	**289,303**	288,978
Merger reserve	14	**138,506**	138,506
Translation reserve	14	**469**	469
Other reserve	14	**(40,077)**	(24,050)
Retained earnings/(accumulated deficit)	14	**199,871**	260,429
Equity attributable to the owners of the Company		**593,515**	669,748
Non-controlling interests	14, 18	**(9,368)**	(16,209)
Total equity		**584,147**	653,539
Non-current liabilities			
Deferred tax liability	25	**89,765**	108,626
Lease liability, non-current	21	**29,040**	32,088
Long-term loan	20	**14,261**	14,818
Liability for share based awards	8	**2,659**	—
Total non-current liabilities		**135,725**	155,531
Current liabilities			
Deferred revenue	3	**65**	1,472
Lease liability, current	21	**3,950**	3,261
Trade and other payables	19	**35,817**	21,826
Subsidiary:			
Notes payable	16, 17	**3,916**	26,455
Warrant liability	16	**6,787**	8,206
Preferred shares	15, 16	**174,017**	118,972
Current portion of long-term loan	20	**857**	—
Other current liabilities		**726**	732
Total current liabilities		**226,135**	180,924
Total liabilities		**361,859**	336,455
Total equity and liabilities		**946,006**	989,994

Please refer to the accompanying Notes to the consolidated financial information. Registered number: 09582467.
The Consolidated Financial Statements were approved by the Board of Directors and authorized for issuance on April 25, 2022 and signed on its behalf by:

Daphne Zohar
Chief Executive Officer
April 25, 2022

The accompanying notes are an integral part of these financial statements.

Consolidated Statements of Changes in Equity

For the years ended December 31

	Share Capital									
	Shares	Amount $000s	Share premium $000s	Merger reserve $000s	Translation reserve $000s	Other reserve $000s	Retained earnings/ (accumulated deficit) $000s	Total Parent equity $000s	Non-controlling interests $000s	Total Equity $000s
Balance January 1, 2019	282,493,867	5,375	278,385	138,506	10	20,923	(166,693)	276,506	(108,535)	167,971
Net income/(loss)	—	—	—	—	—	—	421,144	421,144	(55,079)	366,065
Foreign currency exchange	—	—	—	—	(10)	—	—	(10)	—	(10)
Total comprehensive income/(loss) for the year	**—**	**—**	**—**	**—**	**(10)**	**—**	**421,144**	**421,134**	**(55,079)**	**366,055**
Deconsolidation of subsidiary	—	—	—	—	—	—	—	—	97,178	97,178
Subsidiary note conversion and changes in NCI ownership interest	—	—	—	—	—	(20,631)	—	(20,631)	23,049	2,418
Exercise of share-based awards	237,090	5	499	—	—	—	—	504	—	504
Purchase of subsidiary's non-controlling interest through issuance of shares	2,126,338	28	9,078	—	—	(33,145)	—	(24,039)	24,039	—
Revaluation of deferred tax assets related to share-based awards	—	—	—	—	—	3,061	—	3,061	—	3,061
Equity settled share-based payments	—	—	—	—	—	12,785	—	12,785	1,683	14,468
Vesting of restricted stock units (RSU)	513,324	—	—	—	—	(1,280)	—	(1,280)	—	(1,280)
Other	—	—	—	—	—	5	(7)	(2)	25	23
Balance December 31, 2019	**285,370,619**	**5,408**	**287,962**	**138,506**	**—**	**(18,282)**	**254,444**	**668,037**	**(17,639)**	**650,398**
Net income/(loss)	—	—	—	—	—	—	5,985	5,985	(1,417)	4,568
Foreign currency exchange	—	—	—	—	469	—	—	469	—	469
Total comprehensive income/(loss) for the year	**—**	**—**	**—**	**—**	**469**	**—**	**5,985**	**6,454**	**(1,417)**	**5,037**
Exercise of share-based awards	514,406	9	1,016	—	—	—	—	1,025	11	1,036
Revaluation of deferred tax assets related to share-based awards	—	—	—	—	—	(684)	—	(684)	—	(684)
Equity settled share-based awards	—	—	—	—	—	7,805	—	7,805	2,822	10,627
Settlement of restricted stock units	—	—	—	—	—	(12,888)	—	(12,888)	—	(12,888)
Other	—	—	—	—	—	—	—	—	13	13
As at December 31, 2020	**285,885,025**	**5,417**	**288,978**	**138,506**	**469**	**(24,050)**	**260,429**	**669,748**	**(16,209)**	**653,539**
Net income/(loss)	—	—	—	—	—	—	(60,558)	(60,558)	(2,151)	(62,709)
Foreign currency exchange	—	—	—	—	—	—	—	—	—	—
Total comprehensive income/(loss) for the year	**—**	**—**	**—**	**—**	**—**	**—**	**(60,558)**	**(60,558)**	**(2,151)**	**(62,709)**
Exercise of share-based awards	1,911,560	27	326	—	—	—	—	352	—	352
Revaluation of deferred tax assets related to share-based awards	—	—	—	—	—	615	—	615	—	615
Equity settled share-based awards	—	—	—	—	—	7,109	—	7,109	6,252	13,361
Settlement of restricted stock units	—	—	—	—	—	(10,749)	—	(10,749)	—	(10,749)
Reclassification of equity settled awards to liability awards	—	—	—	—	—	(6,773)	—	(6,773)	—	(6,773)
Vesting of share-based awards and net share exercise	—	—	—	—	—	(2,582)	—	(2,582)	—	(2,582)
Acquisition of subsidiary non-controlling interest	—	—	—	—	—	(9,636)	—	(9,636)	8,668	(968)
NCI exercise of share-based awards in subsidiaries	—	—	—	—	—	5,988	—	5,988	(5,922)	66
Distributions	—	—	—	—	—	—	—	—	(6)	(6)
Balance December 31, 2021	**287,796,585**	**5,444**	**289,303**	**138,506**	**469**	**(40,077)**	**199,871**	**593,515**	**(9,368)**	**584,147**

The accompanying notes are an integral part of these financial statements.

Consolidated Statements of Cash Flows

For the years ended December 31

	Note	**2021 $000s**	2020 $000s	2019 $000s
Cash flows from operating activities				
Income/(loss)		**(62,709)**	4,568	366,065
Adjustments to reconcile net operating loss to net cash used in operating activities:				
Non-cash items:				
Depreciation and amortization	11, 12	**7,287**	6,645	6,665
Impairment of investment in associate	6	**—**	—	42,938
Equity settled share-based payment expense	8	**13,950**	10,718	14,468
(Gain)/loss on investments held at fair value	5	**(179,316)**	(232,674)	37,863
Realized loss on sale of investments		**20,925**	54,976	—
Gain on deconsolidation	5	**—**	—	(264,409)
Gain on loss of significant influence	5	**—**	—	(445,582)
Loss on disposal of assets	11	**53**	66	140
Share of net (income)/loss of associates accounted for using the equity method	6	**73,703**	34,117	(30,791)
Fair value gain on derivative	6	**(800)**	—	—
Income taxes, net	25	**3,756**	14,402	112,077
Finance costs, net	9	**(5,050)**	6,114	46,229
Changes in operating assets and liabilities:				
Accounts receivable	22	**(617)**	(529)	747
Other financial assets	13	**—**	—	(48)
Prepaid expenses and other current assets		**(5,350)**	(3,371)	(25)
Deferred revenues	3	**(1,407)**	(5,223)	186
Trade and other payables	19	**8,338**	605	11,166
Other liabilities		**—**	(7)	3,002
Other		**(103)**	—	—
Income taxes paid		**(27,766)**	(20,737)	—
Interest received		**214**	1,155	3,648
Interest paid	20, 21	**(3,382)**	(2,651)	(2,495)
Net cash used in operating activities		**(158,274)**	(131,827)	(98,156)
Cash flows from investing activities:				
Purchase of property and equipment	11	**(5,571)**	(5,170)	(12,138)
Proceeds from sale of property and equipment		**30**	—	—
Purchases of intangible assets	12	**(90)**	(254)	(400)
Purchase of associate preferred shares held at fair value	5, 6	**—**	(10,000)	(13,670)
Purchase of investments held at fair value	5	**(500)**	(1,150)	(1,556)
Sale of investments held at fair value	5	**218,125**	350,586	9,294
Receipt of payment of sublease	21	**381**	350	191
Purchase of short-term note from associate	16	**(15,000)**	—	—
Purchase of convertible note	6	**—**	—	(6,480)
Cash derecognized upon loss of control over subsidiary		**—**	—	(16,036)
Purchases of short-term investments	22	**—**	—	(69,541)
Proceeds from maturity of short-term investments	22	**—**	30,116	173,995
Net cash provided by investing activities		**197,375**	364,478	63,659
Cash flows from financing activities:				
Receipt of PPP loan		**—**	68	—
Issuance of long term loan	20	**—**	14,720	—
Issuance of subsidiary preferred Shares	15	**37,610**	13,750	51,048
Proceeds from issuance of convertible notes in subsidiary	17	**2,215**	25,000	1,606
Payment of lease liability	21	**(3,375)**	(2,908)	(1,678)
Repayment of long-term debt		**—**	—	(178)
Distribution to Tal shareholders		**—**	—	(112)
Exercise of stock options		**352**	1,036	504
Settlement of RSU's		**(10,749)**	(12,888)	—
Vesting of restricted stock units and net share exercise		**(2,582)**	—	(1,280)
Issuance of shares to NCI in subsidiary	15	**66**	—	—
Issuance of warrants		**—**	92	—
Acquisition of a non-controlling Interest of a subsidiary		**(806)**	—	—
Other		**(5)**	—	—
Net cash provided by financing activities		**22,727**	38,869	49,910
Effect of exchange rates on cash and cash equivalents		**—**	—	(104)
Net increase in cash and cash equivalents		**61,827**	271,520	15,309
Cash and cash equivalents at beginning of year		**403,881**	132,360	117,051
Cash and cash equivalents at end of year		**465,708**	403,881	132,360
Supplemental disclosure of non-cash investment and financing activities:				
Purchase of non controlling interest in consideration for issuance of shares and options		**—**	—	9,106
Purchase of intangible asset and investment held at fair value in consideration for issuance of warrant liability and assumption of other long and short-term liabilities		**—**	—	15,894
Purchase of property, plant and equipment against trade and other payables	11	**1,841**	—	—
Leasehold improvements purchased through lease incentives (deducted from Right of Use Asset)	11	**1,010**	—	10,680
Conversion of subsidiary convertible note into preferred share liabilities	17	**25,797**	—	4,894
Conversion of subsidiary convertible note into subsidiary common stock (NCI)		**—**	—	2,418
Supplemental disclosure of cash paid for income taxes:				
Cash paid for income taxes		**27,766**	20,737	176

The accompanying notes are an integral part of these financial statements.

Notes to the Consolidated Financial Statements

1. Accounting policies

Description of Business

PureTech Health plc ("PureTech," the "Parent" or the "Company") is a public company incorporated, domiciled and registered in the United Kingdom ("UK"). The registered number is 09582467 and the registered address is 8th Floor, 20 Farringdon Street, London EC4A 4AB, United Kingdom.

PureTech's group financial statements consolidate those of the Company and its subsidiaries (together referred to as the "Group"). The Parent company financial statements present financial information about the Company as a separate entity and not about its Group.

The accounting policies set out below have, unless otherwise stated, been applied consistently to all periods presented in these group financial statements.

Basis of Presentation

The consolidated financial statements of the Group are presented as of December 31, 2021 and 2020, and for the years ended December 31, 2021, 2020 and 2019. The Group financial statements have been approved by the Directors on April 25, 2022, and are prepared in accordance with UK-adopted International Financial Reporting Standards (IFRSs). The Consolidated Financial Statements also comply fully with IFRSs as issued by the International Accounting Standards Board (IASB). UK-adopted IFRSs differs in certain respects from IFRS as issued by the IASB. However, the differences have no impact for the periods presented.

For presentation of the Consolidated Statements of Comprehensive Income/(Loss), the Company uses a classification based on the function of expenses, rather than based on their nature, as it is more representative of the format used for internal reporting and management purposes and is consistent with international practice.

Certain amounts in the Consolidated Financial Statements and accompanying notes may not add due to rounding. All percentages have been calculated using unrounded amounts.

Basis of Measurement

The consolidated financial statements are prepared on the historical cost basis except that the following assets and liabilities are stated at their fair value: investments held at fair value, short-term note from associate and liabilities classified as fair value through the profit or loss.

Use of Judgments and Estimates

In preparing these consolidated financial statements, management has made judgements, estimates and assumptions that affect the application of the Group's accounting policies and the reported amounts of assets, liabilities, income and expenses. Actual results may differ from these estimates. Estimates and underlying assumptions are reviewed on an on-going basis.

Significant estimation is applied in determining the following:

- Financial instruments valuations (Note 16): when estimating the fair value of subsidiary warrants, convertible notes and subsidiary preferred shares carried at fair value through profit and loss (FVTPL) as well as investments held at fair value, at initial recognition and upon subsequent measurement. This includes determining the appropriate valuation methodology and making certain estimates of the future earnings potential of the subsidiary businesses, appropriate discount rate, estimated time to exit, marketability and other industry and company specific risk factors. See Note 16 for the sensitivity analysis for key estimates used in these valuations.

Significant judgement is also applied in determining the following:

- Subsidiary preferred shares liability classification (Note 15): when determining the classification of financial instruments in terms of liability or equity. These judgements include an assessment of whether the financial instruments include any embedded derivative features, whether they include contractual obligations of the Group to deliver cash or other financial assets or to exchange financial assets or financial liabilities with another party, and whether that obligation will be settled by the Company exchanging a fixed amount of cash or other financial assets for a fixed number of its own equity instruments. Further information about these critical judgements and estimates is included below under Financial Instruments.
- When the power to control the subsidiaries exists (please refer to Notes 5 and 6 and accounting policy below Subsidiaries). This judgement includes an assessment of whether the Company has (i) power over the investee; (ii) exposure, or rights, to variable returns from its involvement with the investee; and (iii) the ability to use its power over the investee to affect the amount of the investor's returns. The Company considers among others its voting shares, shareholder agreements, ability to appoint board members, representation on the board, rights to appoint management, de facto control, investee dependence on the Company etc. If the power to control investees exists we consolidate the financial statements of such investee in the consolidated financial statements of the Group. Upon issuance of new shares in a subsidiary and a resulting change in any shareholders or governance agreements, the Group reassesses its ability to control the investee based on the revised board composition and revised subsidiary governance and management structure. When such new circumstances result in the Group losing its power to control the investee, the investee is deconsolidated.
- Whether the Company has significant influence over financial and operating policies of investees in order to determine if the Company should account for its investment as an associate based on IAS 28 or based on IFRS 9, Financial Instruments (please refer to Note 5). This judgement includes, among others, an assessment whether the Company has representation on the Board of Directors of the investee, whether the Company participates in the policy making processes of the investee, whether there is any interchange of managerial personnel, whether there is any essential technical information provided to the investee and if there are any transactions between the Company and the investee.
- Upon determining that the Company does have significant influence over the financial and operating policies of an investee, if the Company holds more than a single instrument issued by its equity-accounted investee, judgement is

required to determine whether the additional instrument forms part of the investment in the associate, which is accounted for under IAS 28 and scoped out of IFRS 9, or it is a separate financial instrument that falls in the scope of IFRS 9 (please refer to Notes 5 and 6). This judgement includes an assessment of the characteristics of the financial instrument of the investee held by the Company and whether such financial instrument provides access to returns underlying an ownership interest.

- Where the company has other investments in an equity accounted investee that are not accounted for under IAS 28, judgement is required in determining if such investments constitute Long-Term Interests for the purposes of IAS 28 (please refer to Notes 5 and 6). This determination is based on the individual facts and circumstances and characteristics of each investment, but is driven, among other factors, by the intention and likelihood to settle the instrument through redemption or repayment in the foreseeable future, and whether or not the investment is likely to be converted to common stock or other equity instruments (please also refer to accounting policy with regard to Investments in Associates below). When considering the individual facts and circumstances of the Group's investment in its associate's preferred stock in the manner described above, including the long-term nature of such investment, the ability of the Group to convert its preferred stock investment to an investment in common shares and the likelihood of such conversion, as well the fact that there is no planned redemption or other settlement of the preferred stock by the investee in the foreseeable future, we concluded that such investment is considered a Long Term Interest.

As of December 31, 2021, the Group had cash and cash equivalents of $465.7 million. Considering the Group's and the Company's financial position as of December 31, 2021, and its principal risks and opportunities, a going concern analysis has been prepared for at least the twelve-month period from the date of signing the Consolidated Financial Statements ("the going concern period") utilizing realistic scenarios and applying a severe but plausible downside scenario. Even under the downside scenario, the analysis demonstrates the Group and the Company continue to maintain sufficient liquidity headroom and continue to comply with all financial obligations. The Directors believe the Group and the Company is adequately resourced to continue in operational existence for at least the twelve-month period from the date of signing the Consolidated Financial Statements, irrespective of uncertainty regarding the duration and severity of the COVID-19 pandemic and the global macroeconomic impact of the pandemic. Accordingly, the Directors considered it appropriate to adopt the going concern basis of accounting in preparing the Consolidated Financial Statements and the PureTech Health plc Financial Statements.

Basis of consolidation

The consolidated financial information as of December 31, 2021 and 2020, and for each of the years ended December 31, 2021, 2020 and 2019, comprises an aggregation of financial information of the Company and the consolidated financial information of PureTech Health LLC ("PureTech LLC"). Intra-group balances and transactions, and any unrealized income and expenses arising from intra-group transactions, are eliminated.

Subsidiaries

As used in these financial statements, the term subsidiaries refers to entities that are controlled by the Group. Financial results of subsidiaries of the Group as of December 31, 2021, are reported within the Internal segment, Controlled Founded Entities segment or the Parent Company and Other section (please refer to Note 4). Under applicable accounting rules, the Group controls an entity when it is exposed to, or has the rights to, variable returns from its involvement with the entity and has the ability to affect those returns through its power over the entity. In assessing control, the Group takes into consideration potential voting rights, board representation, shareholders' agreements, ability to appoint Directors and management, de facto control and other related factors. The financial statements of subsidiaries are included in the consolidated financial statements from the date that control commences until the date that control ceases. Losses applicable to the non-controlling interests in a subsidiary are allocated to the non-controlling interests even if doing so causes the non-controlling interests to have a deficit balance.

A list of all current and former subsidiaries organized with respect to classification as of December 31, 2021, and the Group's total voting percentage, based on outstanding voting common and preferred shares as of December 31, 2021, 2020 and 2019, is outlined below. All current subsidiaries are domiciled within the United States and conduct business activities solely within the United States.

	Voting percentage at December 31, through the holdings in					
	2021		2020		2019	
Subsidiary	**Common**	**Preferred**	Common	Preferred	Common	Preferred
Subsidiary operating companies						
Alivio Therapeutics, Inc.[1,2]	**—**	**100.0**	—	91.9	—	91.9
Entrega, Inc. (indirectly held through Enlight)[1,2]	**—**	**77.3**	—	83.1	—	83.1
Follica, Incorporated[1,2,5]	**28.7**	**56.7**	28.7	56.7	28.7	56.7
PureTech LYT (formerly Ariya Therapeutics, Inc.)	**—**	**100.0**	—	100.0	—	100.0
PureTech LYT-100	**—**	**100.0**	—	100.0	—	100.0
PureTech Management, Inc.[3]	**100.0**	**—**	100.0	—	100.0	—
PureTech Health LLC[3]	**100.0**	**—**	100.0	—	100.0	—
Sonde Health, Inc.[1,2]	**—**	**51.8**	—	51.8	—	64.1
Vedanta Biosciences, Inc.[1,2]	**—**	**48.6**	—	59.3	—	61.8
Vedanta Biosciences Securities Corp. (indirectly held through Vedanta)[1,2]	**—**	**48.6**	—	59.3	—	61.8
Deconsolidated former subsidiary operating companies						
Akili Interactive Labs, Inc.[2]	**—**	**26.7**	—	41.9	—	41.9
Gelesis, Inc.[1,2,7,10]	**4.8**	**19.7**	4.9	20.2	5.7	20.2
Karuna Therapeutics, Inc.[1,2,8]	**5.6**	**—**	12.6	—	28.4	—

Vor Biopharma Inc.[1,2,9]	**8.6**	**—**	—	16.4	—	47.5
Nontrading holding companies						
Endra Holdings, LLC (held indirectly through Enlight)[2]	**86.0**	**—**	86.0	—	86.0	—
Ensof Holdings, LLC (held indirectly through Enlight)[2]	**86.0**	**—**	86.0	—	86.0	—
PureTech Securities Corp.[2]	**100.0**	**—**	100.0	—	100.0	—
PureTech Securities II Corp.[2]	**100.0**	**—**	100.0	—	—	—
Inactive subsidiaries						
Appeering, Inc.[2]	**—**	**100.0**	—	100.0	—	100.0
Commense Inc.[2,6]	**—**	**99.1**	—	99.1	—	99.1
Enlight Biosciences, LLC[2]	**86.0**	**—**	86.0	—	86.0	—
Ensof Biosystems, Inc. (held indirectly through Enlight)[1,2]	**57.7**	**28.3**	57.7	28.3	57.7	28.3
Knode Inc. (indirectly held through Enlight)[2]	**—**	**86.0**	—	86.0	—	86.0
Libra Biosciences, Inc.[2]	**—**	**100.0**	—	100.0	—	100.0
Mandara Sciences, LLC[2]	**98.3**	**—**	98.3	—	98.3	—
Tal Medical, Inc.[1,2]	**—**	**100.0**	—	100.0	—	100.0

1 The voting percentage is impacted by preferred shares that are classified as liabilities, which results in the ownership percentage not being the same as the ownership percentage used in allocations to non-controlling interests disclosed in Note 18. The allocation of losses/profits to the noncontrolling interest is based on the holdings of subordinated stock that provide ownership rights in the subsidiaries. The ownership of liability classified preferred shares are quantified in Note 15.

2 Registered address is Corporation Trust Center, 1209 Orange St., Wilmington, DE 19801, USA.

3 Registered address is 2711 Centerville Rd., Suite 400, Wilmington, DE 19808, USA.

4 The Company's interests in its subsidiaries are predominantly in the form of preferred shares, which have a liquidation preference over the common stock, are convertible into common stock at the holder's discretion or upon certain liquidity events, are entitled to one vote per share on all matters submitted to shareholders for a vote and entitled to receive dividends when and if declared. In the case of Enlight, Mandara and PureTech Health LLC, the holdings are membership interests in an LLC. The holders of common stock are entitled to one vote per share on all matters submitted to shareholders for a vote and entitled to receive dividends when and if declared.

5 On July 19, 2019, all of the outstanding notes, plus accrued interest, issued by Follica to PureTech converted into 15,216,214 shares of Series A-3 Preferred Shares and 12,777,287 shares of common share pursuant to a Series A-3 Note Conversion Agreement between Follica and the noteholders. Please refer to Note 16.

6 Commense turned inactive during 2019.

7 On July 1, 2019 PureTech lost control of Gelesis and Gelesis was deconsolidated from the Group's financial statements, resulting in only the profits and losses generated by Gelesis through the deconsolidation date being included in the Group's Consolidated Statement of Comprehensive Income/(Loss). See Notes 5 and 6 for further details about the accounting for the investments in Gelesis subsequent to deconsolidation.

8 On March 15, 2019, PureTech lost control of Karuna, Karuna was deconsolidated from the Group's financial statements and is no longer considered a subsidiary. This results in only the profits and losses generated by Karuna through the deconsolidation date being included in the Group's Consolidated Statement of Comprehensive Income/(Loss).. See Note 5 for further details about the accounting for the investment in Karuna subsequent to deconsolidation.

9 On February 12, 2019, PureTech lost control of Vor, Vor was deconsolidated from the Group's financial statements and is no longer considered a subsidiary. This results in only the profits and losses generated by Vor through the deconsolidation date being included in the Group's Consolidated Statement of Comprehensive Income/(Loss) .See Note 5 for further details about the accounting for the investment in Vor subsequent to deconsolidation.

10 See note 26 regarding Gelesis business combination with Capstar Special Purpose Acquisition Corp after balance sheet date and the Group's ownership rights in the new combined public entity.

Change in subsidiary ownership and loss of control

Changes in the Group's interest in a subsidiary that do not result in a loss of control are accounted for as equity transactions.

Where the Group loses control of a subsidiary, the assets and liabilities are derecognized along with any related non-controlling interest ("NCI"). Any interest retained in the former subsidiary is measured at fair value when control is lost. Any resulting gain or loss is recognized as profit or loss in the Consolidated Statements of Comprehensive Income/(Loss).

Associates

As used in these financial statements, the term associates are those entities in which the Group has no control but maintains significant influence over the financial and operating policies. Significant influence is presumed to exist when the Group holds between 20 and 50 percent of the voting power of an entity, unless it can be clearly demonstrated that this is not the case. The Group evaluates if it maintains significant influence over associates by assessing if the Group has lost the power to participate in the financial and operating policy decisions of the associate.

Application of the equity method to associates

Associates are accounted for using the equity method (equity accounted investees) and are initially recognized at cost, or if recognized upon deconsolidation they are initially recorded at fair value at the date of deconsolidation. The consolidated financial statements include the Group's share of the total comprehensive income and equity movements of equity accounted investees, from the date that significant influence commences until the date that significant influence ceases.

To the extent the Group holds interests in associates that are not providing access to returns underlying ownership interests, the instrument held by PureTech is accounted for in accordance with IFRS 9 as investments held at fair value.

When the Group's share of losses exceeds its equity method investment in the investee, losses are applied against Long-Term Interests, which are investments accounted for under IFRS 9. Investments are determined to be Long-Term Interests when they are long-term in nature and in substance they form part of the Group's net investment in that associate. This determination is impacted by many factors, among others, whether settlement by the investee through redemption or repayment is planned or likely in the foreseeable future, whether the investment can be converted and/or is likely to be converted to common stock or other equity instrument and other factors regarding the nature of the investment. Whilst this assessment is dependent on many specific facts and circumstances of each investment, typically conversion features whereby the investment is likely to convert to common stock or other equity instruments would point to the investment being a Long-Term Interest. Similarly, where the investment is not planned or likely to be settled through redemption or repayment in the foreseeable future, this would indicate that the investment is a Long-Term Interest. When the net investment in the associate, which includes the Group's investments in other long-term interests, is reduced to nil, recognition of further losses is discontinued except to the extent that the Group has incurred legal or constructive obligations or made payments on behalf of an investee.

The Group has also adopted the amendments to IAS 28 Investments in Associates that addresses the dual application of IAS 28 and IFRS 9 (see below) when equity method losses are applied against Long-Term Interests (LTI). The amendments provide the annual sequence in which both standards are to be applied in such a case. The Group has applied the equity method losses to the LTIs presented as part of Investments held at fair value subsequent to remeasuring such investments to their fair value at balance sheet date.

Financial Instruments

Classification

The Group classifies its financial assets in the following measurement categories:

- Those to be measured subsequently at fair value (either through other comprehensive income, or through profit or loss), and
- Those to be measured at amortized cost.

The classification depends on the Group's business model for managing the financial assets and the contractual terms of the cash flows.

For assets measured at fair value, gains and losses will are recorded in profit or loss. For investments in debt instruments, this will depend on the business model in which the investment is held. For investments in equity instruments that are not held for trading, this will depend on whether the Group has made an irrevocable election at the time of initial recognition to account for the equity investment at FVOCI. As of balance sheet dates, none of the Company's financial assets are accounted for as FVOCI.

Measurement

At initial recognition, the Group measures a financial asset at its fair value plus, in the case of a financial asset not at FVTPL, transaction costs that are directly attributable to the acquisition of the financial asset. Transaction costs of financial assets that are carried at FVTPL are expensed.

Impairment

The Group assesses on a forward-looking basis the expected credit losses associated with its debt instruments carried at amortized cost. The Group had no debt instruments carried at amortized cost as of balance sheet date. For trade receivables, the Group applies the simplified approach permitted by IFRS 9, which requires expected lifetime losses to be recognized from initial recognition of the receivables.

Financial Assets

The Group's financial assets consist of cash and cash equivalents, trade and other receivables, investments in equity securities, short-term note, other deposits and investments in associates' preferred shares. The Group's financial assets are classified into the following categories: investments held at fair value, trade and other receivables, short-term investments (if applicable) and cash and cash equivalents. The Group determines the classification of financial assets at initial recognition depending on the purpose for which the financial assets were acquired.

Investments held at fair value are investments in equity instruments that are not held for trading. Such investments consist of the Group's minority interest holdings where the Group has no significant influence or preferred share investments in the Group's associates that are not providing access to returns underlying ownership interests. These financial assets are initially measured at fair value and subsequently re-measured at fair value at each reporting date. The Company elects if the gain or loss will be recognized in Other Comprehensive Income/(Loss) or through profit and loss on an instrument by instrument basis. The Company has elected to record the changes in fair values for the financial assets falling under this category through profit and loss. Please refer to Note 5.

Changes in the fair value of financial assets at FVTPL are recognized in other income/(expense) in the Consolidated Statements of Comprehensive Income/(Loss) as applicable.

The short term note from an associate, since its contractual terms do not consist solely of cash flow payments of principal and interest on the principal amount outstanding, is initially and subsequently measured at fair value, with changes in fair value recognized through profit and loss.

Trade and other receivables are non-derivative financial assets with fixed and determinable payments that are not quoted on active markets. These financial assets are carried at the amounts expected to be received less any expected lifetime losses. Such losses are determined taking into account previous experience, credit rating and economic stability of counterparty and economic conditions. When a trade receivable is determined to be uncollectible, it is written off against the available provision. Trade and other receivables are included in current assets, unless maturities are greater than 12 months after the end of the reporting period.

Financial Liabilities

The Group's financial liabilities consist of trade and other payables, subsidiary notes payable, preferred shares, and warrant liability. Warrant liabilities are initially recognized at fair value. After initial recognition, these financial liabilities are re-measured at FVTPL using an appropriate valuation technique. Subsidiary notes payable without embedded derivatives are accounted for at amortized cost.

The majority of the Group's subsidiaries have preferred shares and notes payable with embedded derivatives, which are classified as current liabilities. When the Group has preferred shares and notes with embedded derivatives that qualify for bifurcation, the Group has elected to account for the entire instrument as FVTPL after determining under IFRS 9 that the instrument qualifies to be accounted for under such FVTPL method.

The Group derecognizes a financial liability when its contractual obligations are discharged, cancelled or expire.

Equity Instruments Issued by the Group

Financial instruments issued by the Group are treated as equity only to the extent that they meet the following two conditions, in accordance with IAS 32:

1. They include no contractual obligations upon the Group to deliver cash or other financial assets or to exchange financial assets or financial liabilities with another party under conditions that are potentially unfavorable to the Group; and
2. Where the instrument will or may be settled in the Group's own equity instruments, it is either a non-derivative that includes no obligation to deliver a variable number of the Group's own equity instruments or is a derivative that will be settled by the Group exchanging a fixed amount of cash or other financial assets for a fixed number of its own equity instruments.

To the extent that this definition is not met, the financial instrument is classified as a financial liability. Where the instrument so classified takes the legal form of the Group's own shares, the amounts presented in the Group's shareholders' equity exclude amounts in relation to those shares.

Changes in the fair value of liabilities at FVTPL are recognized in Net finance income (costs) in the Consolidated Statements of Comprehensive Income/(Loss) as applicable.

IFRS 15, Revenue from Contracts with Customers

The standard establishes a five-step principle-based approach for revenue recognition and is based on the concept of recognizing an amount that reflects the consideration for performance obligations only when they are satisfied and the control of goods or services is transferred.

The majority of the Group's contract revenue is generated from licenses and services, some of which are part of collaboration arrangements.

Management reviewed contracts where the Group received consideration in order to determine whether or not they should be accounted for in accordance with IFRS 15. To date, PureTech has entered into transactions that generate revenue and meet the scope of either IFRS 15 or IAS 20 Accounting for Government Grants. Contract revenue is recognized at either a point-in-time or over time, depending on the nature of the performance obligations.

The Group accounts for agreements that meet the definition of IFRS 15 by applying the following five step model:

- Identify the contract(s) with a customer – A contract with a customer exists when (i) the Group enters into an enforceable contract with a customer that defines each party's rights regarding the goods or services to be transferred and identifies the payment terms related to those goods or services, (ii) the contract has commercial substance and, (iii) the Group determines that collection of substantially all consideration for goods or services that are transferred is probable based on the customer's intent and ability to pay the promised consideration.
- Identify the performance obligations in the contract – Performance obligations promised in a contract are identified based on the goods or services that will be transferred to the customer that are both capable of being distinct, whereby the customer can benefit from the good or service either on its own or together with other resources that are readily available from third parties or from the Group, and are distinct in the context of the contract, whereby the transfer of the goods or services is separately identifiable from other promises in the contract.
- Determine the transaction price – The transaction price is determined based on the consideration to which the Group will be entitled in exchange for transferring goods or services to the customer. To the extent the transaction price includes variable consideration, the Group estimates the amount of variable consideration that should be included in the transaction price utilizing either the expected value method or the most likely amount method depending on the nature of the variable consideration. Variable consideration is included in the transaction price if, in the Group's judgement, it is probable that a significant future reversal of cumulative revenue under the contract will not occur.
- Allocate the transaction price to the performance obligations in the contract – If the contract contains a single performance obligation, the entire transaction price is allocated to the single performance obligation. Contracts that contain multiple performance obligations require an allocation of the transaction price to each performance obligation based on a relative standalone selling price basis.
- Recognize revenue when (or as) the Group satisfies a performance obligation – The Group satisfies performance obligations either over time or at a point in time as discussed in further detail below. Revenue is recognized at the time the related performance obligation is satisfied by transferring a promised good or service to a customer.

Revenue generated from services agreements (typically where licenses and related services were combined into one performance obligation) is determined to be recognized over time when it can be determined that the services meet one of the following: (a) the customer simultaneously receives and consumes the benefits provided by the entity's performance as the entity performs; (b) the entity's performance creates or enhances an asset that the customer controls as the asset is created or enhanced; or (c) the entity's performance does not create an asset with an alternative use to the entity and the entity has an enforceable right to payment for performance completed to date.

It was determined that the Group has contracts that meet criteria (a), since the customer simultaneously receives and consumes the benefits provided by the Company's performance as the Company performs. Therefore revenue is recognized over time using the input method based on costs incurred to date as compared to total contract costs. The Company believes that in research and development service type agreements using costs incurred to date represents the most faithful depiction of the entity's performance towards complete satisfaction of a performance obligation.

Revenue from licenses that are not part of a combined performance obligation are recognized at a point in time due to the licenses relating to intellectual property that has significant stand-alone functionality and as such represent a right to use the entity's intellectual property as it exists at the point in time at which the license is granted.

Royalty income received in respect of licensing agreements is recognized as the related third party sales in the licensee occur.

Amounts that are receivable or have been received per contractual terms but have not been recognized as revenue since performance has not yet occurred or has not yet been completed are recorded as deferred revenue. The Company classifies as non-current deferred revenue amounts received for which performance is expected to occur beyond one year or one operating cycle.

Grant Income

The Company recognizes grants from governmental agencies as grant income in the Consolidated Statement of Comprehensive Income/(Loss), gross of the expenditures that were related to obtaining the grant, when there is reasonable assurance that the Company will comply with the conditions within the grant agreement and there is reasonable assurance that payments under the grants will be received. The Company evaluates the conditions of each grant as of each reporting date to ensure that the Company has reasonable assurance of meeting the conditions of each grant arrangement and that it is expected that the grant payment will be received as a result of meeting the necessary conditions.

The Company submits qualifying expenses for reimbursement after the Company has incurred the research and development expense. The Company records an unbilled receivable upon incurring such expenses. In cases were grant income is received prior to the expenses being incurred or recognized, the amounts received are deferred until the related expense is incurred and/or recognized. Grant income is recognized in the Consolidated Statements of Comprehensive Income/(Loss) at the time in which the Company recognizes the related reimbursable expense for which the grant is intended to compensate.

Functional and Presentation Currency

These consolidated financial statements are presented in United States dollars ("US dollars"). The functional currency of virtually all members of the Group is the U.S. dollar. The assets and liabilities of a previously held subsidiary were translated to U.S. dollars at the exchange rate prevailing on the balance sheet date and revenues and expenses were translated at the average exchange rate for the period. Foreign exchange differences resulting from the translation were reported in Other Comprehensive Income/(Loss).

Foreign Currency

Transactions in foreign currencies are translated to the respective functional currencies of Group entities at the foreign exchange rate ruling at the date of the transaction. Monetary assets and liabilities denominated in foreign currencies at the balance sheet date are retranslated to the functional currency at the foreign exchange rate ruling at that date. Foreign exchange differences arising on remeasurement are recognized in the Consolidated Statement of Comprehensive Income/(Loss). Non-monetary assets and liabilities that are measured in terms of historical cost in a foreign currency are translated using the exchange rate at the date of the transaction.

Cash and Cash Equivalents

Cash and cash equivalents include all highly liquid instruments with original maturities of three months or less.

Share Capital

Ordinary shares are classified as equity. The Group is comprised of share capital, share premium, merger reserve, other reserve, translation reserve, and accumulated deficit.

Property and Equipment

Property and equipment is stated at cost less accumulated depreciation and any accumulated impairment losses. Cost includes expenditures that are directly attributable to the acquisition of the asset. Assets under construction represent leasehold improvements and machinery and equipment to be used in operations or research and development activities. When parts of an item of property and equipment have different useful lives, they are accounted for as separate items (major components) of property and equipment. Depreciation is calculated using the straight-line method over the estimated useful life of the related asset:

Laboratory and manufacturing equipment	2-8 years
Furniture and fixtures	7 years
Computer equipment and software	1-5 years
Leasehold improvements	5-10 years, or the remaining term of the lease, if shorter

Depreciation methods, useful lives and residual values are reviewed at each balance sheet date.

Intangible Assets

Intangible assets, which include purchased patents and licenses with finite useful lives, are carried at historical cost less accumulated amortization, if amortization has commenced. Intangible assets with finite lives are amortized from the time they are available for use. Amortization is calculated using the straight-line method to allocate the costs of patents and licenses over their estimated useful lives.

Research and development intangible assets, which are still under development and have accordingly not yet obtained marketing approval, are presented as In-Process Research and Development (IPR&D). IPR&D is not amortized since it is not yet available for its intended use, but it is evaluated for potential impairment on an annual basis or more frequently when facts and circumstances warrant.

Impairment

Impairment of Non-Financial Assets

The Group reviews the carrying amounts of its property and equipment and intangible assets at each reporting date to determine whether there are indicators of impairment. If any such indicators of impairment exist, then an asset's recoverable amount is estimated. The recoverable amount is the higher of an asset's fair value less cost of disposal and value in use.

The Company's IPR&D intangible assets are not yet available for their intended use. As such, they are tested for impairment at least annually.

An impairment loss is recognized when an asset's carrying amount exceeds its recoverable amount. For the purposes of impairment testing, assets are grouped at the lowest levels for which there are largely independent cash flows. If a non- financial asset instrument is impaired, an impairment loss is recognized in the Consolidated Statements of Comprehensive Income/(Loss).

The Company did not record any impairment of such assets during the reported periods.

Investments in associates are considered impaired if, and only if, objective evidence indicates that one or more events, which occurred after the initial recognition, have had an impact on the future cash flows from the net investment and that impact can be reliably estimated. If an impairment exists the Company measures an impairment by comparing the carrying value of the net investment in the associate to its recoverable amount and recording any excess as an impairment loss. See Note 6 for impairment recorded in respect of an investment in associate during the year ended December 31, 2019.

Employee Benefits

Short-Term Employee Benefits

Short-term employee benefit obligations are measured on an undiscounted basis and expensed as the related service is provided. A liability is recognized for the amount expected to be paid if the Group has a present legal or constructive obligation due to past service provided by the employee, and the obligation can be estimated reliably.

Defined Contribution Plans

A defined contribution plan is a post-employment benefit plan under which an entity pays fixed contributions into a separate entity and has no legal or constructive obligation to pay further amounts. Obligations for contributions to defined contribution plans are recognized as an employee benefit expense in the periods during which related services are rendered by employees. Prepaid contributions are recognized as an asset to the extent that a cash refund or a reduction in future payments is available.

Share-based Payments

Share-based payment arrangements, in which the Group receives goods or services as consideration for its own equity instruments, are accounted for as equity-settled share-based payment transactions (except certain restricted stock units - see below) in accordance with IFRS 2, regardless of how the equity instruments are obtained by the Group. The grant date fair value of employee share-based payment awards is recognized as an expense with a corresponding increase in equity over the requisite service period related to the awards. The amount recognized as an expense is adjusted to reflect the actual number of awards for which the related service and non-market performance conditions are expected to be met, such that the amount ultimately recognized as an expense is based on the number of awards that do meet the related service and non-market performance conditions at the vesting date. For share-based payment awards with market conditions, the grant date fair value is measured to reflect such conditions and there is no true-up for differences between expected and actual outcomes.

Certain restricted stock units are treated as liability settled awards starting in 2021. Such awards are remeasured at every reporting date until settlement date and are recognized as compensation expense over the requisite service period. Differences in remeasurement are recognized in profit and loss. The cumulative cost that will ultimately be recognized in respect of these awards will equal to the amount at settlement.

The fair value of the awards is measured using option pricing models and other appropriate models, which take into account the terms and conditions of the awards granted. See further details in Note 8.

Development Costs

Expenditures on research activities are recognized as incurred in the Consolidated Statements of Comprehensive Income/(Loss). In accordance with IAS 38 development costs are capitalized only if the expenditure can be measured reliably, the product or process is technically and commercially feasible, future economic benefits are probable, the Group can demonstrate its ability to use or sell the intangible asset, the Group intends to and has sufficient resources to complete development and to use or sell the asset, and it is able to measure reliably the expenditure attributable to the intangible asset during its development. The point at which technical feasibility is determined to have been reached is, generally, when regulatory approval has been received where applicable. Management determines that commercial viability has been reached when a clear market and pricing point have been identified, which may coincide with achieving meaningful recurring sales. Otherwise, the development expenditure is recognized as incurred in the Consolidated Statements of Comprehensive Income/(Loss). As of balance sheet date the Group has not capitalized any development costs.

Provisions

A provision is recognized in the Consolidated Statements of Financial Position when the Group has a present legal or constructive obligation due to a past event that can be reliably measured, and it is probable that an outflow of economic benefits will be required to settle the obligation. Provisions are determined by discounting the expected future cash flows at a pre-tax rate that reflects risks specific to the liability.

Leases

The Group leases real estate (and some minor equipment) for use in operations. These leases generally have lease terms of 1 to 10 years. The Group includes options that are reasonably certain to be exercised as part of the determination of the lease term. The group determines if an arrangement is a lease at inception of the contract in accordance with guidance detailed in IFRS 16. ROU assets represent the Group's right to use an underlying asset for the lease term and lease liabilities represent our obligation to make lease payments arising from the lease. Operating lease ROU assets and lease liabilities are recognized at commencement date based on the present value of the lease payments over the lease term. As most of our leases do not provide an implicit rate, we use the Group's estimated incremental borrowing rate based on information available at commencement date in determining the present value of future payments.

The Group's operating leases are virtually all leases of real estate.

The Group has elected to account for lease payments as an expense on a straight-line basis over the life of the lease for:

- Leases with a term of 12 months or less and containing no purchase options; and
- Leases where the underlying asset has a value of less than $5,000.

The right-of-use asset is depreciated on a straight-line basis and the lease liability gives rise to an interest charge.

Further information regarding the subleases, right of use asset and lease liability can be found in Note 21.

Finance Income and Finance Costs

Finance income is comprised of income on funds invested in U.S. treasuries, income on money market funds and income on a finance lease. Financing income is recognized as it is earned. Finance costs comprise mainly of loan, notes and lease liability interest expenses and the changes in the fair value of financial liabilities carried at FVTPL (such changes can consist of finance income when the fair value of such financial liabilities decreases).

Taxation

Tax on the profit or loss for the year comprises current and deferred income tax. In accordance with IAS 12, tax is recognized in the Consolidated Statements of Comprehensive Income/(Loss) except to the extent that it relates to items recognized directly in equity.

Current income tax is the expected tax payable or receivable on the taxable income or loss for the year, using tax rates enacted or substantially enacted at the reporting date, and any adjustment to tax payable in respect of previous years.

Deferred tax is recognized due to temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for taxation purposes. Deferred tax assets are recognized for unused tax losses, unused tax credits and deductible temporary differences to the extent that it is probable that future taxable profits will be available against which they can be used. Deferred tax assets with respect to investments in associates are recognized only to the extent that it is probable the temporary difference will reverse in the foreseeable future and taxable profit will be available against which the temporary difference can be utilised. Deferred tax assets are reviewed at each reporting date and are reduced to the extent that it is no longer probable that the related tax benefit will be realized.

Deferred tax is measured at the tax rates that are expected to be applied to temporary differences when they reverse, using tax rates enacted or substantively enacted at the reporting date.

Deferred income tax assets and liabilities are offset when there is a legally enforceable right to offset current tax assets against current tax liabilities and when the deferred income tax assets and liabilities relate to income taxes levied by the same taxation authority on either the same taxable entity or different taxable entities where there is an intention to settle the balances on a net basis.

Fair Value Measurements

The Group's accounting policies require that certain financial assets and certain financial liabilities be measured at their fair value.

The Group uses valuation techniques that are appropriate in the circumstances and for which sufficient data are available to measure fair value, maximizing the use of relevant observable inputs and minimizing the use of unobservable inputs. Fair values are categorized into different levels in a fair value hierarchy based on the inputs used in the valuation techniques as follows:

- Level 1: quoted prices (unadjusted) in active markets for identical assets or liabilities.
- Level 2: inputs other than quoted prices included in Level 1 that are observable for the asset or liability, either directly (i.e. as prices) or indirectly (i.e. derived from prices).
- Level 3: inputs for the asset or liability that are not based on observable market data (unobservable inputs).

The Group recognizes transfers between levels of the fair value hierarchy at the end of the reporting period during which the change has occurred.

The carrying amount of cash and cash equivalents, accounts receivable, restricted cash, deposits, accounts payable, accrued expenses and other current liabilities in the Group's Consolidated Statements of Financial Position approximates their fair value because of the short maturities of these instruments.

Operating Segments

Operating segments are reported in a manner that is consistent with the internal reporting provided to the chief operating decision maker ("CODM"). The CODM reviews discrete financial information for the operating segments in order to assess their performance and is responsible for making decisions about resources allocated to the segments. The CODM has been identified as the Group's Directors.

2. New Standards and Interpretations Not Yet Adopted

A number of new standards, interpretations, and amendments to existing standards are effective for annual periods commencing on or after January 1, 2022 and have not been applied in preparing the consolidated financial information. The Company's assessment of the impact of these new standards and interpretations is set out below.

Effective January 1, 2023, the definition of accounting estimates has been amended as an amendment to IAS 8 Accounting Policies, Changes in Accounting Estimates and Errors. The amendments clarify how companies should distinguish changes in accounting policies from changes in accounting estimates. The distinction is important because changes in accounting estimates are applied prospectively only to future transactions and future events, but changes in accounting policies are generally also applied retrospectively to past transactions and other past events. This amendment is not expected to have an impact on the Group's financial statements.

Effective January 1, 2023, IAS 1 has been amended to clarify that liabilities are classified as either current or non-current, depending on the rights that exist at the end of the reporting period. Classification is unaffected by the expectations of the entity or events after the reporting date. The Company does not expect this amendment will have a material impact on its financial statements.

Effective January 1, 2023, IAS 12 is amended to narrow the scope of the initial recognition exemption (IRE) so that it does not apply to transactions that give rise to equal and offsetting temporary differences. As a result, companies will need to recognise a deferred tax asset and a deferred tax liability for temporary differences arising on initial recognition of a lease and a decommissioning provision. The amendment is not expected to have an impact on the Group's financial statements as the

Group has already recognized a deferred tax asset and deferred tax liability that arose on initial recognition of its leases (the Group does not have decommissioning provisions).

None of the other new standards, interpretations, and amendments are applicable to the Company's financial statements and therefore will not have an impact on the Company.

3. Revenue

Revenue recorded in the Consolidated Statement of Comprehensive Income/(Loss) consists of the following:

For the years ended December 31,	**2021 $000s**	2020 $000s	2019 $000s
Contract revenue	**9,979**	8,341	8,688
Grant income	**7,409**	3,427	1,119
Total revenue	**17,388**	11,768	9,807

All amounts recorded in contract revenue were generated in the United States. For the years ended December 31, 2021 and 2020 contract revenue includes royalties received from an associate in the amount of $231 thousand and $54 thousand, respectively.

Primarily all of the Company's contracts in the years ended December 31, 2021, 2020 and 2019 were determined to have a single performance obligation which consists of a combined deliverable of license to intellectual property and research and development services (not including the license acquired by Imbrium upon option exercise – see below). Therefore, for such contracts, revenue is recognized over time based on the input method which the Company believes is a faithful depiction of the transfer of goods and services. Progress is measured based on costs incurred to date as compared to total projected costs. Payments for such contracts are primarily made up front at the inception of the contract (or upon achieving a milestone event) and to a lesser extent payments are made periodically over the contract term.

During the year ended December 31, 2021, the company received a $6.5 million payment from Imbrium Therapeutics, Inc. following the exercise of the option to acquire an exclusive license for the Initial Product Candidate, as defined in the agreement. Since the license transferred was a functional license, revenue from the option exercise was recognized at a point in time upon transfer of the license, which occurred during the year ended December 31, 2021.

During the year ended December 31, 2020, the Company received a $2.0 million milestone payment from Karuna Therapeutics, Inc. following initiation of its KarXT Phase 3 clinical study pursuant to the Exclusive Patent License Agreement between PureTech and Karuna. This milestone was recognized as revenue during the year ended December 31, 2020.

Disaggregated Revenue

The Group disaggregates contract revenue in a manner that depicts how the nature, amount, timing, and uncertainty of revenue and cash flows are affected by economic factors. The Group disaggregates revenue based on contract revenue or grant revenue, and further disaggregates contract revenue based on the transfer of control of the underlying performance obligations.

Timing of contract revenue recognition For the years ended December 31,	**2021 $000s**	2020 $000s	2019 $000s
Transferred at a point in time – Licensing Income[1]	**6,809**	2,054	—
Transferred over time[2]	**3,171**	6,286	8,688
	9,979	8,341	8,688

1 2021 – Attributed to Internal segment ($6.5 million), Controlled Founded Entities segment ($74 thousand) and to Parent Company and Other ($235 thousand); 2020 – Attributed to Parent Company and Other. See note 4, Segment information.

2 2021 – Attributed to Internal segment ($1,629 thousand) and Controlled Founded Entities segment ($1,541 thousand); 2020 – Attributed to Internal segment ($5,297 thousand), and Controlled Founded Entities segment ($990 thousand), 2019 – Attributed to Internal segment ($7,077 thousand), Controlled founded entities segment ($1,474 thousand) and Parent Company and Other ($137 thousand). See Note 4, Segment Information.

Customers over 10% of revenue	**2021 $000s**	2020 $000s	2019 $000s
Customer A	**—**	1,518	4,973
Customer B	**1,500**	896	1,433
Customer C	**—**	2,043	1,091
Customer D	**7,250**	1,736	1,013
Customer E	**—**	2,000	—
	8,750	8,193	8,510

Accounts receivables represent rights to consideration in exchange for products or services that have been transferred by the Group, when payment is unconditional and only the passage of time is required before payment is due. Accounts receivables do not bear interest and are recorded at the invoiced amount. Accounts receivable are included within Trade and other receivables on the Consolidated Statement of Financial Position.

Contract liabilities represent the Group's obligation to transfer products or services to a customer for which consideration has been received, or for which an amount of consideration is due from the customer. Contract liabilities are included within deferred revenue on the Consolidated Statement of Financial Position.

Contract Balances	2021 $000s	2020 $000s
Accounts receivable	**704**	711
Deferred revenue – short term	**65**	1,472

During the year ended December 31, 2021, $1.4 million of revenue was recognized from deferred revenue outstanding at December 31, 2020.

Remaining performance obligations represent the transaction price of unsatisfied or partially satisfied performance obligations within contracts with an original expected contract term that is greater than one year and for which fulfillment of the contract has started as of the end of the reporting period. The aggregate amount of transaction consideration allocated to remaining performance obligations as of December 31, 2021, was nil.

4. Segment Information

Basis for Segmentation

The Directors are the Group's strategic decision-makers. The Group's operating segments are reported based on the financial information provided to the Directors periodically for the purposes of allocating resources and assessing performance. The Group has determined that each entity is representative of a single operating segment as the Directors monitor the financial results at this level. When identifying the reportable segments the Group has determined that it is appropriate to aggregate multiple operating segments into a single reportable segment given the high level of operational and financial similarities across the entities.

The Group has identified multiple reportable segments as presented below. There was no change to reportable segments in 2021, except the change in the composition of the segments with respect to Alivio, as explained below. Virtually all of the revenue and profit generating activities of the Group are generated within the United States and accordingly, no geographical disclosures are provided.

During the year ended December 31, 2021, the Company acquired the non-controlling interest in Alivio and since then Alivio is wholly owned by the Company and is managed within the Internal segment. The Company has revised in these financial statements the prior period financial information to conform to the presentation as of and for the period ending December 31, 2021. The change in segments reflects how the Company's Board of Directors reviews the Group's results, allocates resources and assesses performance of the Group at this time.

Internal

The Internal segment (the "Internal segment"), is advancing Wholly Owned Programs which is focused on immunological, fibrotic and lymphatic system disorders and builds upon validated biologic pathways and proven pharmacology. The Internal segment is comprised of the technologies that are wholly owned and will be advanced through either PureTech Health funding or non-dilutive sources of financing in the near-term. The operational management of the Internal segment is conducted by the PureTech Health team, which is responsible for the strategy, business development, and research and development. As of December 31, 2021, this segment included PureTech LYT (formerly Ariya Therapeutics), PureTech LYT-100 and Alivio Therapeutics, Inc.

Controlled Founded Entities

The Controlled Founded Entity segment (the "Controlled Founded Entity segment") is comprised of the Group's subsidiaries that are currently consolidated operational subsidiaries that either have, or have plans to hire, independent management teams and currently have already raised third-party dilutive capital. These subsidiaries have active research and development programs and either have entered into or plan to seek an equity or debt investment partner, who will provide additional industry knowledge and access to networks, as well as additional funding to continue the pursued growth of the company. As of December 31, 2021, this segment included Entrega Inc., Follica Incorporated, Sonde Health Inc., and Vedanta Biosciences, Inc.

Non-Controlled Founded Entities

The Non-Controlled Founded Entities segment (the "Non-Controlled Founded Entities segment") is comprised of the entities in respect of which PureTech Health (i) no longer holds majority voting control as a shareholder and no longer has the right to elect a majority of the members of the subsidiaries' Board of Directors. Upon deconsolidation of an entity the segment disclosure is restated to reflect the change on a retrospective basis, as this constitutes a change in the composition of its reportable segments. The Non-Controlled Founded Entities segment includes Vor Biopharma Inc. ("Vor"), Karuna Therapeutics, Inc. ("Karuna"), and Gelesis Inc. ("Gelesis"), which were deconsolidated during the year ended December 31, 2019.

The Non-Controlled Founded Entities segment incorporates the operational results of the aforementioned entities to the date of deconsolidation. Following the date of deconsolidation, the Company accounts for its investment in each entity at the parent level, and therefore the results associated with investment activity following the date of deconsolidation is included in the Parent Company and Other section.

Parent Company and Other

Parent Company and Other includes activities that are not directly attributable to the operating segments, such as the activities of the Parent, corporate support functions and certain research and development support functions that are not directly attributable to a strategic business segment as well as the elimination of intercompany transactions. Intercompany transactions between segments consist primarily of management fees charged from the Parent Company to the other segments. This section also captures the accounting for the Company's holdings in entities for which control has been lost, which is inclusive of the following items: gain on deconsolidation, gain or loss on investments held at fair value, gain on loss of significant influence, and the share of net income/ (loss) of associates accounted for using the equity method. As of December 31, 2021, this segment included PureTech Health plc, PureTech Health LLC, PureTech Management, Inc., PureTech Securities Corp. and PureTech Securities II Corp., as well as certain other dormant, inactive and shell entities.

Information About Reportable Segments:

	2021 $000s				
	Internal $000s	Controlled Founded Entities $000s	Non-Controlled Founded Entities $000s	Parent Company & Other $000s	Consolidated $000s
Consolidated Statements of Comprehensive Income/(Loss)					
Contract revenue	**8,129**	**1,615**	**—**	**235**	**9,979**
Grant revenue	**1,253**	**6,156**	**—**	**—**	**7,409**
Total revenue	**9,382**	**7,771**	**—**	**235**	**17,388**
General and administrative expenses	**(8,673)**	**(20,729)**	**—**	**(27,797)**	**(57,199)**
Research and development expenses	**(65,444)**	**(43,783)**	**—**	**(1,244)**	**(110,471)**
Total operating expense	**(74,118)**	**(64,512)**	**—**	**(29,041)**	**(167,671)**
Other income/(expense):					
Gain/(loss) on investments held at fair value	**—**	**—**	**—**	**179,316**	**179,316**
Loss realized on sale of investments	**—**	**—**	**—**	**(20,925)**	**(20,925)**
Gain/(loss) on disposal of assets	**(1)**	**(51)**	**—**	**—**	**(53)**
Other income/(expense)	**—**	**121**	**—**	**1,523**	**1,645**
Total other income/(expense)	**(1)**	**70**	**—**	**159,914**	**159,983**
Net finance income/(costs)	**(16)**	**6,744**	**—**	**(1,679)**	**5,050**
Share of net income/(loss) of associates accounted for using the equity method	**—**	**—**	**—**	**(73,703)**	**(73,703)**
Income/(loss) before taxes	**(64,753)**	**(49,927)**	**—**	**55,727**	**(58,953)**
Income/(loss) before taxes pre IFRS 9 fair value accounting, finance costs – subsidiary preferred shares, share-based payment expense, depreciation of tangible assets and amortization of intangible assets	**(60,368)**	**(50,583)**	**—**	**63,628**	**(47,323)**
Finance income/(costs) – IFRS 9 fair value accounting	**—**	**9,606**	**—**	**—**	**9,606**
Share-based payment expense	**(3,066)**	**(6,256)**	**—**	**(4,628)**	**(13,950)**
Depreciation of tangible assets	**(1,319)**	**(1,518)**	**—**	**(1,510)**	**(4,347)**
Amortization of ROU assets	**—**	**(1,174)**	**—**	**(1,764)**	**(2,938)**
Amortization of intangible assets	**—**	**(2)**	**—**	**—**	**(2)**
Taxation	**—**	**—**	**—**	**(3,756)**	**(3,756)**
Income/(loss) for the year	**(64,753)**	**(49,927)**	**—**	**51,971**	**(62,709)**
Other comprehensive income/(loss)	**—**	**—**	**—**	**—**	**—**
Total comprehensive income/(loss) for the year	**(64,753)**	**(49,927)**	**—**	**51,971**	**(62,709)**
Total comprehensive income/(loss) attributable to:					
Owners of the Company	**(64,657)**	**(47,857)**	**—**	**51,956**	**(60,558)**
Non-controlling interests	**(96)**	**(2,069)**	**—**	**15**	**(2,151)**
			December 31, 2021 $000s		
Consolidated Statements of Financial Position:					
Total assets	**125,726**	**66,274**	**—**	**754,007**	**946,006**
Total liabilities[1]	**228,789**	**228,857**	**—**	**(95,787)**	**361,859**
Net assets/(liabilities)	**(103,063)**	**(162,584)**	**—**	**849,794**	**584,147**

1 Parent Company and Other Includes eliminations of intercompany liabilities between the Parent Company and the reportable segments in the amount of $233.3 million.

	2020 $000s				
	Internal $000s	Controlled Founded Entities $000s	Non-Controlled Founded Entities $000s	Parent Company & Other $000s	Consolidated $000s
Consolidated Statements of Comprehensive Income/(Loss)					
Contract revenue	5,297	990	—	2,054	8,341
Grant revenue	1,563	1,864	—	—	3,427
Total revenue	6,860	2,853	—	2,054	11,768
General and administrative expenses	(3,482)	(13,691)	—	(32,267)	(49,440)
Research and development expenses	(45,346)	(36,279)	—	(234)	(81,859)
Total Operating expenses	(48,828)	(49,970)	—	(32,500)	(131,299)
Other income/(expense):					
Gain/(loss) on investments held at fair value	—	—	—	232,674	232,674
Loss realized on sale of investments	—	—	—	(54,976)	(54,976)
Gain/(loss) on disposal of assets	(15)	(15)	—	—	(30)
Other income/(expense)	—	100	—	965	1,065
Other income/(expense)	(15)	85	—	178,662	178,732
Net finance income/(costs)	19	(5,204)	—	(930)	(6,115)
Share of net income/(loss) of associate accounted for using the equity method	—	—	—	(34,117)	(34,117)
Income/(loss) before taxes	(41,964)	(52,236)	—	113,170	18,969
(Loss)/income before taxes pre IFRS 9 fair value accounting, finance costs – subsidiary preferred shares, share-based payment expense, depreciation of tangible assets and amortization of intangible assets	(38,349)	(42,602)	—	121,644	40,694
Finance income/(costs) – subsidiary preferred shares	—	—	—	—	—
Finance income/(costs) – IFRS 9 fair value accounting	—	(4,351)	—	—	(4,351)
Share-based payment expense	(2,762)	(2,552)	—	(5,405)	(10,718)
Depreciation of tangible assets	(854)	(1,544)	—	(1,547)	(3,945)
Amortization of ROU assets	—	(1,186)	—	(1,523)	(2,709)
Amortization of intangible assets	—	(1)	—	—	(1)
Taxation	—	(1)	—	(14,400)	(14,401)
Income/(loss) for the year	(41,964)	(52,237)	—	98,769	4,568
Other comprehensive income/(loss)	—	—	—	469	469
Total comprehensive income/(loss) for the year	(41,964)	(52,237)	—	99,238	5,037
Total comprehensive income/(loss) attributable to:					
Owners of the Company	(41,773)	(51,026)	—	99,253	6,454
Non-controlling interests	(191)	(1,211)	—	(15)	(1,417)
			December 31, 2020 $000s		
Consolidated Statements of Financial Position:					
Total assets	89,214	67,433	—	833,347	989,994
Total liabilities	130,049	200,457	—	5,949	336,455
Net (liabilities)/assets	(40,835)	(133,023)	—	827,397	653,539

The proportion of net assets shown above that is attributable to non-controlling interest is disclosed in Note 18.

	2019 $000s				
	Internal $000s	Controlled Founded Entities $000s	Non-Controlled Founded Entities $000s	Parent Company & Other $000s	Consolidated $000s
Consolidated Statements of Comprehensive Loss					
Contract revenue	7,077	1,474	—	137	8,688
Grant revenue	928	191	—	—	1,119
Total revenue	8,006	1,664	—	137	9,807
General and administrative expenses	(3,252)	(13,569)	(10,439)	(32,098)	(59,358)
Research and development expenses	(28,874)	(39,883)	(15,555)	(1,536)	(85,848)
Total operating expense	(32,126)	(53,451)	(25,994)	(33,634)	(145,206)
Other income/(expense):					
Gain on deconsolidation	—	—	—	264,409	264,409
Gain/(loss) on investments held at fair value	—	—	—	(37,863)	(37,863)
Gain/(loss) on disposal of assets	17	(39)	—	(60)	(82)
Gain on loss of significant influence	—	—	—	445,582	445,582
Other income/(expense)	—	166	—	(45)	121
Other income/(expense)	17	127	—	672,023	672,167
Net finance income/(costs)	—	(16,947)	(30,141)	941	(46,147)
Share of net income/(loss) of associate accounted for using the equity method	—	—	—	30,791	30,791
Impairment of investment in associate	—	—	—	(42,938)	(42,938)
Income/(loss) before taxes	(24,104)	(68,608)	(56,135)	627,320	478,474
(Loss)/income before taxes pre IAS 39 fair value accounting, finance costs – subsidiary preferred shares, share-based payment expense, depreciation of tangible assets and amortization of intangible assets	(23,698)	(47,188)	(21,873)	640,298	547,540
Finance income/(costs) – subsidiary preferred shares	—	107	(1,564)	(1)	(1,458)
Finance income/(costs) – IFRS 9 fair value accounting	—	(17,294)	(28,737)	(444)	(46,475)
Share-based payment expense	(19)	(1,664)	(3,543)	(9,242)	(14,468)
Depreciation of tangible assets	(390)	(1,517)	(207)	(1,114)	(3,228)
Amortization of ROU assets	—	(1,060)	(83)	(2,177)	(3,320)
Amortization of intangible assets	4	7	(128)	—	(117)
Taxation	—	(134)	(162)	(112,113)	(112,409)
Income/(loss) for the year	(24,104)	(68,741)	(56,297)	515,207	366,065
Other comprehensive income/(loss)	—	—	(10)	—	(10)
Total comprehensive income/(loss) for the year	(24,104)	(68,741)	(56,307)	515,207	366,055
Total comprehensive income/(loss) attributable to:					
Owners of the Company	(6,461)	(55,258)	(32,353)	515,207	421,133
Non-controlling interests	(17,643)	(13,483)	(23,953)	—	(55,079)

5. Investments held at fair value

Investments held at fair value include both unlisted and listed securities held by PureTech. These investments, which include interests in Akili, Vor, Karuna, Gelesis (other than the investment in common shares which is accounted for under the equity method), and other insignificant investments, are initially measured at fair value and are subsequently re-measured at fair value at each reporting date with changes in the fair value recorded through profit and loss. Interests in these investments were accounted for as shown below:

Investments held at fair value	$000's
Balance as of January 1, 2020	714,905
Sale of Karuna shares	(347,538)
Sale of resTORbio shares	(3,048)
Loss realised on sale of investments	(54,976)
Cash purchase of Gelesis preferred shares (please refer to Note 6)	10,000
Cash purchase of Vor preferred shares	1,150
Unrealized Loss – fair value through profit and loss	232,674
Balance as of January 1, 2021 before allocation of share in associate loss to long-term interest	553,167
Sale of Karuna shares	(218,125)
Loss realised on sale of investments (see below)	(20,925)
Cash purchase of Vor preferred shares	500
Unrealized gain – fair value through profit and loss	179,271
Balance as of December 31, 2021 before allocation of share in associate loss to long-term interest	**493,888**
Share of associate loss allocated to long-term interest (see Note 6)	(96,709)
Balance as of December 31, 2021 after allocation of share in associate loss to long-term interest[1]	**397,179**

1 Fair value of investments accounted for at fair value, does not take into consideration contribution from milestones that occurred after December 31, 2021, the value of the Group's consolidated Founded Entities (Vedanta, Follica, Sonde and Entrega), the Internal segment, or cash and cash equivalents.

Vor

On February 12, 2019, Vor completed a Series A-2 Preferred Shares financing round with PureTech and several new third party investors. The financing provided for the purchase of 62,819,866 shares of Vor Series A-2 Preferred Shares at the purchase price of $0.40 per share.

As a result of the issuance of Series A-2 preferred shares to third-party investors, PureTech's ownership percentage and corresponding voting rights dropped from 79.5 percent to 47.5 percent, and PureTech simultaneously lost control on Vor's Board of Directors, both of which triggered a loss of control over the entity. As of February 12, 2019, Vor was deconsolidated from the Group's financial statements, resulting in only the profits and losses generated by Vor through the deconsolidation date being included in the Consolidated Statement of Comprehensive Income/(Loss). While the Company no longer controlled Vor, it was concluded that PureTech still had significant influence over Vor by virtue of its large, albeit minority, ownership stake and its continued representation on Vor's Board of Directors. During the year ended December 31, 2019, the Company recognized a $6.4 million gain on the deconsolidation of Vor, which was recorded to the Gain on the deconsolidation of subsidiary line item in the Consolidated Statement of Comprehensive Income/(Loss).

As PureTech did not hold common shares in Vor upon deconsolidation and the preferred shares it held did not have equity-like features, PureTech had no basis to account for its investment in Vor under IAS 28. The preferred shares held by PureTech fell under the guidance of IFRS 9 and were treated as a financial asset held at fair value with changes in fair value recorded in the Consolidated Statement of Comprehensive Income/(Loss). The fair value of the preferred shares at deconsolidation was $12.0 million.

On February 12, 2020, PureTech participated in the second closing of Vor's Series A-2 Preferred Share financing. For consideration of $0.7 million, PureTech received 1,625,000 A-2 shares. On June 30, 2020, PureTech participated in the first closing of Vor's Series B Preferred Share financing. For consideration of $0.5 million, PureTech received 961,538 shares. Upon the conclusion of such Vor financings PureTech no longer had significant influence over Vor.

On January 8, 2021, PureTech participated in the second closing of Vor's Series B Preferred Share financing. For consideration of $0.5 million, PureTech received an additional 961,538 B Preferred shares.

On February 9, 2021, Vor closed its initial public offering (IPO) of 9,828,017 shares of its common stock at a price to the public of $18.00 per share. Subsequent to the closing, PureTech held 3,207,200 shares of Vor common stock, representing 8.6 percent of Vor common stock. Following its IPO, the valuation of Vor common stock is based on level 1 inputs in the fair value hierarchy. See Note 16.

During the years ended December 31, 2021, 2020 and 2019, the Company recognized a gain of $3.9 million, a gain of $19.1 million, and a gain of $0.6 million, respectively for the changes in the fair value of the investment that were recorded in the line item Gain/(loss) on investments held at fair value within the Consolidated Statement of Comprehensive Income/(Loss). Please refer to Note 16 for information regarding the valuation of these instruments.

Gelesis

As of July 1, 2019, Gelesis was deconsolidated from the Group's financial statements, resulting in only the profits and losses generated by Gelesis through the deconsolidation date being included in the Group's Consolidated Statement of Income/(Loss). At the date of deconsolidation, PureTech recorded a $156.0 million gain on the deconsolidation of Gelesis, which was recorded to the Gain on the deconsolidation of subsidiary line item in the Consolidated Statement of Income/(Loss). The preferred shares and warrants held by PureTech fall under the guidance of IFRS 9 and are treated as financial assets held at fair value, where changes to the fair value of the preferred shares and warrant are recorded through the Consolidated Statement

of Income/(Loss). The fair value of the preferred shares and warrants at deconsolidation was $49.2 million. Please refer to Note 6 for information regarding the Company's investment in Gelesis as an associate.

On August 12, 2019, Gelesis issued a convertible promissory note to the Company in the amount of $2.0 million. On October 7, 2019, Gelesis issued an amended and restated convertible note (the “Gelesis Note”) to the Company in the principal amount of up to $6.5 million. The Gelesis Note was payable in installments, with $2.0 million of the note drawn down upon execution of the original note in August 2019 and an additional $3.3 million and $1.2 million drawn down on October 7, 2019 and November 5, 2019, respectively. The Gelesis Note was convertible upon the occurrence of Gelesis' next qualified equity financing, or at the demand of the Company at any date after December 31, 2019. The Gelesis Note fell under the guidance of IFRS 9 and was treated as a financial asset held at fair with all movements to the value of the note recorded through the Consolidated Statement of Income/(Loss).

On December 5, 2019, Gelesis closed its Series 3 Growth Preferred Stock financing, at which point all outstanding principal and interest under the Gelesis Note converted into shares of Series 3 Growth Preferred Stock. In addition to the shares issued upon conversion of the Gelesis Note, PureTech purchased $8.0 million of Series 3 Growth Preferred Stock in the December financing.

On April 1, 2020, PureTech participated in the 2nd closing of Gelesis's Series 3 Growth Preferred Share financing. For consideration of $10.0 million, PureTech received 579,038 Series 3 Growth shares.

During the years ended December 31, 2021, 2020 and 2019, the Company recognized a gain of $34.6 million, a gain of $7.1 million and a loss of $18.7 million, respectively related to the change in the fair value of the preferred shares and warrants that was recorded in the line item Gain/(loss) on investments held at fair value within the Consolidated Statement of Comprehensive Income/(Loss). The loss recorded in 2019 was primarily as a result of the Gelesis Series 3 Growth financing, which was executed with terms that resulted in a decrease in fair value across all other classes of preferred shares. Please refer to Note 16 for information regarding the valuation of these instruments. Additionally, due to the equity method based investment in Gelesis being reduced to zero, the Group allocated a portion of its share in the net loss in Gelesis in the years ended December 31, 2021 and 2020, totaling $73.7 million and $23.0 million, respectively, to its preferred share and warrant investments in Gelesis, which are considered to be long-term interests in Gelesis. As of December 31, 2021, the investment in Gelesis preferred shares and warrants was entirely reduced to nil.

See Note 26 for subsequent event regarding the investment in Gelesis.

Karuna

2019

On March 15, 2019, Karuna completed the closing of a Series B Preferred Share financing with PureTech and several new third party investors. The financing provided for the purchase of 5,285,102 shares of Karuna Series B Preferred Shares at a purchase price of $15.14 per share.

As a result of the issuance of the preferred shares to third-party investors, PureTech's ownership percentage and corresponding voting rights related to Karuna dropped from 70.9 percent to 44.3 percent, and PureTech simultaneously lost control over Karuna's Board of Directors, both of which triggered a loss of control over the entity. As of March 15, 2019, Karuna was deconsolidated from the Group's financial statements, resulting in only the profits and losses generated by Karuna through the deconsolidation date being included in the Group's Consolidated Statement of Comprehensive Income/(Loss). At the date of deconsolidation, PureTech recorded a $102.0 million gain on the deconsolidation of Karuna, which was recorded to the Gain on the deconsolidation of subsidiary line item in the Consolidated Statement of Comprehensive Income/(Loss). While the Company no longer controls Karuna, it was concluded that PureTech still had significant influence over Karuna by virtue of its large, albeit minority, ownership stake and its continued representation on Karuna's Board of Directors. As PureTech had significant influence over Karuna, the entity was accounted for as an associate under IAS 28.

Upon the date of deconsolidation, PureTech held both preferred and common shares in Karuna and a warrant issued by Karuna to PureTech. The preferred shares and warrant held by PureTech fell under the guidance of IFRS 9 and were treated as financial assets held at fair value, and all movements to the value of preferred shares held by PureTech were recorded through the Consolidated Statement of Comprehensive Income/(Loss), in accordance with IFRS 9. The fair value of the preferred shares and warrant at deconsolidation was $72.4 million. Subsequent to deconsolidation, PureTech purchased an additional $5.0 million of Karuna Series B Preferred shares.

Due to the immaterial investment in common shares and overwhelmingly large losses by Karuna, the common share investment accounted for under the equity method was remeasured to nil immediately following both the deconsolidation and the exercise of the warrant in the first half of 2019.

On June 28, 2019, Karuna priced its IPO. PureTech's ownership percentage and corresponding voting rights related to Karuna dropped from 44.3 percent percent to 31.6 percent; however, PureTech retained significant influence due to its continued presence on the board and its large, albeit minority, equity stake in the company. Upon completion of the IPO, the Karuna preferred shares held by PureTech converted to common shares. In light of PureTech's common share holdings in Karuna and corresponding voting rights, PureTech had re-established a basis to account for its investment in Karuna under IAS 28. The preferred shares investment held at fair value was therefore reclassified to investment in associate upon completion of the conversion. During the year ended December 31, 2019 and up to June 28, 2019, the Company recognized a gain of $40.6 million that was recorded on the line item Gain on investments held at fair value within the Consolidated Statement of Comprehensive Income/(Loss) related to the preferred shares that increased in value between the date of deconsolidation and the date of Karuna's IPO.

As of December 2, 2019 it was concluded that the Company no longer exerted significant influence over Karuna owing to the resignation of the PureTech designee from Karuna's Board of Directors, with PureTech retaining no ability to reappoint representation. Furthermore, PureTech was not involved in any manner, or had any influence, on the management of Karuna, or on any of its decision making processes and had no ability to do so. As such, PureTech lost the power to participate in the financial and operating policy decisions of Karuna. As a result, Karuna was no longer deemed an Associate and did not meet

the scope of equity method accounting, resulting in the investment being accounted for as an investment held at fair value. As of December 2, 2019 the Company's interest in Karuna was 28.4 percent. For the period of June 28, 2019 through December 2, 2019, PureTech's investment in Karuna was subject to equity method accounting. In accordance with IAS 28, the Company's investment was adjusted by the share of losses generated by Karuna (weighted average of 31.4 percent based on common stock ownership interest), which resulted in a net loss of associates accounted for using the equity method of $6.3 million during the year ended December 31, 2019.

Upon PureTech's loss of significant influence, the investment in Karuna was reclassified to an investment held at fair value. This change led PureTech to recognize a gain on loss of significant influence of $445.6 million that was recorded to the Consolidated Statement of Comprehensive Income/(Loss) on the line item Gain on loss of significant influence during the year ended December 31, 2019. The investment in Karuna after the recording of the gain on loss of significant influence was $557.2 million, which was reclassified from Investments in associates to Investments held at fair value. Additionally, from December 2, 2019 PureTech recorded a $0.7 million loss on the line item Gain/(loss) on investments held at fair value within the Consolidated Statement of Comprehensive Income/(Loss) for the year ended December 31, 2019.

2020 and 2021

On January 22, 2020, PureTech sold 2,100,000 shares of Karuna common shares for aggregate proceeds of $200.9 million. On May 26, 2020, PureTech sold an additional 555,500 Karuna common shares for aggregate proceeds of $45.0 million. On August 26, 2020, PureTech sold 1,333,333 common shares of Karuna for aggregate proceeds of $101.6 million. As a result of the sales, Puretech recorded a loss of $54.8 million attributable to blockage discount included in the sales price, to the line item Loss Realized on Sale of Investment within the Consolidated Statement of Comprehensive Income/(Loss). See below for gain recorded in respect of the change in fair value of the Karuna investment.

On February 9, 2021, the Group sold 1,000,000 common shares of Karuna for $118.0 million. Following the sale the Group held 2,406,564 common shares of Karuna, which represented 8.2 percent of Karuna common stock at the time of sale. On November 9, 2021, the group sold an additional 750,000 common shares of Karuna for $100.1 million. Following the sale the group holds 1,656,564 common shares of Karuna, which represented 5.6 percent at time of sale. As a result of the aforementioned sales, the Company recorded a loss of $20.9 million, attributable to blockage discount included in the sales price, to the line item Loss Realised on Sale of Investment within the Consolidated Statement of Comprehensive Income/(Loss) for the year ended December 31, 2021. See below for gain recorded in respect of the change in fair value of the Karuna investment.

During the years ended December 31, 2021 and 2020, the Company recognized a gain of $110.0 million and a gain of $191.2 million, respectively for the changes in the fair value of the Karuna investment that were recorded in the line item Gain/(loss) on investments held at fair value within the Consolidated Statement of Comprehensive Income/(Loss). As of December 31, 2021, PureTech continued to hold Karuna common shares or 5.6 percent of total outstanding Karuna common shares. Please refer to Note 16 for information regarding the valuation of these instruments.

Akili

As PureTech does not hold common shares in Akili and the preferred shares it holds do not have equity-like features, PureTech has no basis to account for its investment in Akili under IAS 28. The preferred shares held by PureTech Health fall under the guidance of IFRS 9 and are treated as a financial asset held at fair value and all movements to the value of the preferred shares are recorded through the Consolidated Statements of Comprehensive Income/(Loss), in accordance with IFRS 9.

On May 25, 2021, Akili completed its Series D financing for gross proceeds of $110.0 million in which Akili issued 13,053,508 Series D preferred shares. The Group did not participate in this round of financing and as a result, the Group's interest in Akili was reduced from 41.9 percent to 27.5 percent.

During the years ended December 31, 2021, 2020 and 2019, the Company recognized a gain of $32.2 million, a gain of $14.4 million, and a gain of $11.5 million, respectively for the changes in the fair value of the investment in Akili that was recorded on the line item Gain/(loss) on investments held at fair value within the Consolidated Statement of Comprehensive Income/(Loss). Please refer to Note 16 for information regarding the valuation of these instruments.

resTORbio

On November 15, 2019, resTORbio announced that top line data from the Protector 1 Phase 3 study evaluating the safety and efficacy of RTB101 in preventing clinically symptomatic respiratory illness in adults age 65 and older, did not meet its primary endpoint and the Company has stopped the development of RTB101 in this indication. As a result of ceasing the development of RTB101, resTORbio's share price witnessed a decline in price. In November and December 2019, PureTech Health sold 7,680,700 common shares of resTORbio for aggregate proceeds of $9.3 million. Immediately following the sale of common shares, PureTech Health held 2,119,696 common shares, or 5.8 percent, of resTORbio. During the year ended December 31, 2019 PureTech recorded a loss of $71.9 million for the adjustment to fair value of its investment in resTORbio to the Consolidated Statement of Comprehensive Income/(Loss) in the line item Gain/(loss) on investments held at fair value.

On April 30, 2020, PureTech sold its remaining 2,119,696 resTORbio common shares, for aggregate proceeds of $3.0 million. As a result of the sale, the Company recorded a loss of $0.2 million attributable to blockage discount included in the sales price, to the line item Loss realized on sale of investments within the Consolidated Statement of Comprehensive Income/(Loss). Additionally, during the year ended December 31, 2020, the Company recognized a gain of $0.1 million that was recorded on the line item Gain/(loss) on investments held at fair value within the Consolidated Statement of Comprehensive Income/(Loss).

Gain on deconsolidation

The following table summarizes the gain on deconsolidation recognized by the Company:

Year ended December 31,	**2021 $000s**	2020 $000s	2019 $000s
Gain on deconsolidation of Vor	**—**	—	6,357
Gain on deconsolidation of Karuna	**—**	—	102,038
Gain on deconsolidation of Gelesis [Note 6]	**—**	—	156,014
Total gain on deconsolidation	**—**	—	264,409

6. Investments in Associates

Gelesis

Gelesis was founded by PureTech and raised funding through preferred shares financings as well as issuances of warrants and loans. As of January 1, 2019, PureTech maintained control of Gelesis and Gelesis's financial results were fully consolidated in the Group's consolidated financial statements.

On July 1, 2019, the Gelesis Board of Directors was restructured, resulting in two of the three PureTech representatives resigning from the Board with PureTech retaining no ability to reappoint Directors to these board seats. As a result of this restructuring, PureTech lost control over Gelesis' Board of Directors, which triggered a loss of control over the entity. At the deconsolidation date, PureTech held a 25.2 percent voting interest in Gelesis. As of July 1, 2019, Gelesis was deconsolidated from the Group's financial statements, resulting in only the profits and losses generated by Gelesis through the deconsolidation date being included in the Group's Consolidated Statement of Income/(Loss) and Other Comprehensive Income/(Loss). At the date of deconsolidation, PureTech recorded a $156.0 million gain on the deconsolidation of Gelesis, which was recorded to the Gain on the deconsolidation of subsidiary line item in the Consolidated Statement of Comprehensive Income/(Loss). While the Company no longer controls Gelesis, it was concluded that PureTech still has significant influence over Gelesis by virtue of its large, albeit minority, ownership stake and its continued representation on Gelesis' Board of Directors and as such Gelesis is accounted for as an associate under IAS 28, starting at the date of deconsolidation.

Upon the date of deconsolidation, PureTech held preferred shares and common shares of Gelesis and a warrant issued by Gelesis to PureTech. PureTech's investment in common shares of Gelesis is subject to equity method accounting with an initial investment of $16.4 million. In accordance with IAS 28, PureTech's investment was adjusted by the share of profits and losses generated by Gelesis subsequent to the date of deconsolidation. See table below for the Group's share in the profits and losses of Gelesis for the periods presented.

The preferred shares and warrant held by PureTech fall under the guidance of IFRS 9 and are treated as financial assets held at fair value, where changes to the fair value of the preferred shares and warrant are recorded through the Consolidated Statement of Income/(Loss) and Other Comprehensive Income/(Loss), in accordance with IFRS 9. The fair value of the preferred shares and warrant at deconsolidation was $49.2 million. See Note 5 for changes in the fair value subsequent to deconsolidation date.

Impairment loss for the year ended December 31, 2019

Following the issuance of the Gelesis Series 3 Preferred Shares at a higher valuation than the previous round with some favorable liquidation provisions primarily to PureTech and also to the other Series 3 preferred share investors, which resulted in adjustments to the fair values of other preferred shares, warrant classes and Gelesis common stock, the Company assessed the investment in common shares held in Gelesis for impairment. Management compared the recoverable amount of the investment to its carrying amount as of December 31, 2019, which resulted in an impairment loss to the Investment in Gelesis. The recoverable amount was estimated based on the fair value of the Gelesis common shares held by PureTech, which are considered to be within Level 3 of the fair value hierarchy. The costs of disposal are immaterial for the calculation of Gelesis investment's recoverable amount. The total fair value of common shares was determined utilizing a hybrid valuation approach with significant unobservable inputs within the PureTech valuation framework. The multi-scenario hybrid valuation approach utilized the recent transaction method within an option pricing framework and an IPO scenario within a probability-weighted-expected return framework to determine the value allocation for the common share class of Gelesis. The PWERM maintained a 75.0 percent probability of occurrence while the OPM maintained a 25.0 percent probability of occurrence. The probability weighted term to exit was 1.57 years. The discount rate utilized was 20.0 percent while the risk-free rate and volatility utilized were 1.62 percent and 56.0 percent, respectively.

The impairment loss amounted to $42.9 million and was recorded to Impairment of investment in associate within the Consolidated Statement of Comprehensive Income/(Loss) for the year ended December 31, 2019. As of December 31, 2019 the investment in Gelesis was $10.6 million, which is equal to the fair value of the common shares held by PureTech.

Years ended December 31, 2020 and 2021

During the year ended December 31, 2021 and 2020, the Group recorded its share in the losses of Gelesis. In 2020 the Group's investment in associates accounted for under the equity method was reduced to zero. Since the Group has investments in Gelesis warrants and preferred shares that are deemed to be Long-term interests, the Company continued recognizing its share in Gelesis losses while applying such losses to its preferred share and warrant investment in Gelesis accounted for as an investment held at fair value. In 2021, the total investment in Gelesis, including the Long-term interests, was reduced to zero. Since the Group did not incur legal or constructive obligations or made payments on behalf of Gelesis, the Group discontinued recognizing equity method losses. As of December 31, 2021, unrecognized equity method losses amounted to $38.1 million, which included $0.7 million of unrecognized other comprehensive loss.

During 2021, due to exercise of stock options into common shares in Gelesis the Group's equity interest in Gelesis was reduced from 47.9 percent at December 31, 2020 to 42.0 percent as of December 31, 2021. The gain resulting from the issuance of shares to third parties and the resulting reduction in the Group's share in the accumulated deficit of Gelesis under the equity method was fully offset by the unrecognized equity method losses.

Karuna

For the period of June 28, 2019, through December 2, 2019, PureTech's investment in Karuna was subject to equity method accounting. In accordance with IAS 28, the Company's investment was adjusted by the share of losses generated by Karuna (weighted average of 31.4 percent based on common stock ownership interest), which resulted in a net loss of $6.3 million during the year ended December 31, 2019, recorded in the line item Share of net income/(loss) of associates. Starting December 2, 2019, due to the loss of significant influence in Karuna on such date, the Company is accounting for the investment in Karuna as an investment held at fair value. See Note 5 for further detail on the Group's investment in Karuna.

The following table summarizes the activity related to the investment in associates balance for the years ended December 31, 2021, 2020 and 2019.

Investment in Associates	$000's
As of January 1, 2019	—
Reclassification of Karuna investment at initial public offering	118,006
Investment in Gelesis upon deconsolidation	16,444
Share of net loss of Karuna accounted for using the equity method	(6,345)
Share of net profit of Gelesis accounted for using the equity method	37,136
Impairment of investment in Gelesis	(42,938)
Reclassification of investment upon loss of significant influence	(111,661)
As of December 31, 2019 and January 1, 2020	10,642
Share of net loss in Gelesis	(34,117)
Share of other comprehensive income in Gelesis	469
Share of losses recorded against long term interests	23,006
As of December 31, 2020 and January 1, 2021	—
Share of net loss in Gelesis	(73,703)
Share of losses recorded against long term interests	73,703
As of December 31, 2021	—

Summarized financial information

The following table summarizes the financial information of Gelesis as included in its own financial statements, adjusted for fair value adjustments at deconsolidation and differences in accounting policies. The table also reconciles the summarized financial information to the carrying amount of the Company's interest in Gelesis. The information for the year ended December 31, 2019, includes the results of Gelesis only for the period July 1, 2019 to December 31, 2019, as Gelesis was consolidated prior to this period.

As of and for the year ended December 31,	**2021 $000s**	2020 $000s
Percentage ownership interest	**42.0 %**	47.9 %
Non-current assets	**357,508**	372,184
Current assets	**66,092**	92,875
Non-current liabilities	**(120,786)**	(133,743)
Current liabilities	**(537,432)**	(300,748)
Non controlling interests and options issued to third parties	**(14,216)**	(6,577)
Net assets attributable to shareholders of Gelesis Inc.	**(248,834)**	23,989
Group's share of net assets	**(104,527)**	11,481
Goodwill	**7,211**	8,216
Impairment provision balance	**(37,495)**	(42,702)
Equity method losses recorded against Long-term Interests	**96,709**	23,006
Unrecognized equity method losses (*)	**38,101**	—
Investment in associate	**—**	—

	2021 $000s	2020 $000s	2019 $000s
Revenue	**11,185**	21,442	—
Income/(loss) from continuing operations (100%)	**(271,430)**	(71,157)	74,573
Total comprehensive income/(loss) (100%)	**(273,005)**	(70,178)	74,573
Group's share in net income (losses) - limited to net investment amount	**(73,703)**	(34,117)	37,136
Group's share of total comprehensive income (loss) - limited to net investment amount	**(73,703)**	(33,648)	37,136

(*) Unrecognized equity method losses includes unrecognized other comprehensive loss of $0.7 million.

See Note 26, for the completion of the business combination of Gelesis with Capstar Special Purpose Acquisition Corp ("Capstar") on January 13, 2022. The publicly traded company began trading on the New York Stock exchange under the ticker symbol "GLS" on January 14, 2022.

On December 30, 2021, PureTech signed a Backstop agreement with Capstar according to which PureTech committed to acquire Capstar class A common shares immediately prior to the closing of the business combination between Gelesis and Capstar, in case subsequent to the redemptions of Capstar shares being completed, the Available Funds, as defined in the agreement, are less than$15.0 million. Puretech committed to acquire two thirds of the necessary shares at $10 per share so that the Available Funds increase to $15.0 million. According to the Backstop agreement, in case PureTech is required to acquire any shares under the agreement, PureTech will receive an additional 1,322,500 class A common shares of Capstar (immediately prior to the closing of the business combination) at no additional consideration.

The Company determined that such agreement meets the definition of a derivative under IFRS 9 and as such should be recorded at fair value with changes in fair value recorded through profit and loss. For the year ended December 31, 2021 the changes in fair value were de minimis. The derivative was initially recorded at fair value adjusted to defer the day 1 gain equal to the difference between the fair value of $11.2 million and transaction price of zero on the effective date and as such was initially recorded at zero. The deferred gain is amortized to Other income (expense) in the Consolidated Statement of Income (loss) over the period from the effective date until settlement date. As such, the Group recognized $0.8 million income in 2021 for the portion of the deferred gain amortized in 2021.

On January 13, 2022, as part of the conclusion of the aforementioned Backstop agreement, the Group acquired 496,145 class A common shares of Capstar for $5.0 million and received an additional 1,322,500 common A shares of Capstar for no additional consideration.

7. Operating Expenses

Total operating expenses were as follows:

For the years ending December 31,	**2021 $000s**	2020 $000s	2019 $000s
General and administrative	**57,199**	49,440	59,358
Research and development	**110,471**	81,859	85,848
Total operating expenses	**167,671**	131,299	145,206

The average number of persons employed by the Group during the year, analyzed by category, was as follows:

For the years ending December 31,	**2021**	2020	2019
General and administrative	**52**	43	39
Research and development	**119**	95	90
Total	**171**	138	129

The aggregate payroll costs of these persons were as follows:

For the years ending December 31,	**2021 $000s**	2020 $000s	2019 $000s
General and administrative	**26,438**	22,943	24,468
Research and development	**28,950**	20,674	20,682
Total	**55,388**	43,616	45,150

Detailed operating expenses were as follows:

For the years ending December 31,	**2021 $000s**	2020 $000s	2019 $000s
Salaries and wages	**36,792**	29,403	27,703
Healthcare benefits	**2,563**	1,866	1,511
Payroll taxes	**2,084**	1,629	1,468
Share-based payments	**13,950**	10,718	14,468
Total payroll costs	**55,388**	43,616	45,150
Other selling, general and administrative expenses	**30,761**	26,497	34,890
Other research and development expenses	**81,521**	61,186	65,166
Total other operating expenses	**112,282**	87,683	100,056
Total operating expenses	**167,671**	131,299	145,206

Auditor's remuneration:

For the years ending December 31,	**2021 $000s**	2020 $000s	2019 $000s
Audit of these financial statements	**1,183**	1,145	870
Audit of the financial statements of subsidiaries	**312**	291	290
Audit of the financial statements of associate**	**571**	350	—
Audit-related assurance services*	**1,868**	490	163
Non-audit related services	**—**	173	778
Total	**3,934**	2,449	2,101

* 2021 - $468.2 thousand represents prepaid expenses related to an expected initial public offering of a subsidiary.

** Audit fees of $500.0 thousand and $350.0 thousand in respect of financial statements of associates for the years ended December 31, 2021, and 2020, respectively, are not included within the consolidated financial statements. Fees related to the audit of the financial statements of associates have been disclosed in respect of both 2021 and 2020 as these fees went towards supporting the audit opinion on the Group accounts. Such amounts were not previously disclosed in the 2020 financial statements.

Please refer to Note 8 for further disclosures related to share-based payments and Note 24 for management's remuneration disclosures.

8. Share-based Payments

Share-based payments includes stock options, restricted stock units ("RSUs") and performance-based RSUs in which the expense is recognized based on the grant date fair value of these awards, except for performance based RSUs to executives that are treated as liability awards where expense is recognized based on reporting date fair value up until settlement date.

Share-based Payment Expense

The Group share-based payment expense for the years ended December 31, 2021, 2020 and 2019, were comprised of charges related to the PureTech Health plc incentive stock and stock option issuances and subsidiary stock plans.

The following table provides the classification of the Group's consolidated share-based payment expense as reflected in the Consolidated Statement of Income/(Loss):

Year ended December 31,	**2021 $000s**	2020 $000s	2019 $000s
General and administrative	**9,310**	7,650	10,677
Research and development	**4,640**	3,068	3,791
Total	**13,950**	10,718	14,468

Ariya Stock Option Exchange- 2019

In conjunction with the acquisition of the remaining minority interests of PureTech LYT (previously named Ariya Therapeutics, Inc.) on October 1, 2019 (Please refer to Note 18), PureTech Health exchanged subsidiary stock options previously granted to the co-inventors, advisors and employees of PureTech LYT with stock options to purchase 2,147,965 of the Company's ordinary shares under the PureTech Health Performance Share Plan. As this was an exchange of awards within the consolidated group, whereby the Company's stock options were replacing Ariya's stock options, the exchange was accounted for as a modification of the original award and the incremental fair value on the date of the replacement was amortized over the remaining vesting period of the awards.

The Performance Share Plan

In June 2015, the Group adopted the Performance Stock Plan ("PSP"). Under the PSP and subsequent amendments, awards of ordinary shares may be made to the Directors, senior managers and employees of, and other individuals providing services to the Company and its subsidiaries up to a maximum authorized amount of 10.0 percent of the total ordinary shares outstanding. The shares have various vesting terms over a period of service between two and four years, provided the recipient remains continuously engaged as a service provider.

The share-based awards granted under the PSP are generally equity settled (see cash settlements below) and expire 10 years from the grant date. As of December 31, 2021, the Company had issued share-based awards to purchase an aggregate of 21,756,187 shares under this plan.

RSUs

RSU activity for the years ended December 31, 2021, 2020 and 2019 is detailed as follows:

	Number of Shares/Units	Wtd Avg Grant Date Fair Value (GBP) (*)
Outstanding (Non-vested) at January 1, 2019	**6,598,783**	**1.29**
RSUs Granted in Period	1,775,569	2.95
Vested	(3,738,005)	1.10
Forfeited	—	—
Outstanding (Non-vested) at December 31, 2019 and January 1, 2020	**4,636,347**	**2.08**
RSUs Granted in Period	1,759,011	1.80
Vested	(2,781,687)	1.54
Forfeited	(191,089)	2.37
Outstanding (Non-vested) at December 31, 2020 and January 1, 2021	**3,422,582**	**2.46**
RSUs Granted in Period	2,195,133	2.15
Vested	(1,176,695)	2.93
Forfeited	(808,305)	2.25
Outstanding (Non-vested) at December 31, 2021	**3,632,715**	**1.91**

(*) 2021 – for liability awards based on fair value at reporting date.

Each RSU entitles the holder to one ordinary share on vesting and the RSU awards are generally based on a cliff vesting schedule over a one to three-year requisite service period in which the Company recognizes compensation expense for the RSUs. Following vesting, each recipient will be required to make a payment of one pence per ordinary share on settlement of the RSUs. Vesting of the majority of the RSUs is subject to the satisfaction of performance and market conditions. The grant date fair value of market condition awards that are treated as equity settled awards is measured to reflect such conditions and there is no true-up for differences between expected and actual outcomes. For liability settled awards, see below.

The Company recognizes the estimated fair value of performance-based awards as share-based compensation expense over the performance period based upon its determination of whether it is probable that the performance targets will be achieved. The Company assesses the probability of achieving the performance targets at each reporting period. Cumulative adjustments, if any, are recorded to reflect subsequent changes in the estimated outcome of performance-related conditions.

The fair value of the market and performance-based awards is based on the Monte Carlo simulation analysis utilizing a Geometric Brownian Motion process with 100,000 simulations to value those shares. The model considers share price volatility,

risk-free rate and other covariance of comparable public companies and other market data to predict distribution of relative share performance.

The performance and market conditions attached to the RSU awards are based on the achievement of total shareholder return ("TSR"), based on the achievement of absolute TSR targets, and to a lesser extent based on TSR as compared to the FTSE 250 Index, and the MSCI Europe Health Care Index. The remaining portion is based on the achievement of strategic targets. The RSU award performance criteria have changed over time as the criteria is continually evaluated by the Group's Remuneration Committee.

In 2017, the Company granted certain executives RSUs that vested based on the service, market and performance conditions, as described above. The vesting of all RSUs was achieved by December 31, 2019 where all service, market and performance conditions were met. The remuneration committee of PureTech's Board of Directors approved the achievement of the vesting conditions as of December 31, 2019 and reached the decision during the year ended December 31, 2020 to cash settle the 2017 RSUs. The settlement value was determined based on the 3 day average closing price of the shares. The settlement value was $12.5 million (which after deducting tax withheld on behalf of recipients amounted to $7.2 million). The settlement value did not exceed the fair value at settlement date and as such the cash settlement was treated as an equity transaction in the financial statements as of and for the year ended December 31, 2020, whereby the full repurchase cash settlement amount was charged to equity in Other reserves.

Similarly in 2018, the Company granted certain executives RSUs that vested based on service, market and performance conditions, as described above. The vesting of all RSUs was achieved by December 31, 2020 where all service, market and performance conditions were met. In February 2021 the remuneration committee of PureTech's board of directors approved the achievement of the vesting conditions as of December 31, 2020 and on May 28, 2021 reached the decision to cash settle RSUs to certain employees while others were issued shares. The settlement value was determined based on the three day average closing price of the shares. The settlement value was $10.7 million (which after deducting tax withheld on behalf of recipients amounted to $6.4 million). The settlement value did not exceed the fair value at settlement date and as such the cash settlement was treated as an equity transaction, whereby the full repurchase cash settlement amount was charged to equity in Other reserves in the financial statements as of and for the year ended December 31, 2021.

Following the different cash settlements, the Company concluded that although the remaining RSUs are to be settled by shares according to their respective agreements, and any cash settlement is at the Company's discretion, due to past practice of cash settlement to multiple employees, some for multiple years, these RSUs to the company executives should be treated as liability awards and as such adjusted to fair value at every reporting date with changes in fair value recorded in earnings as stock based compensation expense.

Consequently, the Company reclassified $1.9 million from equity to other non-current liabilities and $4.8 million from equity to other payables equal to the fair value of the awards at the date of reclassification. The Company treated the excess of the fair value at the reclassification date over the grant date fair value of the RSUs (for the portion of the vesting period that has already elapsed) in the amount of $2.9 million as an equity transaction. Therefore the full amount of the liability at reclassification was recorded as a charge to equity. The changes in fair value of the liability from reclassification date to balance sheet date or settlement date are recorded as stock-based compensation expense in the Consolidated Statement of Comprehensive Income (loss).

The Company incurred share-based payment expenses for performance, market and service based RSUs of $1.5 million (including $0.6 million expense in respect of RSU liability awards), $5.7 million and $2.2 million for the years ended December 31, 2021, 2020 and 2019, respectively. The decrease in the share based compensation expense in respect of the RSUs for the year ended December 31, 2021, as compared to the year ended December 31, 2020 is due to reduction in the fair value of the liability awards as compared to their value at the date the awards were reclassified from equity awards to liability awards, as well as forfeitures of certain awards due to unexpected terminations of RSU holders.

As of December 31, 2021, the carrying amount of the RSU liability awards was $7.4 million ($4.7 million current; $2.7 million non current), out of which $4.6 million related to awards that have met all their performance and market conditions.

Stock Options

Stock option activity for the years ended December 31, 2021, 2020 and 2019, is detailed as follows:

	Number of Options	Wtd Average Exercise Price (GBP)	Wtd Average of remaining contractual term (in years)	Wtd Average Stock Price at Exercise (GBP)
Outstanding at January 1, 2019	**5,075,734**	**1.40**	**8.78**	
Granted	3,634,183	0.84		
Exercised	(237,090)	1.98		2.81
Forfeited	—	—		
Options Exercisable at December 31, 2019 and January 1, 2020	**4,349,921**	**0.93**	**8.34**	
Outstanding at December 31, 2019 and January 1, 2020	**8,472,827**	**1.16**	**8.55**	
Granted	4,076,982	3.14		
Exercised	(514,410)	1.52		2.88
Forfeited	(1,119,313)	1.88		
Options Exercisable at December 31, 2020 and January 1, 2021	**5,447,405**	**0.98**	**7.46**	
Outstanding at December 31, 2020 and January 1, 2021	**10,916,086**	**1.81**	**8.38**	
Granted	5,424,000	3.34		
Exercised	(2,238,187)	0.70		3.63
Forfeited	(687,781)	2.53		
Options Exercisable at December 31, 2021	**4,773,873**	**1.42**	**6.50**	
Outstanding at December 31, 2021	**13,414,118**	**2.58**	**8.29**	

The fair value of the stock options awarded by the Company was estimated at the grant date using the Black-Scholes option valuation model, considering the terms and conditions upon which options were granted, with the following weighted-average assumptions:

At December 31,	**2021**	2020	2019
Expected volatility	**41.05 %**	41.25 %	35.68 %
Expected terms (in years)	**6.16**	6.11	5.81
Risk-free interest rate	**1.06 %**	0.53 %	1.85 %
Expected dividend yield	**—**	—	—
Grant date fair value	**$1.87**	$1.72	$2.23

The Company incurred share-based payment expense for the stock options of $6.2 million, $2.1 million and $9.2 million for the years ended December 31, 2021, 2020 and 2019, respectively. The increase in expense for the year ended December 31, 2021, as compared to the year ended December 31, 2020, is due to the new grants granted in 2021. The significant decrease for the year ended December 31, 2020, as compared to the year ended December 31, 2019, is largely attributable to the exchange of the Ariya awards with the Company's stock options in the year ended December 31, 2019, which resulted in an additional expense recorded in such year, as described above.

For shares outstanding as of December 31, 2021, the range of exercise prices is detailed as follow:

Range of Exercise Prices (GBP)	Options Outstanding	Wtd Average Exercise Price (GBP)	Wtd Average of remaining contractual term (in years)
0.01	842,762	—	7.76
1.00 to 2.00	3,521,839	1.42	5.81
2.00 to 3.00	1,251,017	2.47	8.35
3.00 to 4.00	7,798,500	3.39	9.46
Total	**13,414,118**	**2.58**	**8.29**

Subsidiary Plans

Certain subsidiaries of the Group have adopted stock option plans. A summary of stock option activity by number of shares in these subsidiaries is presented in the following table:

	Outstanding as of January 1, 2021	**Granted During the Year**	**Exercised During the Year**	**Expired During the Year**	**Forfeited During the Year**	**Outstanding as of December 31, 2021**
Alivio	**3,888,168**	**197,398**	**(2,373,750)**	**(506,260)**	**(1,205,556)**	**—**
Entrega	**962,000**	**—**	**(525,000)**	**(87,500)**	**—**	**349,500**
Follica	**1,309,040**	**1,383,080**	**—**	**(6,000)**	**—**	**2,686,120**
Sonde	**2,192,834**	**—**	**—**	**(51,507)**	**(92,323)**	**2,049,004**
Vedanta	**1,741,888**	**451,532**	**(52,938)**	**(76,491)**	**(72,354)**	**1,991,637**

	Outstanding as of January 1, 2020	Granted During the Year	Exercised During the Year	Expired During the Year	Forfeited During the Year	Outstanding as of December 31, 2020
Alivio	3,698,244	189,924	—	—	—	3,888,168
Entrega	972,000	—	—	—	(10,000)	962,000
Follica	1,309,040	—	—	—	—	1,309,040
Sonde	1,829,004	363,830	—	—	—	2,192,834
Vedanta	1,450,100	493,951	(813)	—	(201,350)	1,741,888

	Outstanding as of January 1, 2019	Granted During the Year	Exercised During the Year	Expired During the Year	Forfeited During the Year	Outstanding as of December 31, 2019
Gelesis	3,681,732	—	—	(110,386)	(3,571,346)[1]	—
Alivio	2,393,750	1,329,494	(3,125)	—	(21,875)	3,698,244
PureTech LYT	2,180,000	—	—	—	(2,180,000)[2]	—
Commense	540,416	—	—	—	(540,416)	—
Entrega	914,000	58,000	—	—	—	972,000
Follica	1,229,452	79,588	—	—	—	1,309,040
Karuna	1,949,927	—	—	—	(1,949,927)[1]	—
Sonde	22,500	1,806,504	—	—	—	1,829,004
Vedanta	1,373,750	154,193	—	—	(77,843)	1,450,100

1 These shares represent the options outstanding on the date of deconsolidation of Karuna and Gelesis.
2 These shares represent the options outstanding on the date of exchange to PureTech stock options.

The weighted-average exercise prices and remaining contractual life for the options outstanding as of December 31, 2021, were as follows:

Outstanding at December 31, 2021	Number of options	Weighted-average exercise price $	Weighted-average contractual life outstanding
Alivio	**—**	**—**	**0**
Entrega	**349,500**	**1.88**	**4.62**
Follica	**2,686,120**	**1.39**	**7.28**
Sonde	**2,049,004**	**0.20**	**7.71**
Vedanta	**1,991,637**	**13.42**	**5.92**

The weighted average exercise prices for the options granted for the years ended December 31, 2021, 2020 and 2019, were as follows:

For the years ended December 31,	2021 $	2020 $	2019 $
Alivio	**—**	0.47	0.49
Follica	**1.86**	—	0.03
Sonde	**—**	0.18	0.20
Vedanta	**19.69**	19.59	19.13

The weighted average exercise prices for options forfeited during the year ended December 31, 2021, were as follows:

Forfeited during the year ended December 31, 2021	Number of options	Weighted-average exercise price $
Alivio	**1,205,556**	**0.48**
Sonde	**92,323**	**0.18**
Vedanta	**72,354**	**19.36**

The weighted average exercise prices for options exercised during the year ended December 31, 2021, were as follows:

Exercised during the year ended December 31, 2021	Number of options	Weighted-average exercise price $
Alivio	**2,373,750**	**0.03**
Entrega	**525,000**	**0.03**
Vedanta	**52,938**	**0.96**

The weighted average exercise prices for options exercisable as of December 31, 2021, were as follows:

Exercisable at December 31, 2021	Number of Options	Weighted-average exercise price $	Exercise Price Range $
Alivio	**—**	**—**	**—**
Entrega	**349,500**	**1.88**	**0.03-2.36**
Follica	**2,686,120**	**1.01**	**0.03-1.86**
Sonde	**2,049,004**	**0.20**	**0.13-0.20**
Vedanta	**1,991,637**	**9.64**	**0.02-19.94**

Significant Subsidiary Plans

Vedanta 2010 Stock Incentive Plan

In 2010, the Board of Directors for Vedanta approved the 2010 Stock Incentive Plan (the "Vedanta Plan"). Through subsequent amendments, as of December 31, 2021, it allowed for the issuance of 2,797,055 share-based compensation awards through incentive share options, nonqualified share options, and restricted shares to employees, Directors, and nonemployees providing services to Vedanta. At December 31, 2021, 747,270 shares remained available for issuance under the Vedanta Plan.

The options granted under Vedanta Plan are equity settled and expire 10 years from the grant date. Typically, the awards vest in four years but vesting conditions can vary based on the discretion of Vedanta's Board of Directors.

Options granted under the Vedanta Plan are exercisable at a price per share not less than the fair market value of the underlying ordinary shares on the date of grant. The estimated fair value of options, including the effect of estimated forfeitures, is recognized over the options' vesting period.

The fair value of the stock option grants has been estimated at the date of grant using the Black-Scholes option pricing model with the following range of assumptions:

Assumption/Input	**2021**	2020	2019
Expected award life (in years)	**6.00-7.11**	6.00-10.00	5.86-6.07
Expected award price volatility	**88.05%-88.59%**	89.24%-95.46%	89.24%-95.46%
Risk free interest rate	**0.96%-1.32%**	0.32%-0.87%	1.73%-1.88%
Expected dividend yield	**—**	—	—
Grant date fair value	**$13.84-$16.23**	$13.09-$16.54	$14.12-$15.61
Share price at grant date	**$19.00-$21.35**	$19.59	$18.71-$19.94

Vedanta incurred share-based compensation expense of $5.4 million, $2.4 million and $1.7 million for the years ended December 31, 2021, 2020 and 2019, respectively.

Other Plans

The stock compensation expense under plans at other subsidiaries of the Group not including Vedanta amounted to $0.84 million, $0.42 million and $0.01 million for the years ended December 31, 2021, 2020 and 2019, respectively.

9. Finance Cost, net

The following table shows the breakdown of finance income and costs:

For the years ended December 31,	**2021 $000s**	2020 $000s	2019 $000s
Finance income			
Interest income from financial assets	**214**	1,183	4,362
Total finance income	**214**	1,183	4,362
Finance costs			
Contractual interest expense on notes payable	**(1,031)**	(96)	(149)
Interest expense on other borrowings	**(1,502)**	(496)	—
Interest expense on lease liability	**(2,181)**	(2,354)	(2,495)
Gain/(loss) on foreign currency exchange	**(56)**	—	68
Total finance cost – contractual	**(4,771)**	(2,946)	(2,576)
Gain/(loss) from change in fair value of warrant liability	**1,419**	(117)	(11,890)
Gain/(loss) from change in fair value of preferred shares	**8,362**	(4,234)	(34,585)
Gain/(loss) from change in fair value of convertible debt	**(175)**	—	—
Total finance income/(costs) – fair value accounting	**9,606**	(4,351)	(46,475)
Total finance costs – subsidiary preferred shares	**—**	—	(1,458)

Total finance income/(costs)	**9,606**	(4,351)	(47,933)
Finance income/(costs), net	**5,050**	(6,115)	(46,147)

10. Earnings/(Loss) per Share

The basic and diluted loss per share has been calculated by dividing the income/(loss) for the period attributable to ordinary shareholders by the weighted average number of ordinary shares outstanding during the years ended December 31, 2021, 2020 and 2019, respectively. During the year ended December 31, 2021 the Company incurred a net loss and therefore all outstanding potential securities were considered anti-dilutive. The amount of potential securities that were excluded from the calculation amounted to 6,553,905 shares.

Earnings/(Loss) Attributable to Owners of the Company:

	2021		2020		2019	
	Basic $000s	**Diluted $000s**	Basic $000s	Diluted $000s	Basic $000s	Diluted $000s
Income/(loss) for the year, attributable to the owners of the Company	**(60,558)**	**(60,558)**	5,985	5,985	421,144	421,144
Income/(loss) attributable to ordinary shareholders	**(60,558)**	**(60,558)**	5,985	5,985	421,144	421,144

Weighted-Average Number of Ordinary Shares:

	2021		2020		2019	
	Basic	**Diluted**	Basic	Diluted	Basic	Diluted
Issued ordinary shares at January 1,	**285,885,025**	**285,885,025**	285,370,619	285,370,619	282,493,867	282,493,867
Effect of shares issued	**705,958**	**705,958**	233,048	233,048	932,600	932,600
Effect of dilutive shares (please refer to Note 8)	**—**	**—**	—	7,252,246	—	8,355,866
Weighted average number of ordinary shareholders at December 31,	**286,590,983**	**286,590,983**	285,603,667	292,855,913	283,426,467	291,782,333

Earnings/(Loss) per Share:

	2021		2020		2019	
	Basic $	**Diluted $**	Basic $	Diluted $	Basic $	Diluted $
Basic and diluted earnings/(loss) per share	**(0.21)**	**(0.21)**	0.02	0.02	1.49	1.44

11. Property and Equipment

Cost	Laboratory and Manufacturing Equipment $000s	Furniture and Fixtures $000s	Computer Equipment and Software $000s	Leasehold Improvements $000s	Construction in process $000s	Total $000s
Balance as of January 1, 2020	7,385	1,452	1,508	17,656	646	28,647
Additions, net of transfers	1,536	—	51	399	3,347	5,332
Disposals	(642)	—	(40)	—	—	(682)
Reclassifications	141	—	—	—	(141)	—
Balance as of December 31, 2020	8,420	1,452	1,519	18,054	3,852	33,297
Additions, net of transfers	1,424	—	92	183	6,723	8,422
Disposals	(323)	—	(282)	—	—	(605)
Reclassifications	2,211	—	—	248	(2,459)	—
Balance as of December 31, 2021	**11,733**	**1,452**	**1,329**	**18,485**	**8,116**	**41,115**

Accumulated depreciation and impairment loss	Laboratory and Manufacturing Equipment $000s	Furniture and Fixtures $000s	Computer Equipment and Software $000s	Leasehold Improvements $000s	Construction in process $000s	Total $000s
Balance as of January 1, 2020	(2,968)	(239)	(1,030)	(2,955)	—	(7,192)
Depreciation	(1,572)	(215)	(297)	(1,860)	—	(3,944)
Disposals	576	—	40	—	—	616
Balance as of December 31, 2020	(3,965)	(454)	(1,287)	(4,815)	—	(10,520)
Depreciation	(1,973)	(208)	(174)	(1,991)	—	(4,346)
Disposals	251	—	271	—	—	522
Balance as of December 31, 2021	**(5,686)**	**(663)**	**(1,190)**	**(6,806)**	**—**	**(14,344)**

Property and Equipment, net	Laboratory and Manufacturing Equipment $000s	Furniture and Fixtures $000s	Computer Equipment and Software $000s	Leasehold Improvements $000s	Construction in process $000s	Total $000s
Balance as of December 31, 2020	4,456	998	232	13,239	3,852	22,777
Balance as of December 31, 2021	**6,047**	**790**	**139**	**11,679**	**8,116**	**26,771**

Depreciation of property and equipment is included in the General and administrative expenses and Research and development expenses line items in the Consolidated Statements of Comprehensive Income/(Loss). The Company recorded depreciation expense of $4.3 million, $3.9 million and $3.2 million for the years ended December 31, 2021, 2020 and 2019, respectively.

12. Intangible Assets

Intangible assets consist of licenses of intellectual property acquired by the Group through various agreements with third parties and are recorded at the value of the consideration transferred. Information regarding the cost and accumulated amortization of intangible assets is as follows:

Cost	Licenses $000s
Balance as of January 1, 2020	625
Additions	275
Balance as of December 31, 2020	900
Additions	90
Balance as of December 31, 2021	**990**

Accumulated amortization	Licenses $000s
Balance as of January 1, 2020	—
Amortization	(1)
Balance as of December 31, 2020	(1)
Amortization	(2)
Balance as of December 31, 2021	**(3)**

Intangible assets, net	Licenses $000s
Balance as of December 31, 2020	899
Balance as of December 31, 2021	**987**

Substantially all the intangible asset licenses represent in-process-research-and-development assets since they are still being developed and are not ready for their intended use. As such, these assets are not yet amortized but tested for impairment annually.

The Company tested such assets for impairment as of balance sheet date and concluded that none were impaired.

Amortization expense was included in the Research and development expenses line item in the accompanying Consolidated Statements of Comprehensive Income/(Loss). Amortization expense, recorded using the straight-line method, was approximately $0.0 million, $0.0 million and $0.1 million for the years ended December 31, 2021 2020 and 2019, respectively.

13. Other Financial Assets

Other financial assets consist of restricted cash held, which represents amounts that are reserved as collateral against letters of credit with a bank that are issued for the benefit of a landlord in lieu of a security deposit for office space leased by the Group. Information regarding restricted cash was as follows:

As of December 31,	**2021 $000s**	2020 $000s
Restricted cash	**2,124**	2,124
Total other financial assets	**2,124**	2,124

14. Equity

Total equity for PureTech as of December 31, 2021, and 2020, was as follows:

Equity	December 31, 2021 $000s	December 31, 2020 $000s
Share capital, £0.01 par value, issued and paid 287,796,585 and 285,885,025 as of December 31, 2021 and 2020, respectively	**5,444**	5,417
Merger Reserve	**138,506**	138,506
Share premium	**289,303**	288,978
Translation reserve	**469**	469
Other reserves	**(40,077)**	(24,050)
Retained earnings/(accumulated deficit)	**199,871**	260,429
Equity attributable to owners of the Group	**593,515**	669,748
Non-controlling interests	**(9,368)**	(16,209)
Total equity	**584,147**	653,539

Changes in share capital and share premium relate primarily to incentive options exercises during the period.

Shareholders are entitled to vote on all matters submitted to shareholders for a vote. Each ordinary share is entitled to one vote. Each ordinary share is entitled to receive dividends when and if declared by the Company's Directors. The Company has not declared any dividends in the past.

On June 18, 2015, the Company acquired the entire issued share capital of PureTech LLC in return for 159,648,387 Ordinary Shares. This was accounted for as a common control transaction at cost. It was deemed that the share capital was issued in line with movements in share capital as shown prior to the transaction taking place. In addition, the merger reserve records amounts previously recorded as share premium.

Other reserves comprise the cumulative credit to share-based payment reserves corresponding to share-based payment expenses recognized through Consolidated Statements of Comprehensive Income/(Loss), settlements of vested share based payment awards as well as other additions that flow directly through equity such as the excess or deficit from changes in ownership of subsidiaries while control is maintained by the Group.

15. Subsidiary Preferred Shares

Preferred shares issued by subsidiaries and affiliates often contain redemption and conversion features that are assessed under IFRS 9 in conjunction with the host preferred share instrument. This balance represents subsidiary preferred shares issued to third parties.

The subsidiary preferred shares are redeemable upon the occurrence of a contingent event, other than full liquidation of the Company, that is not considered to be within the control of the Company. Therefore these subsidiary preferred shares are classified as liabilities. These liabilities are measured at fair value through profit and loss. The preferred shares are convertible into ordinary shares of the subsidiaries at the option of the holder and mandatorily convertible into ordinary shares upon a subsidiary listing in a public market at a price above that specified in the subsidiary's charter or upon the vote of the holders of subsidiary preferred shares specified in the charter. Under certain scenarios the number of ordinary shares receivable on conversion will change and therefore, the number of shares that will be issued is not fixed. As such the conversion feature is considered to be an embedded derivative that normally would require bifurcation. However, since the preferred share liabilities are measured at fair value through profit and loss, as mentioned above, no bifurcation is required.

The preferred shares are entitled to vote with holders of common shares on an as converted basis.

The Group recognized the preferred share balance upon the receipt of cash financing or upon the conversion of notes into preferred shares at the amount received or carrying balance of any notes and derivatives converted into preferred shares.

The balance as of December 31, 2021 and 2020, represents the fair value of the instruments for all subsidiary preferred shares. The following summarizes the subsidiary preferred share balance:

As of December 31,	2021 $000s	2020 $000s
Entrega	**669**	1,291
Follica	**11,191**	12,792
Sonde	**13,362**	12,821
Vedanta Biosciences	**148,796**	92,068
Total subsidiary preferred share balance	**174,017**	118,972

As is customary, in the event of any voluntary or involuntary liquidation, dissolution or winding up of a subsidiary, the holders of subsidiary preferred shares which are outstanding shall be entitled to be paid out of the assets of the subsidiary available for distribution to shareholders and before any payment shall be made to holders of ordinary shares. A merger, acquisition, sale of voting control or other transaction of a subsidiary in which the shareholders of the subsidiary immediately before the transaction do not own a majority of the outstanding shares of the surviving company shall be deemed to be a liquidation event. Additionally, a sale, lease, transfer or other disposition of all or substantially all of the assets of the subsidiary shall also be deemed a liquidation event.

As of December 31, 2021 and 2020, the minimum liquidation preference reflects the amounts that would be payable to the subsidiary preferred holders upon a liquidation event of the subsidiaries, which is as follows:

As of December 31,	**2021 $000s**	2020 $000s
Entrega	**2,216**	2,216
Follica	**6,405**	6,405
Sonde	**12,000**	12,000
Vedanta Biosciences	**149,568**	86,161
Total minimum liquidation preference	**170,189**	106,782

For the years ended December 31, 2021 and 2020, the Group recognized the following changes in the value of subsidiary preferred shares:

	$000s
Balance as of January 1, 2020	100,989
Issuance of new preferred shares	13,750
Increase in value of preferred shares measured at fair value	4,234
Balance as of January 1, 2021	118,972
Issuance of new preferred shares - financing cash flow	37,610
Conversion of convertible notes into preferred shares - non cash financing activity	25,797
decrease in value of preferred shares measured at fair value - finance costs (income)	(8,362)
Balance as December 31, 2021	**174,017**

2021

On July 21, 2021 Vedanta closed a Series D financing in which Vedanta issued 2,387,675 Preferred D shares for consideration of $68.4 million. From such consideration of $68.4 million, $25.8 million was received from Pfizer through conversion of its convertible note (see Note 17) and $5.0 million was received from PureTech in exchange for 174,520 Preferred D shares. The amount received from PureTech was eliminated in the consolidated financial statements.

2020

In January 2020 and April 2020, Sonde Health issued and sold shares of Series A-2 preferred shares for aggregate proceeds of $4.8 million, of which none was contributed by PureTech.

In April 2020 and July 2020, Vedanta issued and sold shares of Series C-2 preferred shares for aggregate proceeds of $9.0 million, of which none was contributed by PureTech.

16. Financial Instruments

The Group's financial instruments consist of financial liabilities, including preferred shares, convertible notes, warrants and loans payable, as well as financial assets classified as assets held at fair value.

Fair Value Process

For financial instruments measured at fair value under IFRS 9 the change in the fair value is reflected through profit and loss. Using the guidance in IFRS 13, the total business enterprise value and allocable equity of each entity being valued was determined using a discounted cash flow income approach, replacement cost/asset approach, market/asset - PWERM approach, or market backsolve approach through a recent arm's length financing round. The approaches, in order of strongest fair value evidence, are detailed as follows:

Valuation Method	**Description**
Market – Backsolve	The market backsolve approach benchmarks the original issue price (OIP) of the company's latest funding transaction as current value.
Market/Asset – PWERM	Under a PWERM, the company value is based upon the probability-weighted present value of expected future investment returns, considering each of the possible future outcomes available to the enterprise. An Asset approach may be included as an expected future outcome within the PWERM method. Possible future outcomes can include IPO scenarios, potential SPAC transactions, merger and acquisition transactions as well as other similar exit transactions of the investee.
Income Based – DCF	The income approach is used to estimate fair value based on the income streams, such as cash flows or earnings, that an asset or business can be expected to generate.
Asset/Cost	The asset/cost approach considers reproduction or replacement cost as an indicator of value.

As of December 31, 2021 and 2020, at each measurement date, the total fair value of preferred shares and warrants, including embedded conversion rights that are not bifurcated, was determined using the following allocation methods: option pricing model ("OPM"), Probability-Weighted Expected Return Method ("PWERM"), or Hybrid allocation framework. The methods are detailed as follows:

Allocation Method	**Description**
OPM	The OPM model treats preferred stock as call options on the enterprise's equity value, with exercise prices based on the liquidation preferences of the preferred stock.

PWERM	Under a PWERM, share value is based upon the probability-weighted present value of expected future investment returns, considering each of the possible future outcomes available to the enterprise, as well as the rights of each share class.
Hybrid	The hybrid method ("HM") is a combination of the PWERM and OPM. Under the hybrid method, multiple liquidity scenarios are weighted based on the probability of the scenarios occurrence, similar to the PWERM, while also utilizing the OPM to estimate the allocation of value in one or more of the scenarios.

Valuation policies and procedures are regularly monitored by the Company's finance group. Fair value measurements, including those categorized within Level 3, are prepared and reviewed on their issuance date and then on an annual basis for reasonableness and compliance with the fair value measurements guidance under IFRS. The Group measures fair values using the following fair value hierarchy that reflects the significance of the inputs used in making the measurements:

Fair Value Hierarchy Level	**Description**
Level 1	Inputs that are quoted market prices (unadjusted) in active markets for identical instruments.
Level 2	Inputs other than quoted prices included within Level 1 that are observable either directly (i.e. as prices) or indirectly (i.e. derived from prices).
Level 3	Inputs that are unobservable. This category includes all instruments for which the valuation technique includes inputs not based on observable data and the unobservable inputs have a significant effect on the instrument's valuation.

Whilst the Group considers the methodologies and assumptions adopted in fair value measurements as supportable, reasonable and robust, because of the inherent uncertainty of valuation, those estimated values may differ significantly from the values that would have been used had a ready market for the investment existed.

COVID-19 Consideration

At December 31, 2021, the Group assessed certain key assumptions within the valuation of its unquoted instruments and considered the impact of the COVID-19 pandemic on all unobservable inputs (Level 3). The assumptions considered with respect to COVID-19 included but were not limited to the following: exit scenarios and timing, discount rates, revenue assumptions as well as volatilities. The Group views any impact of the COVID-19 pandemic on its unquoted instruments as immaterial as of December 31, 2021.

Subsidiary Preferred Shares Liability and Subsidiary Convertible Notes

The following table summarizes the changes in the Group's subsidiary preferred shares and convertible note liabilities measured at fair value, which were categorized as Level 3 in the fair value hierarchy:

	Subsidiary Preferred Shares $000s	Subsidiary Convertible Notes $000s
Balance at January 1, 2019	217,519	9,333
Value at issuance	51,048	1,607
Conversion to preferred	4,894	(4,894)
Conversion to common	—	(2,418)
Deconsolidation	(207,346)	(5,017)
Change in fair value	33,636	1,389
Finance Costs	1,458	—
Other	(112)	—
Cash distribution	(108)	—
Balance at December 31, 2019 and January 1, 2020	100,989	—
Value at issuance	13,750	25,000
Change in fair value	4,234	—
Balance at December 31, 2020 and January 1, 2021	118,972	25,000
Value at issuance	37,610	2,215
Conversion to subsidiary preferred shares	25,797	(25,797)
Accrued interest – contractual	—	867
Change in fair value	(8,362)	175
Balance at December 31, 2021	**174,017**	**2,461**

The change in fair value of preferred shares and convertible notes are recorded in Finance income/(costs) – fair value accounting in the Consolidated Statements of Comprehensive Income/(Loss).

The table below sets out information about the significant unobservable inputs used at December 31, 2021, in the fair value measurement of the Group's material subsidiary preferred shares liabilities categorized as Level 3 in the fair value hierarchy:

Fair Value at December 31, 2021	Valuation Technique	Unobservable Inputs	Weighted Average	Sensitivity to Decrease in Input
148,796	Market/Asset – PWERM & Hybrid allocation	Estimated time to exit	0.93	
		Discount rate	30.0%	Fair value increase
		Volatility	95.0%	
11,860	Income – DCF & OPM allocation	Estimated time to exit	2.94	Fair value decrease
		Probability of Success	76.5%	
		Discount rate	21.9%	Fair value increase
		Terminal value growth rate	(1.3)%	Fair value decrease
		Volatility	57.1%	
13,362	Market – Backsolve & OPM allocation	Estimated time to exit	2.00	Fair value increase
		Volatility	40.0%	

Subsidiary Preferred Shares Sensitivity

The following summarizes the sensitivity from the assumptions made by the Company with respect to the significant unobservable inputs which are categorized as Level 3 in the fair value hierarchy and used in the fair value measurement of the Group's subsidiary preferred shares liabilities (Please refer to Note 15):

Input	Subsidiary Preferred Share Liability	
As of December 31, 2021	Sensitivity Range	Financial Liability Increase/(Decrease) $000s
Subsidiary Enterprise Value	-2 %	(3,041)
	+2%	3,140
Time to Liquidity	-6 Months	5,934
	+6 Months	(6,838)
Volatility	-10 %	737
	+10%	(682)
Discount Rate	-5 %	10,575
	+5%	(6,068)

Subsidiary Convertible Notes

Vedanta issued convertible promissory notes in December 2020 and Sonde issued convertible notes in April 2021 and November 2021 (collectively the "Notes"). See Note 17 Subsidiary Notes payable for further details. The Notes contain one or more embedded derivatives. The Company elected to account for these Notes as FVTPL liabilities, whereby the embedded derivatives are not bifurcated but rather the Notes are recorded at fair value with changes in fair value recorded in the Finance Income (Cost) line item in the Consolidated statement of comprehensive income (loss).

In July 2021 the entire convertible note issued by Vedanta was converted into Vedanta Series D preferred shares - see Note 15 for further details.

The aggregate fair value of the Sonde Notes was determined to be approximately $2.5 million at December 31, 2021. The valuations of the Notes were each categorized as Level 3 in the fair value hierarchy. In estimating the fair value of these Notes, a probability-weighted methodology was utilized, whereby the Notes' expected returns under various Note-specific liquidity scenarios were analyzed and weighted to arrive at a probability-adjusted fair value at December 31, 2021. The significant unobservable input used at December 31, 2021, in the fair value measurement of Sonde's convertible notes constituted the estimated time to exit, which was 0.59 years.

Financial Assets Held at Fair Value

Karuna and Vor Valuation

Karuna (Nasdaq: KRTX) and Vor (Nasdaq: VOR) and additional immaterial investments are listed entities on an active exchange and as such the fair value for the year ended December 31, 2021, was calculated utilizing the quoted common share price. Please refer to Note 5 for further details.

Akili and Gelesis

In accordance with IFRS 9, the Company accounts for its preferred share investments in Akili and Gelesis as financial assets held at fair value through the profit and loss. During the year ended December 31, 2021, the Company recorded its investment in such preferred shares at fair value and recognized the change in fair value of such investments as a gain of $66.7 million that was recorded to the Consolidated Statements of Comprehensive Income/(Loss) in the line item Gain/(loss) on investments held at fair value.

The following table summarizes the changes in the Group's investments held at fair value, which were categorized as Level 3 in the fair value hierarchy:

	$'000s
Balance at January 1, 2019	85,163
Deconsolidation of Vor	12,028
Deconsolidation of Karuna	77,373
Deconsolidation of Gelesis	49,170
Reclass of Karuna to Associate	(118,006)
Gain/(Loss) on changes in fair value	48,867
Issuance of note receivable	6,480

Conversion of note receivable	(6,630)
Balance at December 31, 2019 and January 1, 2020	154,445
Cash purchase of Gelesis preferred shares (please refer to Note 6)	10,000
Cash purchase of Vor preferred shares	1,150
Gain/(Loss) on changes in fair value	41,297
Balance at January 1, 2021 before allocation of associate loss to long-term interest	206,892
Cash purchase of Vor preferred shares	500
Reclassification of Vor from level 3 to level 1	(33,365)
Gain/(Loss) on changes in fair value	65,505
Balance as of December 31, 2021 before allocation of associate loss to long-term interest	**239,533**
Share of associate loss allocated to long-term interest (please refer to Note 5)	(96,709)
Balance as of December 31, 2021 after allocation of associate loss to long-term interest	**142,824**

The change in fair value of investments held at fair value are recorded in Gain/(loss) on investments held at fair value in the Consolidated Statements of Comprehensive Income/(Loss).

The table below sets out information about the significant unobservable inputs used at December 31, 2021, in the fair value measurement of the Group's material investments held at fair value categorized as Level 3 in the fair value hierarchy:

Fair Value at December 31, 2021	Valuation Technique	Unobservable Inputs	Weighted Average	Sensitivity to Decrease in Input
238,231	Market – PWERM & Hybrid allocation	Estimated time to exit (*)	0.76	
		Discount rate	20.0%	Fair value increase
		Volatility	62.0%	

The following summarizes the sensitivity from the assumptions made by the Company with respect to the significant unobservable inputs which are categorized as Level 3 in the fair value hierarchy and used in the fair value measurement of the Group's investments held at fair value (Please refer to Note 5):

Input	Investments Held at Fair Value	
As of December 31, 2021	Sensitivity Range	Financial Asset Increase/(Decrease) $000s
Investee Enterprise Value	-2 %	(4,559)
	+2%	4,652
Time to Liquidity (*)	-6 Months	11,828
	+6 Months	(14,691)
Discount Rate	-5 %	3,842
	+5%	(3,408)

(*) Gelesis investment in preferred shares was excluded from the sensitivity calculation with regard to the time to liquidity as changing the time to liquidity in the Gelesis valuation would result in an unreasonable assumption leading to an unreasonable alternative value considering the circumstances on the financial reporting date.

Warrants

Warrants issued by subsidiaries within the Group are classified as liabilities, as they will be settled in a variable number of preferred shares. The following table summarizes the changes in the Group's subsidiary warrant liabilities, which were categorized as Level 3 in the fair value hierarchy:

	Subsidiary Warrant Liability $000s
Balance at January 1, 2019	13,012
Warrant Issuance	4,706
Gelesis Deconsolidation	(21,611)
Change in fair value	11,890
Balance at December 31, 2019 and January 1, 2020	7,997
Warrant Issuance	92
Change in fair value	117
Balance at December 31, 2020 and January 1, 2021	8,206
Change in fair value - finance costs (income)	(1,419)
Balance at December 31, 2021	**6,787**

The change in fair value of warrants are recorded in Finance income/(costs) – fair value accounting in the Consolidated Statements of Comprehensive Income/(Loss).

In connection with various amendments to its 2010 Loan and Security Agreement, Follica issued Series A-1 preferred share warrants at various dates in 2013 and 2014. Each of the warrants has an exercise price of $0.14 and a contractual term of ten years from the date of issuance. In 2017, in conjunction with the issuance of convertible notes, the exercise price of the warrants was adjusted to $0.07 per share.

In connection with the September 2, 2020 Oxford Finance LLC loan issuance, Vedanta also issued Oxford Finance LLC 12,886 Series C-2 preferred share warrants with an exercise price of $23.28 per share, expiring September 2030.

The $6.8 million warrant liability at December 31, 2021, was largely attributable to the outstanding Follica preferred share warrants.

The table below sets out the weighted average of significant unobservable inputs used at December 31, 2021, with respect to determining the fair value of the Group's warrants categorized as Level 3 in the fair value hierarchy:

Assumption/Input		Warrants
Expected term		1.66
Expected volatility		49.1 %
Risk free interest rate		0.7 %
Expected dividend yield		— %
Estimated fair value of the preferred share	$	2.72

The following summarizes the sensitivity from the assumptions made by the Company with respect to the significant unobservable inputs which are categorized as Level 3 in the fair value hierarchy and used in the fair value measurement of the Group's warrant liabilities:

Input	Warrant Liability	
As at December 31, 2021	Sensitivity Range	Financial Liability Increase/(Decrease) $000s
Discount Rate used in the calculation of estimated fair value of the preferred share	-5 %	8,390
	+5%	(4,222)

Short-term Note from Associate

On December 7, 2021, Gelesis issued PureTech a $15.0 million note to be repaid the earlier of three business days after the closing of the business combination of Gelesis with Capstar Special Acquisition Corp ("Capstar"), or 30 days following the termination of such business combination. In the event of the business combination termination, the Company, who represented the majority of the note holders, could have elected to convert the note at the next equity financing at a discount of 25% from the financing price. The note bears interest at a rate of 10% per annum.

The note was repaid by Gelesis in January 2022 due to the closing of the business combination between Gelesis and Capstar on January 13, 2022.

The Note is measured at fair value in accordance with IFRS 9 with changes in fair value recorded as profit or loss in the Consolidated Statement of Comprehensive Income/(Loss). The fair value as of December 31, 2021, of $15.1 million approximated the note's contractual amount and the change in fair value from issuance date to December 31, 2021, was not material.

Fair Value Measurement and Classification

The fair value of financial instruments by category at December 31, 2021 and 2020:

	2021					
	Carrying Amount		**Fair Value**			
	Financial Assets $000s	**Financial Liabilities $000s**	**Level 1 $000s**	**Level 2 $000s**	**Level 3 $000s**	**Total $000s**
Financial assets:						
Money Markets[1]	**432,649**	**—**	**432,649**	**—**	**—**	**432,649**
Short-term note from associate	**15,120**	**—**	**—**	**—**	**15,120**	**15,120**
Investments held at fair value[2]	**493,888**	**—**	**254,355**	**—**	**239,533**	**493,888**
Trade and other receivables[3]	**3,174**	**—**	**—**	**3,174**	**—**	**3,174**
Total financial assets	**944,832**	**—**	**687,005**	**3,174**	**254,653**	**944,832**
Financial liabilities:						
Subsidiary warrant liability	**—**	**6,787**	**—**	**—**	**6,787**	**6,787**
Subsidiary preferred shares	**—**	**174,017**	**—**	**—**	**174,017**	**174,017**
Subsidiary notes payable	**—**	**3,916**	**—**	**1,330**	**2,586**	**3,916**
Share based liability awards	**—**	**7,362**	**6,081**	**—**	**1,281**	**7,362**
Total financial liabilities	**—**	**192,082**	**6,081**	**1,330**	**184,671**	**192,082**

1 Issued by a diverse group of corporations, largely consisting of financial institutions, virtually all of which are investment grade.

2 Balance prior to share of associate loss allocated to long-term interest (please refer to Note 5).

3 Outstanding receivables are owed primarily by government agencies, virtually all of which are investment grade.

	2020					
	Carrying Amount		Fair Value			
	Financial Assets $000s	Financial Liabilities $000s	Level 1 $000s	Level 2 $000s	Level 3 $000s	Total $000s
Financial assets:						
Money Markets[1]	394,143	—	394,143	—	—	394,143
Investments held at fair value[2]	553,167	—	346,275	—	206,892	553,167
Loans and receivables:						
Trade and other receivables[3]	2,558	—	—	2,558	—	2,558
Total financial assets	949,867	—	740,417	2,558	206,892	949,867

Financial liabilities:						
Subsidiary warrant liability	—	8,206	—	—	8,206	8,206
Subsidiary preferred shares	—	118,972	—	—	118,972	118,972
Subsidiary notes payable	—	26,455	—	1,330	25,125	26,455
Total financial liabilities	—	153,633	—	1,330	152,303	153,633

1 Issued by a diverse group of corporations, largely consisting of financial institutions, virtually all of which are investment grade.
2 Balance prior to share of associate loss allocated to long-term interest (please refer to Note 5).
3 Outstanding receivables are owed primarily by corporations and government agencies, virtually all of which are investment grade.

17. Subsidiary Notes Payable

The subsidiary notes payable are comprised of loans and convertible notes. As of December 31, 2021 and 2020, the loan in Follica and the financial instruments for Knode and Appeering did not contain embedded derivatives and therefore these instruments continue to be held at amortized cost. The notes payable consist of the following:

As of December 31,	**2021 $000s**	2020 $000s
Loans	**1,330**	1,330
Convertible notes	**2,586**	25,125
Total subsidiary notes payable	**3,916**	26,455

Loans

In October 2010, Follica entered into a loan and security agreement with Lighthouse Capital Partners VI, L.P. The loan is secured by Follica's assets, including Follica's intellectual property and bears interest at a rate of 12.0 percent. The outstanding loan balance totaled approximately $1.3 million and $1.3 million as of December 31, 2021 and December 31, 2020. The accrued interest on such loan balance is presented as Other current liabilities and totaled approximately $0.6 million and $0.5 million as of December 31, 2021 and December 31, 2020, respectively. The increase in 2021 is attributed to interest expense for the year ended December 31, 2021.

Convertible Notes

Convertible Notes outstanding were as follows:

	Vedanta $000s	Knode $000s	Appeering $000s	Sonde $000s	Total $000s
January 1, 2020	—	50	75	—	125
Gross principal - issuance of notes	25,000	—	—	—	25,000
Change in fair value	—	—	—	—	—
December 31, 2020 and January 1, 2021	25,000	50	75	—	25,125
Gross principal - issuance of notes - financing activity	—	—	—	2,215	2,215
Accrued interest on convertible notes - finance costs	797	—	—	70	867
Conversion to subsidiary preferred shares	(25,797)	—	—	—	(25,797)
Change in fair value - finance costs	—	—	—	175	175
December 31, 2021	**—**	**50**	**75**	**2,461**	**2,586**

On December 30, 2020, Vedanta issued a $25.0 million convertible promissory note to an investor. The note bore interest at an annual rate of 6.0 percent and its maturity date was the first anniversary of the note. Prepayment of the note was not allowed and there was no conversion discount feature on the note. The note was mandatorily convertible in a Qualified equity financing and a Qualified Public Offering at the current price of the financing or offering, all as defined in the note purchase agreement. In addition, the note allowed for optional conversion immediately prior to a Non Qualified public offering, Non Qualified Equity financing, or a Corporate transaction and for a pay-out in the case of a change of control transaction. On July 19, 2021, upon the occurrence of Vedanta's Series D preferred share issuance that was considered to be a Qualified Equity Financing, the entire outstanding amount of the note, principal and interest, was converted into Series D preferred shares of Vedanta at the current price of the financing. For further details, please see Note 15.

On April 6, 2021, and on November 24, 2021, Sonde issued unsecured convertible promissory notes to its existing shareholders for a combined total of $4.3 million, of which $2.2 million were issued to third party shareholders (and $2.1 million were issued to the Company and eliminated in consolidation). The notes bear interest at an annual rate of 6.0 percent and mature on the second anniversary of the issuance. The notes mandatorily convert in a Qualified Financing, as defined in the note purchase agreement, at a discount of 20.0 percent from the price per share in the Qualified Financing. In addition, the notes allow for optional conversion concurrently with the closing of a Non-Qualified Equity Financing to the Non-Qualified Equity Securities then issued and sold at a discount of 20.0 percent from the price per share in the Non Qualified Equity Financing. In the event of no conversion or repayment of the notes prior to a Change in Control, the notes shall become immediately due and payable prior to the closing of such Change in Control at three times the outstanding principal plus accrued interest.

For the Vedanta and Sonde convertible notes, since these Notes contain embedded derivatives, the Notes were assessed under IFRS 9 and the entire financial instruments were elected to be accounted for as FVTPL. The Vedanta convertible note was settled through its conversion in July 2021. See above. See Note 16 for further details on the fair value of the Sonde notes.

18. Non-Controlling Interest

During the year ended December 31, 2021, the Company acquired the non-controlling interest in Alivio which resulted in Alivio being transferred to the Internal segment. The Company has revised in the 2021 financial statements the prior period financial information related to the segmentation of NCI, to conform to the presentation as of and for the year ending December 31, 2021. Please refer to Note 4 "Segment Information" for further details regarding reportable segments.

The following table summarizes the changes in the equity classified non-controlling ownership interest in subsidiaries by reportable segment:

	Internal $000s	Controlled Founded Entities $000s	Non-Controlled Founded Entities $000s	Parent Company & Other $000s	Total $000s
Balance at January 1, 2019 *	(15,102)	(20,800)	(73,225)	592	(108,535)
Share of comprehensive loss	(17,643)	(13,483)	(23,953)	—	(55,079)
Deconsolidation of subsidiary	—	—	97,178	—	97,178
Subsidiary note conversion and changes in NCI ownership interest	—	23,049	—	—	23,049
Equity settled share-based payments	—	1,683	—	—	1,683
Acquisition of a subsidiary non controlling interest	24,039	—	—	—	24,039
Other	24	—	—	1	25
Balance at December 31, 2019 and January 1, 2020	(8,682)	(9,551)	—	593	(17,639)
Share of comprehensive loss	(191)	(1,211)	—	(15)	(1,417)
Equity settled share-based payments	305	2,517	—	—	2,822
Other	—	30	—	(6)	24
Balance at December 31, 2020 and January 1, 2021	(8,567)	(8,215)	—	574	(16,209)
Share of comprehensive income (loss)	(96)	(2,069)	—	15	(2,151)
NCI exercise of share-based awards in subsidiaries - change in NCI interest	—	(5,922)	—	—	(5,922)
Equity settled share-based payments	(4)	6,256	—	—	6,252
Acquisition of a subsidiary non controlling interest	8,668	—	—	—	8,668
Other	—	—	—	(6)	(6)
Balance as of December 31, 2021	**—**	**(9,950)**	**—**	**583**	**(9,368)**

(*) Revised to reclassify Alivio into the Internal segment to comply with current period classification. See Note 4.

The following tables summarize the financial information related to the Group's subsidiaries with material non-controlling interests, aggregated for interests in similar entities, and before and after intra group eliminations.

	2021				
For the year ended December 31	Internal $000s	Controlled Founded Entities $000s	Non-Controlled Founded Entities $000s	Intra-group eliminations $000s	Total $000s
Statement of Comprehensive Loss					
Total revenue	**—**	**7,771**	**—**	**—**	**7,771**
Income/(loss) for the year	**—**	**(50,436)**	**—**	**792**	**(49,644)**
Other comprehensive income/(loss)	**—**	**—**	**—**	**—**	**—**
Total comprehensive income/(loss) for the year	**—**	**(50,436)**	**—**	**792**	**(49,644)**
Statement of Financial Position					
Total assets	**—**	**66,279**	**—**	**(161)**	**66,118**
Total liabilities	**—**	**228,856**	**—**	**(10,755)**	**218,101**
Net assets/(liabilities)	**—**	**(162,576)**	**—**	**10,594**	**(151,982)**

As of December 31, 2021, Controlled Founded Entities with non-controlling interests primarily include Follica Incorporated, Sonde Health Inc., Entrega Inc. and Vedanta Biosciences, Inc. Ownership interests of the non-controlling interests in Follica Incorporated, Entrega Inc., Sonde Health Inc., and Vedanta Biosciences, Inc are 19.9 percent, 11.7 percent, 6.2 percent and 3.7 percent, respectively. In addition, Non-controlling interests include the amounts recorded for subsidiary stock options, with the vast majority comprising of Vedanta stock options.

For the year ended December 31	2020 Internal $000s	Controlled Founded Entities $000s	Non-Controlled Founded Entities $000s	Intra-group eliminations $000s	Total $000s
Statement of Comprehensive Loss					
Total revenue	3,267	1,957	—	—	5,224
Income/(loss) for the year	(2,407)	(53,535)	—	1,073	(54,869)
Total comprehensive income/(loss) for the year	(2,407)	(53,535)	—	1,073	(54,869)
Statement of Financial Position					
Total assets	1,297	67,048	—	(7)	68,339
Total liabilities	12,086	188,345	—	(14,621)	185,809
Net assets/(liabilities)	(10,788)	(121,296)	—	14,615	(117,470)

As of December 31, 2020, Internal segment with non-controlling interests include Alivio, Controlled Founded Entities with non-controlling interests primarily include, Follica Incorporated, Sonde Health Inc., and Vedanta Biosciences, Inc. Ownership interests of the non-controlling interests in Alivio Therapeutics, Inc., Follica Incorporated, Sonde Health Inc., and Vedanta Biosciences, Inc are 8.1 percent, 19.9 percent, 4.5 percent and 0.4 percent, respectively. In addition, Non-controlling interests include the amounts recorded for subsidiary stock options, with the vast majority comprising of Vedanta stock options.

For the year ended December 31	2019 Internal $000s	Controlled Founded Entities $000s	Non-Controlled Founded Entities $000s
Statement of Comprehensive Loss			
Total revenue	8,006	41	—
Income/(loss) for the year	(26,668)	(23,871)	(47,905)
Other comprehensive income/(loss)	—	—	(10)
Total comprehensive income/(loss) for the year	(26,668)	(23,871)	(47,915)

On July 19, 2019 PureTech and a third party investor converted their convertible debt in Follica to Follica Preferred shares (presented as liabilities) and Follica common shares. The amount of convertible debt converted by the third party investor into Follica common shares amounted to $2.4 million (see also Note 16). As a result of the conversion Follica NCI share (in Follica common stock) was reduced from 68 percent to 19.9 percent, which resulted in a reduction in the NCI share in Follica's shareholders' deficit of $19.9 million. The excess of the change in the book value of NCI ($19.9 million noted above) over the contribution made by NCI ($2.4 million) amounted to $17.5 million and was recorded as a loss directly in shareholders' equity.

During 2019 a subsidiary of the Company fully funded by the Company ceased its operations and became inactive. This resulted in a change in the NCI share in the subsidiary deficit. As a result the Company recorded a loss directly in equity of $3.1 million.

On October 1, 2019, PureTech acquired the remaining 10.0 percent of minority non-controlling interests of PureTech LYT, Inc. (previously named Ariya Therapeutics, Inc.), increasing its ownership from 90.0 percent to 100.0 percent. In consideration for the acquisition of minority interests, PureTech issued 2,126,338 shares of common shares. The fair value of the shares issued in consideration for the minority non-controlling interest amounted to $9.1 million. The carrying amount of the non-controlling interest at the acquisition was a $24.0 million deficit and the excess of the consideration paid over the book value of the non-controlling interest of approximately $33.1 million was recorded directly in shareholders' equity.

On June 11, 2021, PureTech acquired the remaining 17.1 percent of the minority non-controlling interests of Alivio (after exercise of all in the money stock options) increasing its ownership to 100.0 percent of Alivio. The consideration for such non controlling interests amounted to $1.2 million, to be paid in three equal installments, with the first installment of $0.4 million paid at the effective date of the transaction and two additional installment to be paid upon the occurrence of certain contingent events. The Group recorded a contingent consideration liability of $0.6 million at fair value for the two additional installments, resulting in a total acquisition cost of $1.0 million. The excess of the consideration paid over the book value of the non-controlling interest of approximately $9.6 million was recorded directly as a charge to shareholders' equity. The second installment of $0.4 million was paid in July 2021, upon the occurrence of the contingent event specified in the agreement. The contingent consideration liability is adjusted to fair value at the end of each reporting period with changes in fair value recorded in earnings. Changes in fair value of the aforementioned contingent consideration liability were not material.

On December 1, 2021, options holders in Entrega exercised options into shares of common stock, increasing the NCI interest held from 0.2 percent to 11.7 percent. During 2021 option holders in Vedanta exercised options and increased the NCI interest to 3.7 percent. The exercise of the options resulted in an increase in the NCI share in Entrega's and Vedanta's shareholder's deficit of $5.9 million. The consideration paid by NCI ($0.1 million) together with the increase in NCI share in Entrega's and Vedanta's shareholder deficit ($5.9 million) amounted to $6.0 million and was recorded as a gain directly in shareholders' equity.

19. Trade and Other Payables

Information regarding Trade and other payables was as follows:

As of December 31,	2021 $000s	2020 $000s
Trade payables	**11,346**	8,871
Accrued expenses	**17,309**	9,090
Income tax payable	**57**	1,260
Liability settled share based awards	**4,703**	—
Other	**2,403**	2,606
Total trade and other payables	**35,817**	21,826

20. Long-term loan

In September 2020, Vedanta entered into a $15.0 million loan and security agreement with Oxford Finance LLC. The loan is secured by Vedanta's assets, including equipment, inventory and intellectual property. The loan bears a floating interest rate of 7.7 percent plus the greater of (i) 30 day U.S. Dollar LIBOR reported in the Wall Street Journal or (ii) 0.17 percent. The loan matures September 2025 and requires interest only payments for the initial 24 months. The loan also carries a final fee upon full repayment of 7.0 percent of the original principal, or $1.1 million. For loan consideration, Vedanta also issued Oxford Finance LLC 12,886 Series C-2 preferred share warrants with an exercise price of $23.28 per share, expiring September 2030. The outstanding loan balance totaled approximately $15.1 million as of December 31, 2021.

The following table summarizes long-term loan activity for the years ended December 31, 2021 and 2020:

	Long-term loan	
	2021 $000s	2020 $000s
Balance at January 1,	**14,818**	—
Net loan proceeds	**—**	14,720
Accrued interest	**1,502**	496
Interest paid	**(1,201)**	(296)
Other	**—**	(102)
Balance at December 31,	**15,118**	14,818

The following table summarizes Vedanta's future principal payments for the long-term loan as of December 31, 2021:

Balance Type	2022	2023	2024	2025	Total
Principal	857	5,143	5,143	3,857	15,000
Balance of accreted premium net of unamortized issuance costs					118
Total					**15,118**

The long-term loan is presented as follows in the Statement of Financial Position as of December 31, 2021 and 2020:

	Long-term loan	
	2021 $000s	2020 $000s
Current portion of Long-term loan	**857**	—
Long-term loan	**14,261**	14,818
Total Long-term loan	**15,118**	14,818

21. Leases

The activity related to the Group's right of use asset and lease liability for the years ended December 31, 2021 and 2020 is as follows:

	Right of use asset, net	
	2021 $000s	2020 $000s
Balance at January 1,	**20,098**	22,383
Additions	**739**	—
Tenant improvement - lease incentive	**(733)**	—
Depreciation	**(2,938)**	(2,699)
Adjustments	**—**	414
Balance at December 31,	**17,166**	20,098

	Total lease liability	
	2021 $000s	2020 $000s
Balance at January 1,	**35,348**	37,843
Additions	**1,016**	—
Cash paid for rent - principal - financing cash flow	**(3,375)**	(2,908)
Cash paid for rent - interest	**(2,181)**	(2,354)
Interest expense	**2,181**	2,354
Adjustments	**—**	414
Balance at December 31,	**32,990**	35,348

Depreciation of the right-of-use assets, which virtually all consist of leased real estate, is included in the General and administrative expenses and Research and development expenses line items in the Consolidated Statements of Comprehensive Income/(Loss). The Company recorded depreciation expense of $2.9 million, $2.7 million and $3.2 million for the years ended December 31, 2021, 2020 and 2019, respectively.

The following details the short term and long-term portion of the lease liability as at December 31, 2021 and 2020:

	Total lease liability	
	2021 $000s	2020 $000s
Short-term Portion of Lease Liability	**3,950**	3,261
Long-term Portion of Lease Liability	**29,040**	32,088
Total Lease Liability	**32,990**	35,348

The following table details the future maturities of the lease liability, showing the undiscounted lease payments to be paid after the reporting date:

	2021 $000s
Less than one year	**5,927**
One to two years	**6,591**
Two to three years	**6,754**
Three to four years	**5,168**
Four to five years	**4,419**
More than five years	**12,033**
Total undiscounted lease maturities	**40,893**
Interest	**7,903**
Total lease liability	**32,990**

During the year ended December 31, 2019, PureTech entered into a lease agreement for certain premises consisting of approximately 50,858 rentable square feet of space located at 6 Tide Street. The lease commenced on April 26, 2019 ("Commencement Date") for an initial term consisting of ten years and three months and there is an option to extend for two consecutive periods of five years each. The Company assessed at lease commencement date whether it is reasonably certain to exercise the extension options and deemed such options not reasonably certain to be exercised. The Company will reassess whether it is reasonably certain to exercise the options only if there is a significant event or significant changes in circumstances within its control.

On June 26, 2019, PureTech executed a sublease agreement with Gelesis. The lease is for the approximately 9,446 rentable square feet located on the sixth floor of the Company's former offices at the 501 Boylston Street building. The sublessee obtained possession of the premises on June 1, 2019 and the rent period term began on June 1, 2019 and expires on August 31, 2025. The sublease was determined to be a finance lease. As of December 31, 2021, the balances related to the sublease were as follows:

	Total lease receivable $000s
Short-term Portion of Lease Receivable	415
Long-term Portion of Lease Receivable	1,285
Total Lease Receivable	**1,700**

The following table details the future maturities of the lease receivable, showing the undiscounted lease payments to be received after the reporting date:

	2021 $000s
Less than one year	**504**
One to two years	**513**
Two to three years	**523**
Three to four years	**353**
Total undiscounted lease receivable	**1,892**
Unearned Finance income	**192**
Net investment in the lease	**1,700**

On August 6, 2019, PureTech executed a sublease agreement with Dewpoint Therapeutics, Inc. ("Dewpoint"). The sublease was for approximately 11,852 rentable square feet located on the third floor of the 6 Tide Street building, where the Company's offices are currently located. Dewpoint obtained possession of the premises on September 1, 2019 with a rent period term that began on September 1, 2019, and expired on August 31, 2021. The sublease was determined to be an operating lease.

Rental income recognized by the Company during the years ended December 31, 2021, 2020 and 2019, was $0.65 million, $1.08 million and $0.4 million, respectively and is included in the Other income/(expense) line item in the Consolidated Statements of Comprehensive Income/(Loss).

22. Capital and Financial Risk Management

Capital Risk Management

The Group's capital and financial risk management policy is to maintain a strong capital base so as to support its strategic priorities, maintain investor, creditor and market confidence as well as sustain the future development of the business. The Group's objectives when managing capital are to safeguard its ability to continue as a going concern in order to provide returns for shareholders and benefits for other stakeholders and to maintain an optimal capital structure to reduce the cost of capital. To maintain or adjust the capital structure, the Group may issue new shares or incur new debt. The Group has some external debt and no material externally imposed capital requirements. The Group's share capital is clearly set out in Note 14.

Management continuously monitors the level of capital deployed and available for deployment in the Internal and Parent segments as well as at Controlled Founded Entities. The Directors seek to maintain a balance between the higher returns that might be possible with higher levels of deployed capital and the advantages and security afforded by a sound capital position.

The Group's Directors have overall responsibility for establishment and oversight of the Group's capital and risk management framework. The Group is exposed to certain risks through its normal course of operations. The Group's main objective in using financial instruments is to promote the development and commercialization of intellectual property through the raising and investing of funds for this purpose. The Group's policies in calculating the nature, amount and timing of investments are determined by planned future investment activity. Due to the nature of activities and with the aim to maintain the investors' funds as secure and protected, the Group's policy is to hold any excess funds in highly liquid and readily available financial instruments and maintain insignificant exposure to other financial risks.

COVID-19

In March 2020, the World Health Organization declared the COVID-19 outbreak a pandemic. The pandemic has since caused widespread and significant disruption to daily life and the global economy as governments have taken actions, including the issuance of stay-at-home orders and social distancing guidelines, and businesses have adjusted their activities. While our business, operations and financial condition and results have not been significantly impacted in 2020 or 2021, as a result of the COVID-19 pandemic, we have taken swift action to ensure the safety of our employees and other stakeholders. The Group continues to monitor the latest developments regarding the COVID-19 pandemic on business, operations, and financial condition and results, and has made certain assumptions regarding the pandemic for purposes of the Group's operational planning and financial projections, including assumptions regarding the duration and severity of the pandemic and the global macroeconomic impact of the pandemic. Despite careful tracking and planning, however, the Group is unable to accurately predict the extent of the impact of the pandemic on the business, operations, and financial condition and results in future periods due to the uncertainty of future developments. The Group is focused on all aspects of the business and is implementing measures aimed at mitigating issues where possible.

Credit Risk

The Group has exposure to the following risks arising from financial instruments:

Credit risk is the risk of financial loss to the Group if a customer or counterparty to a financial instrument fails to meet its contractual obligations. Financial instruments that potentially subject the Group to concentrations of credit risk consist principally of cash and cash equivalents and trade and other receivables. The Group held the following balances (not including the income tax receivable resulting from overpayment of income taxes, see Note 25):

As of December 31	**2021 $000s**	2020 $000s
Cash and cash equivalents	**465,708**	403,881
Trade and other receivables	**3,174**	2,558
Total	**468,882**	406,438

The Group invests its excess cash in U.S. Treasury Bills, U.S. debt obligations and money market accounts, which the Group believes are of high credit quality. Further the Group's cash and cash equivalents and short-term investment are held at diverse, investment-grade financial institutions.

The Group assesses the credit quality of customers on an ongoing basis. The credit quality of financial assets is assessed by historical and recent payment history, counterparty financial position, reference to credit ratings (if available) or to historical information about counterparty default rates. The Group does not have expected credit losses owing largely to a small number of counterparties and the high credit quality of such counterparties (primarily the US government and large funds in respect of grant income).

The aging of trade and other receivables that were not impaired at December 31 is as follows:

As of December 31	**2021 $000s**	2020 $000s
Not impaired	**3,174**	2,558
Total	**3,174**	2,558

Liquidity Risk

Liquidity risk is the risk that the Group will encounter difficulty in meeting the obligations associated with its financial liabilities that are settled by delivering cash or another financial asset. The Group actively manages its risk of a funds shortage by closely monitoring the maturity of its financial assets and liabilities and projected cash flows from operations, under both normal and stressed conditions, without incurring unacceptable losses or risking damage to the Group's reputation. Due to the nature of these financial liabilities, the funds are available on demand to provide optimal financial flexibility.

The table below summarizes the maturity profile of the Group's financial liabilities, including subsidiary preferred shares that have customary liquidation preferences, as of December 31, 2021 and 2020, based on contractual undiscounted payments:

As of December 31	2021 Carrying Amount $000s	Within Three Months $000s	Three to Twelve Months $000s	One to Five Years $000s	Total $000s (*)
Long-term loan (non-current + current)	**15,118**	**296**	**2,182**	**16,274**	**18,752**
Subsidiary notes payable	**3,916**	**3,916**	**—**	**—**	**3,916**
Trade and other payables	**35,817**	**35,817**	**—**	**—**	**35,817**
Warrants[2]	**6,787**	**6,787**	**—**	**—**	**6,787**
Subsidiary preferred shares (Note 15)[1]	**174,017**	**174,017**	**—**	**—**	**174,017**
Total	**235,656**	**220,833**	**2,182**	**16,274**	**239,290**

As of December 31	2020 Carrying Amount $000s	Within Three Months $000s	Three to Twelve Months $000s	One to Five Years $000s	Total $000s (*)
Long-term loan	14,818	296	905	18,780	19,981
Subsidiary notes payable	26,455	1,455	25,000	—	26,455
Trade and other payables	21,826	21,826	—	—	21,826
Warrants[2]	8,206	8,206	—	—	8,206
Subsidiary preferred shares (Note 15)[1]	118,972	118,972	—	—	118,972
Total	190,278	150,756	25,905	18,780	195,441

1 Redeemable only upon a liquidation or Deemed liquidation event, as defined in the applicable shareholder documents.

2 Warrants issued by subsidiaries to third parties to purchase preferred shares.

(*) Does not include payments in respect of lease obligations. For the contractual future payments related to lease obligations, see Note 21.

Interest Rate Sensitivity

As of December 31, 2021, the Group had cash and cash equivalents of $465.7 million. The Group's exposure to interest rate sensitivity is impacted by changes in the underlying U.K. and U.S. bank interest rates. The Group has not entered into investments for trading or speculative purposes. Due to the conservative nature of the Group's investment portfolio, which is predicated on capital preservation and investments in short duration, high-quality U.S. Treasury Bills and U.S. debt obligations and related money market accounts, a change in interest rates would not have a material effect on the fair market value of the Group's portfolio, and therefore the Group does not expect operating results or cash flows to be significantly affected by changes in market interest rates.

Controlled Founded Entity Investments

The Group maintains investments in certain Controlled Founded Entities. The Group’s investments in Controlled Founded Entities are eliminated as intercompany transactions upon financial consolidation. The Group is however exposed to a preferred share liability owing to the terms of existing preferred shares and the ownership of Controlled Founded Entities preferred shares by third parties. As discussed in Note 15, certain of the Group’s subsidiaries have issued preferred shares that include the right to receive a payment in the event of any voluntary or involuntary liquidation, dissolution or winding up of a subsidiary, including in the event of "deemed liquidation" as defined in the incorporation documents of the entities, which shall be paid out of the assets of the subsidiary available for distribution to shareholders and before any payment shall be made to holders of ordinary shares. The liability of preferred shares is maintained at fair value through the profit and loss. The Group’s strong cash position, budgeting and forecasting processes, as well as decision making and risk mitigation framework enable the Group to robustly monitor and support the business activities of the Controlled Founded Entities to ensure no exposure to dissolution or liquidation. Accordingly, the Group views exposure to 3rd party preferred share liability as low.

Non-Controlled Founded Entity Investments

The Group maintains certain investments in Non-Controlled Founded Entities which are deemed either as investments and accounted for as investments held at fair value or associates and accounted for under the equity method (please refer to Note 1). The Group's exposure to investments held at fair value is $397.2 million as of December 31, 2021, and the Group may or may not be able to realize the value in the future. Accordingly, the Group views the risk as high. The Group’s exposure to investments in associates is limited to the carrying amount of the investment in an Associate. The Group is not exposed to further contractual obligations or contingent liabilities beyond the value of initial investment. As of December 31, 2021, Gelesis was the only associate. The carrying amount of the investment in Gelesis as an associate was zero. Accordingly, the Group does not view this as a risk. Please refer to Notes 5,6 and 16 for further information regarding the Group's exposure to Non-Controlled Founded Entity Investments.

Equity Price Risk

As of December 31, 2021, the Group held 1,656,564 common shares of Karuna and 3,207,200 common shares of Vor. The fair value of the Group's investment in the common stock of Karuna and Vor was $217.0 million and $37.3 million respectively.

The investments in Karuna and Vor are exposed to fluctuations in the market price of these common shares. The effect of a 10.0 percent adverse change in the market price of Karuna and Vor common shares as of December 31, 2021, would have been a loss of approximately $21.7 million and $3.7 million respectively, recognized as a component of Other income (expense) in the Consolidated Statements of Comprehensive Income/(Loss).

Foreign Exchange Risk

The Group maintains consolidated financial statements in the Group's functional currency, which is the U.S. dollar. Monetary assets and liabilities denominated in currencies other than the functional currency are translated into the functional currency at rates of exchange prevailing at the balance sheet dates. Non-monetary assets and liabilities denominated in foreign currencies are translated into the functional currency at the exchange rates prevailing at the date of the transaction. Exchange gains or

losses arising from foreign currency transactions are included in the determination of net income (loss) for the respective periods. Such foreign currency gains or losses were not material for all reported periods. See Note 9.

The Group does not currently engage in currency hedging activities since its foreign currency risk is limited, but the Group may begin to do so in the future if and when its foreign currency risk exposure changes. Instruments that may be used to hedge future risks include foreign currency forward and swap contracts. These instruments may be used to selectively manage risks, but there can be no assurance that the Group will be fully protected against material foreign currency fluctuations.

23. Commitments and Contingencies

The Group is party to certain licensing agreements where the Group is licensing IP from third parties. In consideration for such licenses the Group has made upfront payments and may be required to make additional contingent payments based on developmental and sales milestones and/or royalty on future sales. As of December 31, 2021, these milestone events have not yet occurred and therefore the Group does not have a present obligation to make the related payments in respect of the licenses. Such milestones are dependent on events that are outside of the control of the Group and many of these milestone events are remote of occurring. As of December 31, 2021, payments in respect of developmental milestones that are dependent on events that are outside the control of the Group but are reasonably possible to occur amounted to approximately $10.3 million. These milestone amounts represent an aggregate of multiple milestone payments depending on different milestone events in multiple agreements. The probability that all such milestone events will occur in the aggregate is remote. Payments made to license IP represent the acquisition cost of intangible assets. See Note 12.

The Group is party to certain sponsored research arrangements as well as arrangements with contract manufacturing and contract research organizations, whereby the counterparty provides the Company with research and/or manufacturing services. As of December 31, 2021, the noncancellable commitments in respect of such contracts amounted to approximately $6.7 million.

24. Related Parties Transactions

Related Party Subleases and royalties

During 2019, PureTech executed sublease agreements with a related party, Gelesis. Please refer to Note 21 for further details regarding the sublease.

The Group receives royalties from Gelesis on its product sales. Such royalties amounted to $231 thousand and $54 thousand for the years ended December 31, 2021 and 2020, respectively and are presented in Contract revenue in the Consolidated Statements of Comprehensive Income/(Loss).

Key Management Personnel Compensation

Key management includes executive directors and members of the executive management team of the Group (not including compensation provided to independent directors). Full details for Directors' remuneration can be found in the Directors' Remuneration Report. The key management personnel compensation of the Group was as follows for the years ended December 31:

As of December 31	**2021 $000s**	2020 $000s	2019 $000s
Short-term employee benefits	**4,666**	4,833	5,543
Share-based payments	**4,045**	5,822	2,774
Total	**8,711**	10,656	8,317

Short-term employee benefits include salaries, health care and other non-cash benefits. Share-based payments are generally subject to vesting terms over future periods.

For cash settlements of share based awards – see Note 8 .

During the year ended December 31, 2021, the company incurred $782 thousand of general administrative expenses that was paid to a related party.

Convertible Notes Issued to Directors

Certain members of the Group have invested in convertible notes issued by the Group's subsidiaries. As of December 31, 2021, 2020 and 2019, the outstanding related party notes payable totaled $94 thousand, $89 thousand and $84 thousand respectively, including principal and interest.

The notes issued to related parties bear interest rates, maturity dates, discounts and other contractual terms that are the same as those issued to outside investors during the same issuances, as described in Note 17.

Directors' and Senior Managers' Shareholdings and Share Incentive Awards

The Directors and senior managers hold beneficial interests in shares in the following businesses and sourcing companies as at December 31, 2021:

	Business Name (Share Class)	**Number of shares held as of December 31, 2021**	**Number of options held as of December 31, 2021**	**Ownership Interest[1]**
Directors:				
Ms Daphne Zohar[2]	Gelesis (Common)	**179,443**	**1,207,006**	**5.03 %**
Dr Robert Langer	Entrega (Common)	**250,000**	**82,500**	**4.09 %**

Dr Raju Kucherlapati	Enlight (Class B Common)	**—**	**30,000**	**3.00 %**
Dr John LaMattina[3]	Akili (Series A-2 Preferred)	**37,372**	**—**	**0.80 %**
	Akili (Series C Preferred)	**11,755**	**—**	**0.20 %**
	Gelesis (Common)[3]	**50,540**	**—**	**0.18 %**
	Gelesis (Common)[4]	**33,051**	**33,578**	**0.24 %**
	Gelesis (Series A-1 Preferred)[3]	**49,523**	**—**	**0.18 %**
	Vedanta Biosciences (Common)	**25,000**	**—**	**0.17 %**
Senior Managers:				
Dr Bharatt Chowrira	Karuna (Common)[4]	**5,000**	**—**	**0.02 %**
Dr Joseph Bolen	Vor (Common)	**—**	**9,191**	**0.02 %**

1 Ownership interests as of December 31, 2021 are calculated on a diluted basis, including issued and outstanding shares, warrants and options (and written commitments to issue options) but excluding unallocated shares authorized to be issued pursuant to equity incentive plans and any shares issuable upon conversion of outstanding convertible promissory notes.

2 Common shares and options held by Yishai Zohar, who is the husband of Ms. Zohar. Ms. Zohar does not have any direct interest in the share capital of Gelesis. Ms Zohar recuses herself from any and all material decisions with regard to Gelesis.

3 Dr John and Ms Mary LaMattina hold 50,540 shares of common shares and 49,523 shares of Series A-1 preferred shares in Gelesis. Individually, Dr LaMattina holds 33,051 shares of Gelesis and convertible notes issued by Appeering in the aggregate principal amount of $50,000.

4 Options to purchase the listed shares were granted in connection with the service on such founded entity's Board of Directors and any value realized therefrom shall be assigned to PureTech Health, LLC.

Directors and senior managers hold 24,676,165 ordinary shares and 8.6 percent voting rights of the Company as of December 31, 2021. This amount excludes options to purchase 4,750,000 ordinary shares. This amount also excludes 4,666,514 shares, which are issuable based on the terms of performance based RSU awards granted to certain senior managers covering the financial years 2021, 2020 and 2019, and 67,140 shares, which are issuable to directors immediately prior to the Company's 2022 Annual General Meeting of Stockholders based on the terms of the RSU awards granted to non-executive directors in 2021. Such shares will be issued to such senior managers and non executive directors in future periods provided that performance and/or service conditions are met and certain of the shares will be withheld for payment of customary withholding taxes.

Short term Note from Associate

See Note 16 for details on the $15.0 million note issued by Gelesis to the Company. The Company recognized income of $0.1 million with respect to interest and changes in fair value related to the short term note.

25. Taxation

Tax on the profit or loss for the year comprises current and deferred income tax. Tax is recognized in the Consolidated Statements of Comprehensive Income/(Loss) except to the extent that it relates to items recognized directly in equity.

For the years ended December 31, 2021, 2020 and 2019, the Group filed a consolidated U.S. federal income tax return which included all subsidiaries in which the Company owned greater than 80 percent of the vote and value. For the years ended December 31, 2021, 2020 and 2019, the Group filed certain consolidated state income tax returns which included all subsidiaries in which the Company owned greater than 50 percent of the vote and value. The remaining subsidiaries file separate U.S. tax returns.

Amounts recognized in Consolidated Statements of Comprehensive Income/(Loss):

As of December 31	**2021 $000s**	2020 $000s	2019 $000s
Income/(loss) for the year	**(62,709)**	4,568	366,065
Income tax expense/(benefit)	**3,756**	14,401	112,409
Income/(loss) before taxes	**(58,953)**	18,969	478,474

Recognized income tax expense/(benefit):

As of December 31	**2021 $000s**	2020 $000s	2019 $000s
Federal	**22,138**	21,796	—
Foreign	**—**	—	—
State	**109**	—	—
Total current income tax expense/(benefit)	**22,247**	21,796	—
Federal	**(15,416)**	(7,349)	83,776
Foreign	**—**	—	—
State	**(3,075)**	(46)	28,633
Total deferred income tax expense/(benefit)	**(18,491)**	(7,395)	112,409
Total income tax expense/(benefit), recognized	**3,756**	14,401	112,409

The tax expense was $3.8 million, $14.4 million and $112.4 million in 2021, 2020 and 2019 respectively. The decrease in tax expense is primarily the result of the decrease in profit before tax in entities in the U.S. Federal and Massachusetts consolidated return groups of the Company.

Reconciliation of Effective Tax Rate

The Group is primarily subject to taxation in the U.S. A reconciliation of the U.S. federal statutory tax rate to the effective tax rate is as follows:

As of December 31	2021 $000s	2021 %	2020 $000s	2020 %	2019 $000s	2019 %
US federal statutory rate	**(12,380)**	**21.00**	3,984	21.00	97,183	21.00
Effects of state tax rate in U.S.	**(4,484)**	**7.61**	1,844	9.72	22,111	4.78
R&D and orphan drug tax credits	**(5,056)**	**8.58**	(5,642)	(29.74)	(6,321)	(1.37)
Non deductible share based payment expenses	**555**	**(0.94)**	327	1.73	433	0.09
Finance income/(costs) – fair value accounting	**(2,017)**	**3.42**	919	4.84	3,725	0.80
Loss with respect to associate for which no deferred tax asset is recognized	**11,542**	**(19.58)**	—	—	—	—
Transaction Costs	**309**	**(0.52)**	361	1.91	—	—
Interest Expense	**217**	**(0.37)**	(2,258)	(11.91)	1,030	0.22
Executive Compensation	**746**	**(1.27)**	827	4.36	—	—
Deconsolidation adjustments	**—**	**0.00**	—	—	(13,658)	(2.95)
Recognition of deferred tax assets and tax benefits not previously recognized	**(414)**	**0.70**	—	—	(6,251)	(1.35)
Current year losses for which no deferred tax asset is recognized	**14,375**	**(24.38)**	13,948	73.53	14,514	3.14
Other	**363**	**(0.62)**	91	0.48	(356)	(0.06)
	3,756	**(6.37)**	14,401	75.92	112,409	24.29

The Company is also subject to taxation in the UK but to date no taxable income has been generated in the UK. Changes in corporate tax rates can change both the current tax expense (benefit) as well as the deferred tax expense (benefit).

Deferred Tax Assets and Liabilities

Deferred tax assets have been recognized in the U.S. jurisdiction in respect of the following items:

As of December 31	2021 $000s	2020 $000s
Operating tax losses	**46,982**	39,901
Tax credits	**10,673**	10,805
Share-based payments	**7,265**	5,429
Deferred revenue	**—**	358
Investment in Associates	**11,542**	—
Lease Liability	**8,969**	9,657
Other temporary differences	**2,665**	2,078
Deferred tax assets	**88,096**	68,228
Investments held at fair value	**(96,804)**	(120,676)
ROU asset	**(4,667)**	(5,491)
Fixed assets	**(3,547)**	(3,588)
Other temporary differences	**—**	(27)
Deferred tax liabilities	**(105,018)**	(129,782)
Deferred tax assets (liabilities), net	**(16,922)**	(61,554)
Deferred tax liabilities, net, recognized	**(89,765)**	(108,626)
Deferred tax assets, net, recognized	**—**	—
Deferred tax assets (liabilities), net, not recognized	**72,843**	47,072

We have recognized deferred tax assets related to entities in the U.S. Federal and Massachusetts consolidated return groups due to future reversals of existing taxable temporary differences that will be sufficient to recover the net deferred tax assets. Our unrecognized deferred tax assets of $72.8 million are primarily related to tax credit, loss carryforwards and deductible temporary differences in subsidiaries outside the U.S. Federal and Massachusetts consolidated return groups. Such deferred tax assets have not been recognized because it is not probable that future taxable profits will be available to support their realizability. The unrecognized deferred tax assets, to a lesser extent, also relate to unrecognized deferred tax assets with respect to an investment in an associate since the Group does not believe it is probable that such tax benefits will be realized in the foreseeable future.

There was movement in deferred tax recognized, which impacted income tax expense by approximately $18.5 million benefit, primarily related to changes in the value of investments. The Company sold a portion of its stock in Karuna during 2021 and was able to partially offset its gains by using various attributes (i.e. net operating losses, research and development credits, etc.) resulting in current tax expense of $22.2 million.

Unrecognized Deferred Tax Assets

Deferred tax assets have not been recognized in respect of the following carryforward losses, credits and temporary differences, because it is not probable that future taxable profit will be available against which the Group can use the benefits therefrom.

	2021 $000s		2020 $000s	
As of December 31	**Gross Amount**	**Tax Effected**	Gross Amount	Tax Effected
Deductible Temporary Difference	**59,925**	**16,224**	7,997	1,679
Tax Losses	**215,425**	**46,982**	169,731	36,273
Tax Credits	**9,636**	**9,636**	9,120	9,120
Total	**284,986**	**72,843**	186,848	47,072

Tax Losses and tax credits carryforwards

Tax losses and tax credits for which no deferred tax asset was recognized

	2021 $000s		2020 $000s	
As of December 31	**Gross Amount**	**Tax Effected**	Gross Amount	Tax Effected
Tax losses expiring:				
Within 10 years	**19,735**	**4,343**	12,530	2,760
More than 10 years	**47,937**	**11,611**	55,312	12,117
Available Indefinitely	**147,753**	**31,028**	101,889	21,397
Total	**215,425**	**46,982**	169,731	36,273
Tax credits expiring:				
Within 10 years	**4**	**4**	13	13
More than 10 years	**9,632**	**9,632**	9,107	9,107
Available indefinitely	**—**	**—**	—	—
Total	**9,636**	**9,636**	9,120	9,120

The Group had U.S. federal net operating losses carry forwards ("NOLs") of approximately $215.4 million, $169.7 million and $243.0 million as of December 31, 2021, 2020 and 2019, respectively, which are available to offset future taxable income. These NOLs expire through 2037 with the exception of $147.8 million which is not subject to expiration. The Group had U.S. Federal research and development tax credits of approximately $3.9 million, $3.9 million and $7.4 million as of December 31, 2021, 2020 and 2019, respectively, which are available to offset future taxes that expire at various dates through 2041. The Group also had Federal Orphan Drug credits of approximately $5.7 million and $5.2 million as of December 31, 2021, and 2020, which are available to offset future taxes that expire at various dates through 2041. A portion of these Federal NOLs and credits can only be used to offset the profits from the Company's subsidiaries who file separate Federal tax returns. These NOLs and credits are subject to review and possible adjustment by the Internal Revenue Service.

The Group had Massachusetts net operating losses carry forwards ("NOLs") of approximately $27.9 million, $67.4 million and $273.0 million for the years ended December 31, 2021, 2020 and 2019, respectively, which are available to offset future taxable income. These NOLs expire at various dates beginning in 2030. The Group had Massachusetts research and development tax credits of approximately $1.3 million, $2.1 million and $1.6 million for the years ended December 31, 2021, 2020 and 2019, respectively, which are available to offset future taxes and expire at various dates through 2036. These NOLs and credits are subject to review and possible adjustment by the Massachusetts Department of Revenue.

Utilization of the NOLs and research and development credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986 due to ownership change limitations that have occurred previously or that could occur in the future. These ownership changes may limit the amount of NOL and research and development credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. The Company notes that a 382 analysis was performed through December 31, 2021. The results of this analysis concluded that certain net operating losses were subject to limitation under Section 382 of the Internal Revenue Code. None of the Company's tax attributes which are subject to a restrictive Section 382 limitation have been recognized in the financial statements.

Tax Balances

The current tax related balances are presented in the Statement of Financial Position as follows:

As of December 31	2021 $000s	2020 $000s
Income tax receivable - current	**4,514**	—
Trade and Other Payables	**(57)**	(1,260)

Uncertain Tax Positions

The Company has no uncertain tax positions as of December 31, 2021. U.S. corporations are routinely subject to audit by federal and state tax authorities in the normal course of business.

26. Subsequent Events

The Company has evaluated subsequent events after December 31, 2021, the date of issuance of the Consolidated Financial Statements, and has not identified any recordable or disclosable events not otherwise reported in these Consolidated Financial Statements or notes thereto, except for the following:

On January 13, 2022 Gelesis completed its business combination with Capstar Special Purpose Acquisition Corp ("Capstar"). As part of the business combination all shares held in Gelesis, common and preferred, were exchanged for common shares of the merged entity. In addition, the Group invested $15.0 million in the class A common shares of Capstar as part of the PIPE transaction that took place immediately prior to the closing of the business combination and an additional approximately $5.0 million, as part of the Backstop agreement signed with Capstar on December 30, 2021 (see Note 6). Pursuant to the business combination, Gelesis became a wholly-owned subsidiary of Capstar and Capstar changed its name to Gelesis Holdings, Inc., which began trading on the New York Stock exchange under the ticker symbol "GLS" on January 14, 2022. Following the closing of the business combination, the PIPE transaction and the settlement of the aforementioned Backstop agreement with Capstar, PureTech holds 16,727,582 common shares of Gelesis Holdings Inc., which is equal to approximately 23.2% of Gelesis Holdings Inc's outstanding common shares.

On January 26, 2022, Akili Interactive and Social Capital Suvretta Holdings Corp a special purpose acquisition company announced they had entered into a definitive business combination agreement. Upon completion of the transaction, the combined company's securities are expected to be traded on the Nasdaq Stock Market under the ticker symbol "AKLI". The transaction is expected to close in mid-2022. As part of this transaction the Akili Interactive shares held by the Company will be exchanged for the combined company's securities and the Company's interest in the combined public entity is expected to decrease from its current voting interest in Akili of 26.7%.

Exhibit 2.3

Description of Securities

The following description of the securities registered under Section 12 of the Securities Exchange Act of 1934 of PureTech Health plc ("PureTech," "us," "our," "we" or the "Company") is a summary of the rights of our American Depository Shares and certain provisions of our articles of association in effect as of December 31, 2021 (the "Articles"). This summary does not purport to be complete and is qualified in its entirety by the provisions of our Articles previously filed with the Securities and Exchange Commission and incorporated by reference as an exhibit to the Annual Report on Form 20-F of which this Exhibit 2.3 is a part, as well as to the applicable provisions of the laws and regulations of England and Wales. We encourage you to read our Articles and applicable legislation on England and Wales carefully.

Ordinary Shares

The holders of our ordinary shares, par value £0.01 per share, are entitled to receive dividends in proportion to the number of ordinary shares held by them and according to the amount paid up on such ordinary shares during any portion or portions of the period in respect of which the dividend is paid. Holders of ordinary shares are entitled, in proportion to the number of ordinary shares held by them and to the amounts paid up thereon, to share in any surplus in the event of our winding up. The holders of ordinary shares are entitled to receive notice of, attend either in person or by proxy or, being a corporation, by a duly authorized representative, and vote at general meetings of shareholders.

Share Register

We are required by the Companies Act 2006 to keep a register of our shareholders. Under English law, the ordinary shares are deemed to be issued when the name of the shareholder is entered in our share register. The share register therefore is prima facie evidence of the identity of our shareholders, and the shares that they hold. The share register generally provides limited, or no, information regarding the ultimate beneficial owners of our ordinary shares. Our share register is maintained by our registrar, Computershare Investor Services PLC.

Under the Companies Act 2006, we must enter an allotment of shares in our share register as soon as practicable and in any event within two months of the allotment. We are also required by the Companies Act 2006 to register a transfer of shares (or give the transferee notice of and reasons for refusal) as soon as practicable and in any event within two months of receiving notice of the transfer.

We, any of our shareholders or any other affected person may apply to the court for rectification of the share register if:

- the name of any person is wrongly entered in or omitted from our register of members; or
- there is a failure or unnecessary delay in amending the register of members to show the date a member ceased to be a member.

Objects

Section 31 of the Companies Act 2006 provides that the objects of a company are unrestricted unless any restrictions are set out in the articles. There are no such restrictions in the Articles and our objects are therefore unrestricted.

Voting Rights

Subject to any rights or restrictions attached to any shares, on a show of hands:

- every shareholder who is entitled to vote on the resolution and who is present in person has one vote;
- every proxy present who has be duly appointed by one or more shareholders entitled to vote on the resolution(s) has one vote;
- a proxy has one vote for and one vote against the resolution(s) if he has been duly appointed by more than one shareholder entitled to vote on the resolution and either (i) is instructed by one or more of those shareholders to vote for the resolution and by one or more others to vote against it; or (ii) is instructed by one or more of those shareholders to vote in one way and is given a discretion as to how to vote by one or more others (and wishes to use that discretion to vote in the other way);
- subject to any rights or restrictions attached to any shares, on a poll every shareholder who is entitled to vote on the resolutions and is present in person or by proxy shall have one vote for every share of which he is the holder;
- where there are joint holders of a share, the vote of the senior who tenders a vote, whether in person or by proxy, shall be accepted to the exclusion of the vote or votes of the other joint holder or holders. Seniority is determined by the order in which the names of the holders stand in the register; and
- unless the Board otherwise determines, a shareholder shall not be entitled to vote unless all calls or other sums due and payable from him in respect of shares in our company have been paid.

Dividends

Subject to the Companies Act 2006 and the Articles, we may by ordinary resolution declare dividends, but no such dividends shall exceed the amount recommended by the Board. Subject to the Companies Act 2006, the Board may declare and pay such interim dividends (including any dividend payable at a fixed rate) as appear to the Board to be justified by the profits of our company available for distribution.

Except as otherwise provided by the rights attached to shares, all dividends shall be declared and paid according to the amounts paid up or credited as paid up (other than amounts paid in advance of calls) on the shares in respect of which the dividend is paid and shall be apportioned and paid proportionately to the amounts paid up on such shares during any portion or portions of the period in respect of which the dividend is paid.

Dividends may be declared or paid in whatever currency the Board decides. Unless otherwise provided by the rights attached to the shares, dividends shall not carry a right to receive interest.

All dividends unclaimed for a period of 12 years after having been declared or becoming due for payment shall be forfeited and cease to remain owing by us.

The Board may, with the authority of an ordinary resolution of our company:

- offer holders of ordinary shares the right to elect to receive further ordinary shares, credited as fully paid, instead of cash in respect of all or part of any dividend or dividends specified by the ordinary resolution; and

- direct that payment of all or part of any dividend declared may be satisfied by the distribution of specific assets.

There are no fixed or specified dates on which entitlements to dividends payable by us arise.

Pre-Emption Rights

In certain circumstances, shareholders may have statutory pre-emption rights under the Companies Act 2006 in respect of the allotment of new shares in our company. These statutory pre-emption rights would require us to offer new shares for allotment to existing shareholders on a pro rata basis before allotting them to other persons. In such circumstances, the procedure for the exercise of such statutory pre-emption rights would be set out in the documentation by which such shares would be offered to shareholders.

Distribution of Assets on a Winding-Up

On a winding up, a liquidator may, with the authority of a special resolution of our company and any other sanction required by law divide among the shareholders in kind the whole or any part of the assets of our company, whether or not the assets consist of property of one kind or different kinds and may for such purposes set such value as he considers fair upon any one or more class or classes of property and may determine how such division shall be carried out as between the Shareholders or different classes of Shareholders. The liquidator may, with the same authority, transfer any part of the assets to trustees on such trusts for the benefit of shareholders as the liquidator, with the same authority, thinks fit and the liquidation may then be closed and our company dissolved, but so that no Shareholder shall be compelled to accept any shares or other property in respect of which there is a liability.

Transfer of Shares

Every transfer of shares which are in certificated form must be in writing in any usual form or in any form approved by the Board and shall be executed by or on behalf of the transferor and (in the case of a transfer of a share which is not fully paid up) by or on behalf of the transferee.

Every transfer of shares which are in uncertificated form must be made by means of a relevant system (such as CREST).

The Board may, in its absolute discretion and without giving reason, refuse to register any transfer of certificated shares if: (a) it is in respect of a share which is not fully paid up (provided that, if such share is admitted to trading

on a recognised investment exchange, the refusal does not prevent dealings in our company's shares from taking place on an open and proper basis); (b) it is in respect of more than one class of share; (c) it is not duly stamped (if so required)or duly certified or otherwise shown to the satisfaction of the Board to be exempt from stamp duty; or (d) it is not delivered for registration to the registered office of our company or such other place as the Board may from time to time determine, accompanied (except in the case of a transfer by a recognized person (as defined in the Articles) where a certificate has not been issued) by the relevant share certificate and such other evidence as the Board may reasonably require to show the right of the transferor to make the transfer and, if the transfer is signed by some other person on his behalf, the authority of that person to do so.

The Board may, in its absolute discretion and without giving reason, refuse to register any transfer or allotment of shares which is in favor of: (a) a child, bankrupt or person of unsound mind; or (b) more than four joint transferees

Restrictions on Voting Rights

If a member or any person appearing to be interested in shares held by such a member has been duly served with a notice under section 793 of the Companies Act 2006 and has failed in relation to any shares ("default shares")

Variation of Class Rights

Subject to the Companies Act 2006, all or any of the rights or privileges attached to any class of shares in our company may be varied or abrogated in such manner (if any) as may be provided by such rights, or, in the absence of any such provision, either with the consent in writing of the holders of at least three-fourths of the nominal amount of the issued shares of that class or with the sanction of a special resolution passed at a separate meeting of such holders of shares of that class, but not otherwise. The quorum at any such meeting (other than an adjourned meeting) is two persons holding or representing by proxy at least one third in nominal amount of the issued shares of the class in question.

The rights attached to any class of shares shall not, unless otherwise expressly provided in the rights attaching to such shares, be deemed to be varied or abrogated by the creation or issue of shares ranking pari passu with or subsequent to them or by the purchase or redemption by us of any of our own shares.

Share Capital, Changes in Capital and Purchase of Own Shares

Subject to the Companies Act 2006 and to the Articles, the power to allot and issue shares shall be exercised by the Board at such times and on such terms and conditions as the Board may determine.

Subject to the Articles and to any rights attached to any existing shares, any share may be issued with such rights or restrictions as we may from time to time determine by ordinary resolution.

We may issue redeemable shares and the Board may determine the terms, conditions and manner of redemption of such shares, provided it does so before the shares are allotted.

General Meetings

The Board may convene a general meeting whenever it thinks fit.

Pursuant to the Companies Act 2006, an annual general meeting shall be called on not less than 21 clear days' notice. All other general meetings shall be called by not less than 14 clear days' notice.

The quorum for a general meeting is two shareholders present in person or by proxy and entitled to vote.

The Board and, at any general meeting, the chairman of the meeting may make any arrangement and impose any requirement or restriction which it or he considers appropriate to ensure the security or orderly conduct of the meeting. This may include requirements for evidence of identity to be produced by those attending, the searching of their personal property and the restriction of items which may be taken into the meeting place.

Appointment of Directors

Unless otherwise determined by ordinary resolution, there shall be no maximum number of directors, but the number of directors shall not be less than two. Subject to the Companies Act 2006 and the Articles, we may by ordinary resolution appoint any person who is willing to act as a director either as an additional director or to fill a vacancy. The Board may also appoint any person who is willing to act as a director, subject to the Companies Act 2006 and the Articles. Any person appointed by the Board as a director will hold office only until conclusion of the next annual general meeting, unless he is re-elected during such meeting.

The Board may appoint any director to hold any employment or executive office in our company and may also revoke or terminate any such appointment (without prejudice to any claim for damages for breach of any service contract between the director and our company). The Board may by ordinary resolution appoint any person who is willing to act as a director either as an additional director or to fill a vacancy. The Board may also appoint any person who is willing to act as a director, subject to the Companies Act 2006 and the Articles. Any person appointed by the Board as a director will hold office only until conclusion of the next annual general meeting, unless he is re-elected during such meeting.

The Board may appoint any director to hold any employment or executive office in our company and may also revoke or terminate any such appointment (without prejudice to any claim for damages for breach of any service contract between the director and our company).

Retirement and Removal of Directors

Our Articles provide that at each annual general meeting of our company, one-third of the directors who are subject to retirement by rotation or, if their number is not three, the number nearest to but not exceeding one third shall retire from office unless there are fewer than three directors who are subject to retirement by rotation, in which case only one shall retire from office. However, in accordance with the U.K. Corporate Governance Code and best practice, at each annual general meeting all of our directors retire from office and put themselves forward for re-election. In addition, any director who has been a director at each of the preceding two annual general meetings shall also retire. Each such director may, if eligible, offer himself for re-election. If our company, at the meeting at which a director retires, does not fill the vacancy the retiring director shall, if willing, be deemed to have been reappointed unless it is expressly resolved not to fill the vacancy or a resolution for the reappointment of the director is put to the meeting and lost.

Without prejudice to the provisions of the Companies Act 2006, our company may by ordinary resolution remove any director before the expiration of his period of office and may by ordinary resolution appoint another director in his place.

Directors' Interests

Subject to the Companies Act 2006 and provided that he has disclosed to the directors the nature and extent of any interest, a director is able to enter into contracts or other arrangements with us, hold any other office (except auditor) with us or be a director, employee or otherwise interested in any company in which our company is interested. Such a director shall not be liable to account to us for any profit, remuneration or other benefit realized by any such office, employment, contract, arrangement or proposal.

Save as otherwise provided by the Articles, a director shall not vote on, or be counted in the quorum in relation to, any resolution of the Board concerning any contract, arrangement, transaction or proposal to which our company is or is to be a party and in which he (together with any person connected with him) is to his knowledge materially interested, directly or indirectly. Interests of which the director is not aware, interests which cannot reasonably be regarded as likely to give rise to a conflict of interest and interests arising purely as a result of an interest in our company's shares, debentures or other securities are disregarded. However, a director can vote and be counted in the quorum where the resolution relates to any of the following:

- the giving of any guarantee, security or indemnity in respect of (i) money lent or obligations incurred by him or by any other person at the request of or for the benefit of our company or any of its subsidiary undertakings or (ii) a debt or obligation of our company or any of its subsidiary undertakings for which the director himself has assumed responsibility in whole or in part under a guarantee or indemnity or by the giving of security;

- the participation of the director, in an offer of securities of our company or any of its subsidiary undertakings, including participation in the underwriting or sub-underwriting of the offer;

- a proposal involving another company in which he and any persons connected with him has a direct or indirect interest of any kind, unless he and any persons connected with him hold an interest in shares representing one percent or more of either any class of equity share capital, or the voting rights, in such company;

- any arrangement for the benefit of employees of our company or of any of its subsidiary undertakings which does not award the director any privilege or benefit not generally awarded to the employees to whom such arrangement relates;

- any proposal concerning the purchase or maintenance of any insurance policy under which he may benefit;

- any proposal concerning indemnities in favor of directors or the funding of expenditure by one or more directors on defending proceedings against such director(s).

A director shall not vote or be counted in the quorum on any resolution of the Board concerning his own appointment (including fixing or varying the terms of his appointment or its termination) as the holder of any office or place of profit with our company or any company in which our company is interested.

The Board may authorize any matter that would otherwise involve a Director breaching his duty under the Companies Act 2006 to avoid conflicts of interest, provided that the interested director(s) do not vote or count in the quorum in relation to any resolution authorizing the matter. The Board may authorize the relevant matter on such terms as it may determine including:

- whether the interested director(s) may vote or be counted in the quorum in relation to any resolution relating to the relevant matter;
- the exclusion of the interested director(s) from all information and discussion by our company of the relevant matter; and
- the imposition of confidentiality obligations on the interested director(s).

An interested director must act in accordance with any terms determined by the Board. An authorization of a relevant matter may also provide that where the interested director obtains information that is confidential to a third party (other than through his position as director) he will not be obliged to disclose it to our company or to use it in relation to our company's affairs, if to do so would amount to a breach of that confidence.

Powers of the Directors

Subject to the Articles and to any directions given by special resolution of the Company, the business of the Company shall be managed by the Board, which may exercise all the powers of the Company whether relating to the management of the business or not.

Differences in Corporate Law

The applicable provisions of the Companies Act 2006 differ from laws applicable to U.S. corporations and their shareholders. Set forth below is a summary of certain differences between the provisions of the Companies Act 2006 applicable to us and the Delaware General Corporation Law relating to shareholders' rights and protections. This summary is not intended to be a complete discussion of the respective rights and it is qualified in its entirety by reference to Delaware law and English law.

	ENGLAND AND WALES	DELAWARE
Number of Directors	Under the Companies Act 2006, a public limited company must have at least two directors and the number of directors may be fixed by or in the manner provided in a company's articles of association.	Under Delaware law, a corporation must have at least one director and the number of directors shall be fixed by or in the manner provided in the bylaws.

Removal of Directors	Under the Companies Act 2006, shareholders may remove a director without cause by an ordinary resolution (which is passed by a simple majority of those voting in person or by proxy at a general meeting) irrespective of any provisions of any service contract the director has with the company, provided 28 clear days' notice of the resolution has been given to the company and its shareholders. On receipt of notice of an intended resolution to remove a director, the company must forthwith send a copy of the notice to the director concerned. Certain other procedural requirements under the Companies Act 2006 must also be followed such as allowing the director to make representations against his or her removal either at the meeting or in writing.	Under Delaware law, any director or the entire board of directors may be removed, with or without cause, by the holders of a majority of the shares then entitled to vote at an election of directors, except (a) unless the certificate of incorporation provides otherwise, in the case of a corporation whose board of directors is classified, shareholders may effect such removal only for cause, or (b) in the case of a corporation having cumulative voting, if less than the entire board of directors is to be removed, no director may be removed without cause if the votes cast against his removal would be sufficient to elect him if then cumulatively voted at an election of the entire board of directors, or, if there are classes of directors, at an election of the class of directors of which he is a part.
Vacancies on the Board of Directors	Under English law, the procedure by which directors, other than a company's initial directors, are appointed is generally set out in a company's articles of association, provided that where two or more persons are appointed as directors of a public limited company by resolution of the shareholders, resolutions appointing each director must be voted on individually.	Under Delaware law, vacancies and newly created directorships may be filled by a majority of the directors then in office (even though less than a quorum) or by a sole remaining director unless (a) otherwise provided in the certificate of incorporation or by-laws of the corporation or (b) the certificate of incorporation directs that a particular class of stock is to elect such director, in which case a majority of the other directors elected by such class, or a sole remaining director elected by such class, will fill such vacancy.

Annual General Meeting	Under the Companies Act 2006, a public limited company must hold an annual general meeting within the six-month period following the company's annual accounting reference date.	Under Delaware law, the annual meeting of stockholders shall be held at such place, on such date and at such time as may be designated from time to time by the board of directors or as provided in the certificate of incorporation or by the bylaws.
General Meeting	Under the Companies Act 2006, a general meeting of the shareholders of a public limited company may be called by the directors. Shareholders holding at least 5 percent of the paid-up capital of the company carrying voting rights at general meetings can require the directors to call a general meeting and, if the directors fail to do so within 21 days (with the meeting to be held not more than 28 days after the date of the notice), may themselves convene a general meeting.	Under Delaware law, special meetings of the stockholders may be called by the board of directors or by such person or persons as may be authorized by the certificate of incorporation or by the bylaws.

Notice of General Meetings	Under the Companies Act 2006, 21 clear days' notice must be given for an annual general meeting and any resolutions to be proposed at the meeting. Subject to a company's articles of association providing for a longer period, at least 14 clear days' notice is required for any other general meeting. In addition, certain matters, such as the removal of directors or auditors, require special notice, which is 28 clear days' notice. The shareholders of a company may in all cases consent to a shorter notice period, the proportion of shareholders' consent required being 100 percent of those entitled to attend and vote in the case of an annual general meeting and, in the case of any other general meeting, a majority in number of the members having a right to attend and vote at the meeting, being a majority who together hold not less than 95 percent in nominal value of the shares giving a right to attend and vote at the meeting.	Under Delaware law, unless otherwise provided in the certificate of incorporation or bylaws, written notice of any meeting of the stockholders must be given to each stockholder entitled to vote at the meeting not less than ten nor more than 60 days before the date of the meeting and shall specify the place, date, hour, and purpose or purposes of the meeting.
Proxy	Under the Companies Act 2006, at any meeting of shareholders, a shareholder may designate another person to attend, speak and vote at the meeting on their behalf by proxy.	Under Delaware law, at any meeting of stockholders, a stockholder may designate another person to act for such stockholder by proxy, but no such proxy shall be voted or acted upon after three years from its date, unless the proxy provides for a longer period. A director of a Delaware corporation may not issue a proxy representing the director's voting rights as a director.

Pre-emptive Rights	Under the Companies Act 2006, "equity securities", being (i) shares in the company other than shares that, with respect to dividends and capital, carry a right to participate only up to a specified amount in a distribution ("ordinary shares") or (ii) rights to subscribe for, or to convert securities into, ordinary shares, proposed to be allotted for cash must be offered first to the existing equity shareholders in the company in proportion to the respective nominal value of their holdings, unless an exception applies or a special resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise in each case in accordance with the provisions of the Companies Act 2006.	Under Delaware law, shareholders have no preemptive rights to subscribe to additional issues of stock or to any security convertible into such stock unless, and except to the extent that, such rights are expressly provided for in the certificate of incorporation.

Authority to Allot	Under the Companies Act 2006 the directors of a company must not allot shares or grant of rights to subscribe for or to convert any security into shares unless an exception applies or an ordinary resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise in each case in accordance with the provisions of the Companies Act 2006 default, breach of duty or breach of trust in relation to the company is void.	Under Delaware law, if the corporation's charter or certificate of incorporation so provides, the board of directors has the power to authorize the issuance of stock. It may authorize capital stock to be issued for consideration consisting of cash, any tangible or intangible property or any benefit to the corporation or any combination thereof. It may determine the amount of such consideration by approving a formula. In the absence of actual fraud in the transaction, the judgment of the directors as to the value of such consideration is conclusive can limit the liability of a director for:
	Any provision by which a company directly or indirectly provides an indemnity, to any extent, for a director of the company or of an associated company against any liability attaching to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company of which he is a director is also void except as permitted by the Companies Act 2006, which provides exceptions for the company to (a) purchase and maintain insurance against such liability; (b) provide a "qualifying third party indemnity" (being an indemnity against liability incurred by the director to a person other than the company or an associated company or criminal proceedings in which he is not convicted); and (c) provide a "qualifying pension scheme indemnity" (being an indemnity against liability incurred in connection with the company's activities as trustee of an occupational pension plan).	• any breach of the director's duty of loyalty to the corporation or its stockholders; • acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law; • intentional or negligent payment of unlawful dividends or stock purchases or redemptions; or • any transaction from which the director derives an improper personal benefit

Voting Rights	Under English law, unless a poll is demanded by the shareholders of a company or is required by the chairman of the meeting or the company's articles of association, shareholders shall vote on all resolutions on a show of hands. Under the Companies Act 2006, a poll may be demanded by (a) not fewer than five shareholders having the right to vote on the resolution; (b) any shareholder(s) representing not less than 10 percent of the total voting rights of all the shareholders having the right to vote on the resolution; or (c) any shareholder(s) holding shares in the company conferring a right to vote on the resolution being shares on which an aggregate sum has been paid up equal to not less than 10 percent of the total sum paid up on all the shares conferring that right. A company's articles of association may provide more extensive rights for shareholders to call a poll. Under English law, an ordinary resolution is passed on a show of hands if it is approved by a simple majority (more than 50 percent) of the votes cast by shareholders present (in person or by proxy) and entitled to vote. If a poll is demanded, an ordinary resolution is passed if it is approved by holders representing a simple majority of the total voting rights of shareholders present, in person or by proxy, who, being entitled to vote, vote on the resolution. Special resolutions require the affirmative vote of not less than 75 percent of the votes cast by shareholders present, in person or by proxy, at the meeting and entitled to vote.	Delaware law provides that, unless otherwise provided in the certificate of incorporation, each stockholder is entitled to one vote for each share of capital stock held by such stockholder.

Shareholder Vote on Certain Transactions	The Companies Act 2006 provides for schemes of arrangement, which are arrangements or compromises between a company and any class of shareholders or creditors and used in certain types of reconstructions, amalgamations, capital reorganizations or takeovers. These arrangements require: • the approval at a shareholders' or creditors' meeting convened by order of the court, of a majority in number of shareholders or creditors representing 75 percent in value of the capital held by, or debt owed to, the class of shareholders or creditors, or class thereof present and voting, either in person or by proxy; and • the approval of the court.	Generally, under Delaware law, unless the certificate of incorporation provides for the vote of a larger portion of the stock, completion of a merger, consolidation, sale, lease or exchange of all or substantially all of a corporation's assets or dissolution requires: • the approval of the board of directors; and • approval by the vote of the holders of a majority of the outstanding stock or, if the certificate of incorporation provides for more or less than one vote per share, a majority of the votes of the outstanding stock of a corporation entitled to vote on the matter.

Standard of Conduct for Directors		
	Under English law, a director owes various statutory and fiduciary duties to the company, including: • to act in the way he considers, in good faith, would be most likely to promote the success of the company for the benefit of its members as a whole; • to avoid a situation in which he has, or can have, a direct or indirect interest that conflicts, or possibly conflicts, with the interests of the company; • to act in accordance with the company's constitution and only exercise his powers for the purposes for which they are conferred; • to exercise independent judgment; • to exercise reasonable care, skill and diligence; • not to accept benefits from a third party conferred by reason of his being a director or doing, or not doing, anything as a director; and • a duty to declare any interest that he has, whether directly or indirectly, in a proposed or existing transaction or arrangement with the company.	Delaware law does not contain specific provisions setting forth the standard of conduct of a director. The scope of the fiduciary duties of directors is generally determined by the courts of the State of Delaware. In general, directors have a duty to act without self-interest, on a well-informed basis and in a manner they reasonably believe to be in the best interest of the stockholders. Directors of a Delaware corporation owe fiduciary duties of care and loyalty to the corporation and to its shareholders. The duty of care generally requires that a director act in good faith, with the care that an ordinarily prudent person would exercise under similar circumstances. Under this duty, a director must inform himself of all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director act in a manner he reasonably believes to be in the best interests of the corporation. He must not use his corporate position for personal gain or advantage. In general, but subject to certain exceptions, actions of a director are presumed to have been made on an informed basis, in good faith and in the honest belief that the action taken was in the best interests of the corporation. However, this presumption may be rebutted by evidence of a breach of one of the fiduciary duties. Delaware courts have also imposed a heightened standard of conduct upon directors of a Delaware corporation who take any action designed to defeat a threatened change in control of the corporation. In addition, under Delaware law, when the board of directors of a Delaware corporation approves the sale or break-up of a corporation, the board of directors may, in certain circumstances, have a duty to obtain the highest value reasonably available to the shareholders.

Stockholder Suits	Under English law, generally, the company, rather than its shareholders, is the proper claimant in an action in respect of a wrong done to the company or where there is an irregularity in the company's internal management. Notwithstanding this general position, the Companies Act 2006 provides that (i) a court may allow a shareholder to bring a derivative claim (that is, an action in respect of and on behalf of the company) in respect of a cause of action arising from a director's negligence, default, breach of duty or breach of trust and (ii) a shareholder may bring a claim for a court order where the company's affairs have been or are being conducted in a manner that is unfairly prejudicial to some of its shareholders.	Under Delaware law, a stockholder may initiate a derivative action to enforce a right of a corporation if the corporation fails to enforce the right itself. The complaint must: • state that the plaintiff was a stockholder at the time of the transaction of which the plaintiff complains or that the plaintiffs shares thereafter devolved on the plaintiff by operation of law; and • allege with particularity the efforts made by the plaintiff to obtain the action the plaintiff desires from the directors and the reasons for the plaintiff's failure to obtain the action; or • state the reasons for not making the effort. Additionally, the plaintiff must remain a stockholder through the duration of the derivative suit. The action will not be dismissed or compromised without the approval of the Delaware Court of Chancery.

Description of American Depository Shares

Citibank, N.A. has agreed to act as the depositary bank for our American Depositary Shares. Citibank's depositary offices are located at 388 Greenwich Street, New York, New York, 10013. American Depositary Shares are frequently referred to as "ADSs" and represent ownership interests in securities that are on deposit with the depositary bank. ADSs may be represented by certificates that are commonly known as "American Depositary Receipts" or "ADRs." The depositary bank typically appoints a custodian to safekeep the securities on deposit. In this case, the custodian is Citibank, N.A.—London Branch, located at Citigroup Centre Canary Wharf, London E14 5LB D.

We have appointed Citibank as depositary bank pursuant to a deposit agreement. A copy of the deposit agreement is on file with the SEC under cover of a Registration Statement on Form F-6. You may obtain a copy of the deposit agreement from the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549 and from the SEC's website (www.sec.gov). Please refer to Registration Number 333-249809 when retrieving such copy.

We are providing you with a summary description of the material terms of the ADSs and of your material rights as an owner of ADSs. Please remember that summaries by their nature lack the precision of the information summarized and that the rights and obligations of an owner of ADSs will be determined by reference to the terms of the deposit agreement and not by this summary. We urge you to review the deposit agreement in its entirety. The portions of this summary description that are italicized describe matters that may be relevant to the ownership of ADSs but that may not be contained in the deposit agreement.

Each ADS represents the right to receive, and to exercise the beneficial ownership interests in, ordinary shares that are on deposit with the depositary bank and/or custodian. An ADS also represents the right to receive, and to exercise the beneficial interests in, any other property received by the depositary bank or the custodian on behalf of the owner of the ADS but that has not been distributed to the owners of ADSs because of legal restrictions or practical considerations. We and the depositary bank may agree to change the ADS-to-Share ratio by amending the deposit agreement. This amendment may give rise to, or change, the depositary fees payable by ADS owners. The custodian, the depositary bank and their respective nominees hold all deposited property for the benefit of the holders and beneficial owners of ADSs. The deposited property does not constitute the proprietary assets of the depositary bank, the custodian or their nominees. Beneficial ownership in the deposited property under the terms of the deposit agreement are vested in the beneficial owners of the ADSs. The depositary bank, the custodian and their respective nominees are the record holders of the deposited property represented by the ADSs for the benefit of the holders and beneficial owners of the corresponding ADSs. A beneficial owner of ADSs may or may not be the holder of ADSs. Beneficial owners of ADSs are able to receive, and to exercise beneficial ownership interests in, the deposited property only through the registered holders of the ADSs, the registered holders of the ADSs (on behalf of the applicable ADS owners) only through the depositary bank, and the depositary bank (on behalf of the owners of the corresponding ADSs) directly, or indirectly, through the custodian or their respective nominees, in each case upon the terms of the deposit agreement.

If you become (or already are) an owner of ADSs, you will become (or already are) a party to the deposit agreement and therefore will be (or are) bound to its terms and to the terms of any ADR that represents your ADSs. The deposit agreement and the ADR specify our rights and obligations as well as your rights and obligations as owner of ADSs and those of the depositary bank. As an ADS holder you appoint the depositary bank to act on your behalf in certain circumstances. The deposit agreement and the ADRs are governed by New York law. However, our obligations to the holders of ordinary shares will continue to be governed by the laws of England and Wales, which may be different from the laws of the United States.

In addition, applicable laws and regulations may require you to satisfy reporting requirements and obtain regulatory approvals in certain circumstances. You are solely responsible for complying with such reporting requirements and obtaining such approvals. Neither the depositary bank, the custodian, us or any of their or our respective agents or affiliates shall be required to take any actions whatsoever on your behalf to satisfy such reporting requirements or obtain such regulatory approvals under applicable laws and regulations.

As an owner of ADSs, we will not treat you as one of our shareholders and you will not have direct shareholder rights. The depositary bank will hold on your behalf the shareholder rights attached to the ordinary shares underlying your ADSs. An owner of ADSs is able to exercise the shareholders rights for the ordinary shares represented by ADSs through the depositary bank only to the extent contemplated in the deposit agreement. To exercise any shareholder rights not contemplated in the deposit agreement you will, as an ADS owner, need to arrange for the cancellation of your ADSs and become a direct shareholder.

The manner in which you own the ADSs (e.g., in a brokerage account vs. as registered holder, or as holder of certificated vs. uncertificated ADSs) may affect your rights and obligations, and the manner in which, and extent to which, the depositary bank's services are made available to you. As an owner of ADSs, you may hold your ADSs either by means of an ADR registered in your name, through a brokerage or safekeeping account, or through an account established by the depositary bank in your name reflecting the registration of uncertificated ADSs directly on the books of the depositary bank (commonly referred to as the "direct registration system" or "DRS"). The direct registration system reflects the uncertificated (book-entry) registration of ownership of ADSs by the depositary bank. Under the direct registration system, ownership of ADSs is evidenced by periodic statements issued by the depositary bank to the holders of the ADSs. The direct registration system includes automated transfers between the depositary bank and The Depository Trust Company ("DTC"), the central book-entry clearing and settlement system for equity securities in the United States. If you decide to hold your ADSs through your brokerage or safekeeping account, you must rely on the procedures of your broker or bank to assert your rights as ADS owner. Banks and brokers typically hold securities such as the ADSs through clearing and settlement systems such as DTC. The procedures of such clearing and settlement systems may limit your ability to exercise your rights as an owner of ADSs. Please consult with your broker or bank if you have any questions concerning these limitations and procedures. All ADSs held through DTC will be registered in the name of a nominee of DTC. This summary description assumes you have opted to own the ADSs directly by means of an ADS registered in your name and, as such, we will refer to you as the "holder." When we refer to "you," we assume the reader owns ADSs and will own ADSs at the relevant time.

The registration of the ordinary shares in the name of the depositary bank or the custodian shall, to the maximum extent permitted by applicable law, vest in the depositary bank or the custodian the record ownership in the applicable ordinary shares with the beneficial ownership rights and interests in such ordinary shares being at all times vested with the beneficial owners of the ADSs representing the ordinary shares. The depositary bank or the custodian shall at all times be entitled to exercise the beneficial ownership rights in all deposited property, in each case only on behalf of the holders and beneficial owners of the ADSs representing the deposited property.

Dividends and Distributions

As a holder of ADSs, you generally have the right to receive the distributions we make on the securities deposited with the custodian. Your receipt of these distributions may be limited, however, by practical considerations and legal limitations. Holders of ADSs will receive such distributions under the terms of the deposit agreement in proportion to the number of ADSs held as of the specified record date, after deduction of the applicable fees, taxes and expenses.

Distributions of Cash

Whenever we make a cash distribution for the securities on deposit with the custodian, we will deposit the funds with the custodian. Upon receipt of confirmation of the deposit of the requisite funds, the depositary bank will arrange for the funds received in a currency other than U.S. dollars to be converted into U.S. dollars and for the distribution of the U.S. dollars to the holders, subject to the laws and regulations of England and Wales.

The conversion into U.S. dollars will take place only if practicable and if the U.S. dollars are transferable to the United States. The depositary bank will apply the same method for distributing the proceeds of the sale of any property (such as undistributed rights) held by the custodian in respect of securities on deposit.

The distribution of cash will be made net of the fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. The depositary bank will hold any cash amounts it is unable to distribute in a non-interest bearing account for the benefit of the applicable holders and beneficial owners of ADSs until the distribution can be effected or the funds that the depositary bank holds must be escheated as unclaimed property in accordance with the laws of the relevant states of the United States.

Distributions of Shares

Whenever we make a free distribution of ordinary shares for the securities on deposit with the custodian, we will deposit the applicable number of ordinary shares with the custodian. Upon receipt of confirmation of such deposit, the depositary bank will either distribute to holders new ADSs representing the ordinary shares deposited or modify the ADS-to-ordinary shares ratio, in which case each ADS you hold will represent rights and interests in the additional ordinary shares so deposited. Only whole new ADSs will be distributed. Fractional entitlements will be sold and the proceeds of such sale will be distributed as in the case of a cash distribution.

The distribution of new ADSs or the modification of the ADS-to-ordinary shares ratio upon a distribution of ordinary shares will be made net of the fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. In order to pay such taxes or governmental charges, the depositary bank may sell all or a portion of the new ordinary shares so distributed.

No such distribution of new ADSs will be made if it would violate a law (*e.g.*, the U.S. securities laws) or if it is not operationally practicable. If the depositary bank does not distribute new ADSs as described above, it may sell the ordinary shares received upon the terms described in the deposit agreement and will distribute the proceeds of the sale as in the case of a distribution of cash.

Distributions of Rights

Whenever we intend to distribute rights to subscribe for additional ordinary shares, we will give prior notice to the depositary bank and we will assist the depositary bank in determining whether it is lawful and reasonably practicable to distribute rights to subscribe for additional ADSs to holders.

The depositary bank will establish procedures to distribute rights to subscribe for additional ADSs to holders and to enable such holders to exercise such rights if it is lawful and reasonably practicable to make the rights available to holders of ADSs, and if we provide all of the documentation contemplated in the deposit agreement (such as opinions to address the lawfulness of the transaction). You may have to pay fees, expenses, taxes and other governmental charges to subscribe for the new ADSs upon the exercise of your rights. The depositary bank is not

obligated to establish procedures to facilitate the distribution and exercise by holders of rights to subscribe for new ordinary shares other than in the form of ADSs.

The depositary bank will *not* distribute the rights to you if:

- We do not timely request that the rights be distributed to you or we request that the rights not be distributed to you; or
- We fail to deliver satisfactory documents to the depositary bank; or
- It is not reasonably practicable to distribute the rights.

The depositary bank will sell the rights that are not exercised or not distributed if such sale is lawful and reasonably practicable. The proceeds of such sale will be distributed to holders as in the case of a cash distribution. If the depositary bank is unable to sell the rights, it will allow the rights to lapse.

Elective Distributions

Whenever we intend to distribute a dividend payable at the election of shareholders either in cash or in additional shares, we will give prior notice thereof to the depositary bank and will indicate whether we wish the elective distribution to be made available to you. In such case, we will assist the depositary bank in determining whether such distribution is lawful and reasonably practicable.

The depositary bank will make the election available to you only if it is reasonably practicable and if we have provided all of the documentation contemplated in the deposit agreement. In such case, the depositary bank will establish procedures to enable you to elect to receive either cash or additional ADSs, in each case as described in the deposit agreement.

If the election is not made available to you, you will receive either cash or additional ADSs, depending on what a shareholder in England and Wales would receive upon failing to make an election, as more fully described in the deposit agreement.

Other Distributions

Whenever we intend to distribute property other than cash, ordinary shares or rights to subscribe for additional ordinary shares, we will notify the depositary bank in advance and will indicate whether we wish such distribution to be made to you. If so, we will assist the depositary bank in determining whether such distribution to holders is lawful and reasonably practicable.

If it is reasonably practicable to distribute such property to you and if we provide to the depositary bank all of the documentation contemplated in the deposit agreement, the depositary bank will distribute the property to the holders in a manner it deems practicable.

The distribution will be made net of fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. In order to pay such taxes and governmental charges, the depositary bank may sell all or a portion of the property received.

The depositary bank will *not* distribute the property to you and will sell the property if:

- We do not request that the property be distributed to you or if we request that the property not be distributed to you; or
- We do not deliver satisfactory documents to the depositary bank; or
- The depositary bank determines that all or a portion of the distribution to you is not reasonably practicable.

The proceeds of such a sale will be distributed to holders as in the case of a cash distribution.

Redemption

Whenever we decide to redeem any of the securities on deposit with the custodian, we will notify the depositary bank in advance. If it is practicable and if we provide all of the documentation contemplated in the deposit agreement, the depositary bank will provide notice of the redemption to the holders. The custodian will be instructed to surrender the shares being redeemed against payment of the applicable redemption price. The depositary bank will convert into U.S. dollars, upon the terms of the deposit agreement, the redemption funds received in a currency other than U.S. dollars and will establish procedures to enable holders to receive the net proceeds from the redemption upon surrender of their ADSs to the depositary bank. You may have to pay fees, expenses, taxes and other governmental charges upon the redemption of your ADSs. If less than all ADSs are being redeemed, the ADSs to be retired will be selected by lot or on a *pro rata* basis, as the depositary bank may determine.

Changes Affecting Ordinary Shares

The ordinary shares held on deposit for your ADSs may change from time to time. For example, there may be a change in nominal or par value, split-up, cancellation, consolidation or any other reclassification of such ordinary shares or a recapitalization, reorganization, merger, consolidation or sale of assets of the company.

If any such change were to occur, your ADSs would, to the extent permitted by law and the deposit agreement, represent the right to receive the property received or exchanged in respect of the ordinary shares held on deposit.

The depositary bank may in such circumstances deliver new ADSs to you, amend the deposit agreement, the ADRs and the applicable Registration Statement(s) on Form F-6, call for the exchange of your existing ADSs for new ADSs and take any other actions that are appropriate to reflect as to the ADSs the change affecting the ordinary shares. If the depositary bank may not lawfully distribute such property to you, the depositary bank may sell such property and distribute the net proceeds to you as in the case of a cash distribution.

Issuance of ADSs upon Deposit of Ordinary Shares

The ordinary shares have been deposited by us with the custodian and the depositary bank has issued ADSs to the holders thereof.

The depositary bank may create ADSs on your behalf if you or your broker deposit ordinary shares with the custodian. The depositary bank will deliver these ADSs to the person you indicate only after you pay any applicable

issuance fees and any charges and taxes payable for the transfer of the ordinary shares to the custodian. Your ability to deposit ordinary shares and receive ADSs may be limited by U.S. and English legal considerations applicable at the time of deposit.

The issuance of ADSs may be delayed until the depositary bank or the custodian receives confirmation that all required approvals have been given and that the ordinary shares have been duly transferred to the custodian. The depositary bank will only issue ADSs in whole numbers.

When you make a deposit of ordinary shares, you will be responsible for transferring good and valid title to the depositary bank. As such, you will be deemed to represent and warrant that:

- The ordinary shares are duly authorized, validly issued, fully paid, non-assessable and legally obtained.
- All preemptive (and similar) rights, if any, with respect to such ordinary shares have been validly waived or exercised.
- You are duly authorized to deposit the ordinary shares.
- The ordinary shares presented for deposit are free and clear of any lien, encumbrance, security interest, charge, mortgage or adverse claim, and are not, and the ADSs issuable upon such deposit will not be, "restricted securities" (as defined in the deposit agreement).
- The ordinary shares presented for deposit have not been stripped of any rights or entitlements.

If any of the representations or warranties are incorrect in any way, we and the depositary bank may, at your cost and expense, take any and all actions necessary to correct the consequences of the misrepresentations.

Transfer, Combination and Split Up of ADRs

As an ADR holder, you are entitled to transfer, combine or split up your ADRs and the ADSs evidenced thereby. For transfers of ADRs, you will have to surrender the ADRs to be transferred to the depositary bank and also must:

- ensure that the surrendered ADR is properly endorsed or otherwise in proper form for transfer;
- provide such proof of identity and genuineness of signatures as the depositary bank deems appropriate;
- provide any transfer stamps required by the State of New York or the United States; and
- pay all applicable fees, charges, expenses, taxes and other government charges payable by ADR holders pursuant to the terms of the deposit agreement, upon the transfer of ADRs.

To have your ADRs either combined or split up, you must surrender the ADRs in question to the depositary bank with your request to have them combined or split up, and you must pay all applicable fees, charges and expenses payable by ADR holders, pursuant to the terms of the deposit agreement, upon a combination or split up of ADRs.

Withdrawal of Ordinary Shares Upon Cancellation of ADSs

As a holder, you are entitled to present your ADSs to the depositary bank for cancellation and then receive the corresponding number of underlying ordinary shares at the custodian's offices. Your ability to withdraw the ordinary shares held in respect of the ADSs may be limited by U.S. and English law considerations applicable at the time of withdrawal. In order to withdraw the ordinary shares represented by your ADSs, you will be required to pay to the depositary bank the fees for cancellation of ADSs and any charges and taxes payable upon the transfer of the ordinary shares. You assume the risk for delivery of all funds and securities upon withdrawal. Once canceled, the ADSs will not have any rights under the deposit agreement.

If you hold ADSs registered in your name, the depositary bank may ask you to provide proof of identity and genuineness of any signature and such other documents as the depositary bank may deem appropriate before it will cancel your ADSs. The withdrawal of the ordinary shares represented by your ADSs may be delayed until the depositary bank receives satisfactory evidence of compliance with all applicable laws and regulations. Please keep in mind that the depositary bank will only accept ADSs for cancellation that represent a whole number of securities on deposit.

You have the right to withdraw the securities represented by your ADSs at any time except for:

- Temporary delays that may arise because (i) the transfer books for the ordinary shares or ADSs are closed, or (ii) ordinary shares are immobilized on account of a shareholders' meeting or a payment of dividends.

- Obligations to pay fees, taxes and similar charges.

- Restrictions imposed because of laws or regulations applicable to ADSs or the withdrawal of securities on deposit.

The deposit agreement may not be modified to impair your right to withdraw the securities represented by your ADSs except to comply with mandatory provisions of law.

Each holder and beneficial owner of ADSs agrees to provide such information as the company may request in a disclosure notice given pursuant to the U.K. Companies Act 2006, as amended, or the Companies Act, or the Articles. Each holder and beneficial owner of ADSs acknowledges that it understands that failure to comply with such request may result in the imposition of sanctions against the holder of the ordinary shares in respect of which the non-complying person is or was, or appears to be or has been, interested as provided in the Companies Act and the Articles which currently include, the withdrawal of the voting rights of such Shares and the imposition of restrictions on the rights to receive dividends on and to transfer such Shares.

Voting Rights

As a holder, you generally have the right under the deposit agreement to instruct the depositary bank to exercise the voting rights for the ordinary shares represented by your ADSs. The voting rights of holders of ordinary shares are described in herein above.

At our request, the depositary bank will distribute to you any notice of shareholders' meeting received from us together with information explaining how to instruct the depositary bank to exercise the voting rights of the

securities represented by ADSs. In lieu of distributing such materials, the depositary bank may distribute to holders of ADSs instructions on how to retrieve such materials upon request.

If the depositary bank timely receives voting instructions from a holder of ADSs, it will endeavor to vote the securities (in person or by proxy) represented by the holder's ADSs as follows:

- In the event of voting by show of hands, the depositary bank will vote (or cause the custodian to vote) all ordinary shares held on deposit at that time in accordance with the voting instructions received from a majority of holders of ADSs who provide timely voting instructions.

- In the event of voting by poll, the depositary bank will vote (or cause the Custodian to vote) the ordinary shares held on deposit in accordance with the voting instructions received from the holders of ADSs.

Securities for which no voting instructions have been received will not be voted (except as otherwise contemplated in the deposit agreement). Please note that the ability of the depositary bank to carry out voting instructions may be limited by practical and legal limitations and the terms of the securities on deposit. We cannot assure you that you will receive voting materials in time to enable you to return voting instructions to the depositary bank in a timely manner.

Fees and Charges

As an ADS holder, you are required to pay the following fees under the terms of the deposit agreement:

SERVICE	FEES
• Issuance of ADSs (e.g., an issuance of ADS upon a deposit of ordinary shares, upon a change in the ADS(s)-to-ordinary share(s) ratio, or for any other reason), excluding ADS issuances as a result of distributions of ordinary shares)	Up to U.S.$0.05 per ADS issued
• Cancellation of ADSs (e.g., a cancellation of ADSs for delivery of deposited property, upon a change in the ADS(s)-to-ordinary share(s) ratio, or for any other reason)	Up to U.S.$0.05 per ADS cancelled
• Distribution of cash dividends or other cash distributions (e.g., upon a sale of rights and other entitlements)	Up to U.S.$0.05 per ADS held
• Distribution of ADSs pursuant to (i) share dividends or other free share distributions, or (ii) exercise of rights to purchase additional ADSs	Up to U.S.$0.05 per ADS held
• Distribution of securities other than ADSs or rights to purchase additional ADSs (e.g., upon a spin-off)	Up to U.S.$0.05 per ADS held
• ADS Services	Up to U.S.$0.05 per ADS held on the applicable record date(s) established by the depositary bank
• Registration of ADS transfers (e.g., upon a registration of the transfer of registered ownership of ADSs, upon a transfer of ADSs into DTC and *vice versa*, or for any other reason)	Up to U.S.$0.05 per ADS (or fraction thereof) transferred
• Conversion of ADSs of one series for ADSs of another series (e.g., upon conversion of partial entitlement ADSs for full entitlement ADSs, or upon conversion of restricted ADSs (each as defined in the deposit agreement) into freely transferable ADSs, and *vice versa*).	Up to U.S.$0.05 per ADS (or fraction thereof) converted

As an ADS holder you will also be responsible to pay certain charges such as:

- taxes (including applicable interest and penalties) and other governmental charges;
- the registration fees as may from time to time be in effect for the registration of ordinary shares on the share register and applicable to transfers of ordinary shares to or from the name of the custodian, the depositary bank or any nominees upon the making of deposits and withdrawals, respectively;
- certain cable, telex and facsimile transmission and delivery expenses;
- the fees, expenses, spreads, taxes and other charges of the depositary bank and/or service providers (which may be a division, branch or affiliate of the depositary bank) in the conversion of foreign currency;
- the reasonable and customary out-of-pocket expenses incurred by the depositary bank in connection with compliance with exchange control regulations and other regulatory requirements applicable to ordinary shares, ADSs and ADRs; and
- the fees, charges, costs and expenses incurred by the depositary bank, the custodian, or any nominee in connection with the ADR program.

ADS fees and charges for (i) the issuance of ADSs, and (ii) the cancellation of ADSs are charged to the person for whom the ADSs are issued (in the case of ADS issuances) and to the person for whom ADSs are cancelled (in the case of ADS cancellations). In the case of ADSs issued by the depositary bank into DTC, the ADS issuance and cancellation fees and charges may be deducted from distributions made through DTC, and may be charged to the DTC participant(s) receiving the ADSs being issued or the DTC participant(s) holding the ADSs being cancelled, as the case may be, on behalf of the beneficial owner(s) and will be charged by the DTC participant(s) to the account of the applicable beneficial owner(s) in accordance with the procedures and practices of the DTC participants as in effect at the time. ADS fees and charges in respect of distributions and the ADS service fee are charged to the holders as of the applicable ADS record date. In the case of distributions of cash, the amount of the applicable ADS fees and charges is deducted from the funds being distributed. In the case of (i) distributions other than cash and (ii) the ADS service fee, holders as of the ADS record date will be invoiced for the amount of the ADS fees and charges and such ADS fees and charges may be deducted from distributions made to holders of ADSs. For ADSs held through DTC, the ADS fees and charges for distributions other than cash and the ADS service fee may be deducted from distributions made through DTC, and may be charged to the DTC participants in accordance with the procedures and practices prescribed by DTC and the DTC participants in turn charge the amount of such ADS fees and charges to the beneficial owners for whom they hold ADSs. In the case of (i) registration of ADS transfers, the ADS transfer fee will be payable by the ADS Holder whose ADSs are being transferred or by the person to whom the ADSs are transferred, and (ii) conversion of ADSs of one series for ADSs of another series, the ADS conversion fee will be payable by the Holder whose ADSs are converted or by the person to whom the converted ADSs are delivered.

In the event of refusal to pay the depositary bank fees, the depositary bank may, under the terms of the deposit agreement, refuse the requested service until payment is received or may set off the amount of the depositary bank fees from any distribution to be made to the ADS holder. Certain depositary fees and charges (such as the ADS services fee) may become payable shortly after the purchase of ADSs. Note that the fees and charges you may be required to pay may vary over time and may be changed by us and by the depositary bank. You will receive prior notice of such changes. The depositary bank may reimburse us for certain expenses incurred by us in respect of the ADR program, by making available a portion of the ADS fees charged in respect of the ADR program or otherwise, upon such terms and conditions as we and the depositary bank agree from time to time.

Amendments and Termination

We may agree with the depositary bank to modify the deposit agreement at any time without your consent. We undertake to give holders 30 days' prior notice of any modifications that would materially prejudice any of their substantial rights under the deposit agreement. We will not consider to be materially prejudicial to your substantial rights any modifications or supplements that are reasonably necessary for the ADSs to be registered under the Securities Act or to be eligible for book-entry settlement, in each case without imposing or increasing the fees and charges you are required to pay. In addition, we may not be able to provide you with prior notice of any modifications or supplements that are required to accommodate compliance with applicable provisions of law.

You will be bound by the modifications to the deposit agreement if you continue to hold your ADSs after the modifications to the deposit agreement become effective. The deposit agreement cannot be amended to prevent you from withdrawing the ordinary shares represented by your ADSs (except as permitted by law).

We have the right to direct the depositary bank to terminate the deposit agreement. Similarly, the depositary bank may in certain circumstances on its own initiative terminate the deposit agreement. In either case, the depositary bank must give notice to the holders at least 30 days before termination. Until termination, your rights under the deposit agreement will be unaffected.

Termination

After termination, the depositary bank will continue to collect distributions received (but will not distribute any such property until you request the cancellation of your ADSs) and may sell the securities held on deposit. After the sale, the depositary bank will hold the proceeds from such sale and any other funds then held for the holders of ADSs in a non-interest bearing account. At that point, the depositary bank will have no further obligations to holders other than to account for the funds then held for the holders of ADSs still outstanding (after deduction of applicable fees, taxes and expenses).

In connection with any termination of the deposit agreement, the depositary bank may make available to owners of ADSs a means to withdraw the ordinary shares represented by ADSs and to direct the depositary of such ordinary shares into an unsponsored American depositary share program established by the depositary bank. The ability to receive unsponsored American depositary shares upon termination of the deposit agreement would be subject to satisfaction of certain U.S. regulatory requirements applicable to the creation of unsponsored American depositary shares and the payment of applicable depositary fees.

Books of Depositary

The depositary bank maintains ADS holder records at its depositary office. You may inspect such records at such office during regular business hours but solely for the purpose of communicating with other holders in the interest of business matters relating to the ADSs and the deposit agreement.

The depositary bank will maintain in New York facilities to record and process the issuance, cancellation, combination, split-up and transfer of ADSs. These facilities may be closed from time to time, to the extent not prohibited by law.

Limitations on Obligations and Liabilities

The deposit agreement limits our obligations and the depositary bank's obligations to you. Please note the following:

- We and the depositary bank are obligated only to take the actions specifically stated in the deposit agreement without negligence or bad faith.
- The depositary bank disclaims any liability for any failure to carry out voting instructions, for any manner in which a vote is cast or for the effect of any vote, provided it acts in good faith and in accordance with the terms of the deposit agreement.
- The depositary bank disclaims any liability for any failure to determine the lawfulness or practicality of any action, for the content of any document forwarded to you on our behalf or for the accuracy of any translation of such a document, for the investment risks associated with investing in ordinary shares, for the validity or worth of the ordinary shares, for any tax consequences that result from the ownership of ADSs, for the credit-worthiness of any third party, for allowing any rights to lapse under the terms of the deposit agreement, for the timeliness of any of our notices or for our failure to give notice.
- We and the depositary bank are not obligated to perform any act that is inconsistent with the terms of the deposit agreement.
- We and the depositary bank disclaim any liability if we or the depositary bank are prevented or forbidden from or subject to any civil or criminal penalty or restraint on account of, or delayed in, doing or performing any act or thing required by the terms of the deposit agreement, by reason of any provision, present or future of any law or regulation, or by reason of present or future provision of any provision of our Articles, or any provision of or governing the securities on deposit, or by reason of any act of God or war or other circumstances beyond our control.
- We and the depositary bank disclaim any liability by reason of any exercise of, or failure to exercise, any discretion provided for in the deposit agreement or in our Articles or in any provisions of or governing the securities on deposit.

- We and the depositary bank further disclaim any liability for any action or inaction in reliance on the advice or information received from legal counsel, accountants, any person presenting Shares for deposit, any holder of ADSs or authorized representatives thereof, or any other person believed by either of us in good faith to be competent to give such advice or information.

- We and the depositary bank also disclaim liability for the inability by a holder to benefit from any distribution, offering, right or other benefit that is made available to holders of ordinary shares but is not, under the terms of the deposit agreement, made available to you.

- We and the depositary bank may rely without any liability upon any written notice, request or other document believed to be genuine and to have been signed or presented by the proper parties.

- We and the depositary bank also disclaim liability for any consequential or punitive damages for any breach of the terms of the deposit agreement.
- No disclaimer of any Securities Act liability is intended by any provision of the deposit agreement.

- Nothing in the deposit agreement gives rise to a partnership or joint venture, or establishes a fiduciary relationship, among us, the depositary bank and you as ADS holder.

- Nothing in the deposit agreement precludes Citibank, N.A. (or its affiliates) from engaging in transactions in which parties adverse to us or the holders or beneficial owners of ADS have interests, and nothing in the deposit agreement obligates Citibank, N.A. to disclose those transactions, or any information obtained in the course of those transactions, to us or to the holders or beneficial owners of ADS, or to account for any payment received as part of those transactions.

Taxes

You are responsible for the taxes and other governmental charges payable on the ADSs and the securities represented by the ADSs. We, the depositary bank and the custodian may deduct from any distribution the taxes and governmental charges payable by holders and may sell any and all property on deposit to pay the taxes and governmental charges payable by holders. You are liable for any deficiency if the sale proceeds do not cover the taxes that are due.

The depositary bank may refuse to issue ADSs, to deliver, transfer, split and combine ADRs or to release securities on deposit until all taxes and charges are paid by the applicable holder. The depositary bank and the custodian may take reasonable administrative actions to obtain tax refunds and reduced tax withholding for any distributions on your behalf. However, you may be required to provide to the depositary bank and to the custodian proof of taxpayer status and residence and such other information as the depositary bank and the custodian may require to fulfill legal obligations. You are required to indemnify us, the depositary bank and the custodian for any claims with respect to taxes based on any tax benefit obtained for you.

Foreign Currency Conversion

The depositary bank will arrange for the conversion of all foreign currency received into U.S. dollars if such conversion is practical, and it will distribute the U.S. dollars in accordance with the terms of the deposit agreement. You may have to pay fees and expenses incurred in converting foreign currency, such as fees and expenses incurred in complying with currency exchange controls and other governmental requirements.

If the conversion of foreign currency is not practical or lawful, or if any required approvals are denied or not obtainable at a reasonable cost or within a reasonable period, the depositary bank may take the following actions in its discretion:

- Convert the foreign currency to the extent practical and lawful and distribute the U.S. dollars to the holders for whom the conversion and distribution is lawful and practical.
- Distribute the foreign currency to holders for whom the distribution is lawful and practical.
- Hold the foreign currency (without liability for interest) for the applicable holders.

Governing Law/Waiver of Jury Trial

The deposit agreement, the ADRs, and the ADSs will be interpreted in accordance with the laws of the State of New York. The rights of holders of ordinary shares (including ordinary shares represented by ADSs) is governed by the laws of England and Wales.

AS A PARTY TO THE DEPOSIT AGREEMENT, YOU IRREVOCABLY WAIVE, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, YOUR RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING ARISING OUT OF, OR RELATING TO, THE DEPOSIT AGREEMENT OR THE ADRs, OR ANYTHING CONTAINED THEREIN AGAINST US AND/OR THE DEPOSITARY.

The deposit agreement provides that, to the extent permitted by law, ADS holders waive the right to a jury trial of any claim they may have against us or the depositary arising out of or relating to our ordinary shares, the ADSs or the deposit agreement, including any claim under U.S. federal securities laws. If we or the depositary opposed a jury trial demand based on the waiver, the court would determine whether the waiver was enforceable in the facts and circumstances of that case in accordance with applicable case law. However, you will not be deemed, by agreeing to the terms of the deposit agreement, to have waived our or the depositary's compliance with U.S. federal securities laws and the rules and regulations promulgated thereunder.

Exhibit 4.24

CERTAIN IDENTIFIED INFORMATION HAS BEEN EXCLUDED (INDICATED BY: [***]) FROM THE EXHIBIT BECAUSE IT IS BOTH (I) NOT MATERIAL AND (II) THE TYPE OF INFORMATION THAT THE REGISTRANT CUSTOMARILY AND ACTUALLY TREATS AS PRIVATE OR CONFIDENTIAL.

EXECUTION VERSION

AKILI INTERACTIVE LABS, INC.
THIRD AMENDED AND RESTATED
INVESTORS' RIGHTS AGREEMENT

THIS THIRD AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT (the "Agreement") is made as of the 25th day of May, 2021, by and among Akili Interactive Labs, Inc., a Delaware corporation (the "Company"), the holders of the Company's Series A-1 Preferred Stock, par value $0.0001 per share (the "Series A-1 Preferred Stock"), the holders of the Company's Series A-2 Preferred Stock, par value $0.0001 per share (the "Series A-2 Preferred Stock"), the holders of the Company's Series B Preferred Stock, par value $0.0001 per share (the "Series B Preferred Stock"), the holders of the Company's Series C Preferred Stock, par value $0.0001 per share (the "Series C Preferred Stock"), the holders of the Company's Series D Preferred Stock, par value $0.0001 per share (the "Series D Preferred Stock", and together with the Series A-1 Preferred Stock, Series A-2 Preferred Stock, Series B Preferred Stock and Series C Preferred Stock, the "Preferred Stock"), listed on Schedule A hereto (the "Investors") and the holders of the Company's Common Stock, par value $0.0001 per share (the "Common Stock"), or options to purchase Common Stock, listed on the Schedule of Key Holders attached as Schedule B hereto (the "Key Holders"). The Investors and the Key Holders are individually referred to herein as a "Stockholder" and are collectively referred to herein as the "Stockholders" (and, together with the Company, the "Parties").

RECITALS

WHEREAS, certain of the Investors (the "Existing Investors") hold shares of the Company's Series A-1 Preferred Stock, Series A-2 Preferred Stock, Series B Preferred Stock, Series C Preferred Stock and/or shares of Common Stock issued upon conversion thereof and possess registration rights, information rights, rights of first offer and other rights pursuant to that certain Amended and Restated Investors' Rights Agreement dated [***] by and among the Company, certain holders of Common Stock and such Existing Investors (the "Prior Agreement");

WHEREAS, the Prior Agreement may be amended, and any provision therein waived, with the consent of the Company and the holders of [***] of the outstanding Preferred Stock (as such term is defined in the Prior Agreement);

WHEREAS, the Existing Investors as holders of [***] of the outstanding Preferred Stock (as such term is defined in the Prior Agreement) of the Company desire to terminate the Prior Agreement and to accept the rights created pursuant hereto in lieu of the rights granted to them under the Prior Agreement; and

WHEREAS, certain Investors are parties to that certain Series D Preferred Stock Purchase Agreement of even date herewith by and among the Company and certain of the

Investors (the "Series D Agreement"), which provides that as a condition to the closing of the sale of the Series D Preferred Stock, this Agreement must be executed and delivered by such Investors, Existing Investors holding [***] of the outstanding Preferred Stock (as such term is defined in the Prior Agreement) of the Company, and the Company.

NOW, THEREFORE, in consideration of the mutual promises and covenants set forth herein, the Company and the Existing Investors hereby agree that the Prior Agreement shall be superseded and replaced in its entirety by this Agreement, and the parties hereto further agree as follows:

1. Definitions. For purposes of this Agreement:

1.1 The term "1934 Act" means the Securities Exchange Act of 1934, as amended.

1.2 The term "Act" means the Securities Act of 1933, as amended, and the rules and regulations promulgated thereunder.

1.3 The term "Affiliate" means, (i) with respect to any specified Person, any other Person who or which, directly or indirectly, controls, is controlled by, or is under common control with such specified Person, including, without limitation, any general partner, officer, director, member, manager or stockholder of such Person and any venture capital fund now or hereafter existing that is controlled by one or more general partners or managing members of, or is under common investment management with, such Person, in each case where the term "control" means ownership of at least 50% of the voting securities of an entity [***].

1.4 The term "Board" means the Company's Board of Directors, as constituted from time to time.

1.5 The term "Form S-3" means such form under the Act as in effect on the date hereof or any registration form under the Act subsequently adopted by the SEC that permits inclusion or incorporation of substantial information by reference to other documents filed by the Company with the SEC.

1.6 The term "Free Writing Prospectus" means a free-writing prospectus, as defined in Rule 405.

1.7 The term "Holder" means any Person owning Registrable Securities who is a party to this Agreement.

1.8 The term "Initial Offering" means the Company's first firm commitment underwritten public offering of its Common Stock under the Act.

1.9 The term "Person" shall mean any individual, corporation, partnership, trust, limited liability company, association or other entity.

1.10 The terms "register," "registered," and "registration" refer to a registration effected by preparing and filing a registration statement or similar document in compliance with the Act, and the declaration or ordering of effectiveness of such registration statement or document.

1.11 The term "Registrable Securities" means (i) the Common Stock issuable or issued upon conversion of the Preferred Stock and (ii) any Common Stock of the Company issued as (or issuable upon the conversion or exercise of any warrant, right or other

security that is issued as) a dividend or other distribution with respect to, or in exchange for, or in replacement of, the shares referenced in (i) above or any other Common Stock held by a holder of Preferred Stock, excluding in all cases, however, any Registrable Securities sold by a Person in a transaction in which such Person's rights under Section 2 of this Agreement are not assigned. In addition, the number of shares of Registrable Securities outstanding shall equal the aggregate of the number of shares of Common Stock outstanding that are, and the number of shares of Common Stock issuable pursuant to then exercisable or convertible securities that are, Registrable Securities.

1.12 The term "Restated Certificate" means the Company's Amended and Restated Certificate of Incorporation, as amended from time to time.

1.13 The term "Rule 144" shall mean Rule 144 under the Act.

1.14 The term "Rule 144(b)(1)(i)" shall mean subsection (b)(1)(i) of Rule 144 under the Act as it applies to Persons who have held shares for more than one (1) year.

1.15 The term "Rule 405" shall mean Rule 405 under the Act.

1.16 The term "SEC" shall mean the Securities and Exchange Commission.

1.17 The term "Shares" shall mean any shares of, or securities convertible into or exchangeable or exercisable for any shares of, the Company's capital stock.

2. Registration Rights.

2.1 Request for Registration.

(a) Subject to the conditions of this Section 2.1, if the Company shall receive at any time after the earlier of (i) [***] of the date of this Agreement; or (ii) [***] following the effective date of the Initial Offering, a written request from any Holders of the Registrable Securities (for purposes of this Section 2.1, the "Initiating Holders"), including Neuberger or Temasek for clause (i), that the Company file two (2) registration statements under the Act covering the registration of Registrable Securities with an anticipated aggregate offering price of at least [***], then the Company shall, within [***] of the receipt thereof, give written notice of such request to all Holders, and subject to the limitations of this Section 2.1, use its commercially reasonable efforts to effect, as soon as practicable, the registration under the Act of all Registrable Securities that the Holders request to be registered in a written request received by the Company within [***] of the mailing of the Company's notice pursuant to this Section 2.1(a).

(b) If the Initiating Holders intend to distribute the Registrable Securities covered by their request by means of an underwriting, they shall so advise the Company as a part of their request made pursuant to this Section 2.1, and the Company shall include such information in the written notice referred to in Section 2.1(a). In such event the right of any Holder to include its Registrable Securities in such registration shall be conditioned upon such Holder's participation in such underwriting and the inclusion of such Holder's Registrable Securities in the underwriting (unless otherwise mutually agreed by [***] of the Initiating Holders and such Holder) to the extent provided herein. All Holders proposing to distribute their securities through such underwriting shall enter into an underwriting agreement in customary form with the underwriter or underwriters selected for such underwriting by the Company (which underwriter or underwriters shall be reasonably acceptable to those Initiating Holders holding [***] of the Registrable Securities then held by all Initiating Holders).

Notwithstanding any other provision of this Section 2.1, if the underwriter advises the Company that marketing factors require a limitation on the number of securities underwritten (including Registrable Securities), then the Company shall so advise all Holders of Registrable Securities that would otherwise be underwritten pursuant hereto, and the number of shares that may be included in the underwriting shall be allocated to the Holders of such Registrable Securities pro rata based on the number of Registrable Securities held by all such Holders (including the Initiating Holders). In no event shall any Registrable Securities be excluded from such underwriting unless all other securities are first excluded. Any Registrable Securities excluded or withdrawn from such underwriting shall be withdrawn from the registration.

(c) Notwithstanding the foregoing, the Company shall not be required to effect a registration pursuant to this Section 2.1:

(i) in any particular jurisdiction in which the Company would be required to execute a general consent to service of process in effecting such registration, unless the Company is already subject to service in such jurisdiction and except as may be required under the Act; or

(ii) after the Company has effected [***] registrations pursuant to this Section 2.1, and such registrations have been declared or ordered effective; or

(iii) during the period starting with the date [***] prior to the Company's good faith estimate of the date of the filing of and ending on a date [***] following the effective date of a Company initiated registration subject to Section 2.2 below, provided that the Company is actively employing in good faith its commercially reasonable efforts to cause such registration statement to become effective; or

(iv) if the Initiating Holders propose to dispose of Registrable Securities that may be registered on Form S-3 pursuant to Section 2.3 hereof; or

(v) if the Company shall furnish to Holders requesting a registration statement pursuant to this Section 2.1 a certificate signed by the Company's Chief Executive Officer or Chairman of the Board stating that in the good faith judgment of the Board, it would be seriously detrimental to the Company and its stockholders for such registration statement to be effected at such time, in which event the Company shall have the right to defer such filing for a period of not more than [***] after receipt of the request of the Initiating Holders; provided that such right shall be exercised by the Company not more than [once] in any [***] period.

2.2 Company Registration.

(a) If (but without any obligation to do so) the Company proposes to register (including for this purpose a registration effected by the Company for stockholders other than the Holders) any of its stock or other securities under the Act in connection with the public offering of such securities (other than (i) a registration relating to a demand pursuant to Section 2.1 of this Agreement, (ii) a registration relating solely to the sale of securities of participants in a Company stock plan, (iii) a registration relating to a corporate reorganization or transaction under Rule 145 of the Act, (iv) a registration on any form that does not include substantially the same information as would be required to be included in a registration statement covering the sale of the Registrable Securities, or (v) a registration in which the only Common Stock being registered is Common Stock issuable upon conversion of debt securities that are also being registered), the Company shall, at such time, promptly give each Holder written notice of such registration. Upon the written request of each Holder given within [***] after mailing of such notice by the Company in accordance with Section 5.5 of this

Agreement, the Company shall, subject to the provisions of Section 2.2(c) of this Agreement, use its commercially reasonable efforts to cause to be registered under the Act all of the Registrable Securities that each such Holder requests to be registered.

(b) Right to Terminate Registration. The Company shall have the right to terminate or withdraw any registration initiated by it under this Section 2.2 prior to the effectiveness of such registration whether or not any Holder has elected to include securities in such registration. The expenses of such withdrawn registration shall be borne by the Company in accordance with Section 2.6 hereof.

(c) Underwriting Requirements. In connection with any offering involving an underwriting of shares of the Company's capital stock, the Company shall not be required under this Section 2.2 to include any of the Holders' securities in such underwriting unless they accept the terms of the underwriting as agreed upon between the Company and the underwriters selected by the Company (or by other Persons entitled to select the underwriters) and enter into an underwriting agreement in customary form with such underwriters, and then only in such quantity as the underwriters determine in their sole discretion will not jeopardize the success of the offering by the Company. If the total amount of securities, including Registrable Securities, requested by stockholders to be included in such offering exceeds the amount of securities sold other than by the Company that the underwriters determine in their sole discretion is compatible with the success of the offering, then the Company shall be required to include in the offering only that number of such securities, including Registrable Securities, that the underwriters determine in their sole discretion will not jeopardize the success of the offering. In the event that the underwriters determine that less than all of the Registrable Securities requested to be registered can be included in such offering, then the Registrable Securities that are included in such offering shall be apportioned pro rata among the selling Holders based on the number of Registrable Securities held by all selling Holders or in such other proportions as shall mutually be agreed to by all such selling Holders. Notwithstanding the foregoing, in no event shall any Registrable Securities be excluded from such offering unless all other stockholders' securities have been first excluded from the offering. For purposes of the preceding sentence concerning apportionment, for any selling stockholder that is a Holder of Registrable Securities and that is a venture capital fund, partnership or corporation, the affiliated venture capital funds, partners, members, retired partners and stockholders of such Holder, or the estates and family members of any such partners, members and retired partners and any trusts for the benefit of any of the foregoing Persons, or any Person who shares an investment advisor with the Holder, shall be deemed to be a single "selling Holder," and any pro rata reduction with respect to such "selling Holder" shall be based upon the aggregate amount of Registrable Securities owned by all such related entities and individuals.

2.3 Form S-3 Registration. In case the Company shall receive from any Holders of the Registrable Securities (for purposes of this Section 2.3, the "S-3 Initiating Holders") a written request or requests that the Company effect a registration on Form S-3 covering the registration of Registrable Securities with an anticipated aggregate offering price of at least [***] and any related qualification or compliance with respect to all or a part of the Registrable Securities owned by such Holder or Holders, the Company shall:

(a) promptly give written notice of the proposed registration, and any related qualification or compliance, to all other Holders; and

(b) use its commercially reasonable efforts to effect, as soon as practicable, such registration and all such qualifications and compliances as may be so requested and as would permit or facilitate the sale and distribution of all or such portion of such Holders' Registrable Securities as are specified in such request, together with all or such portion of the Registrable Securities of any other Holders joining in such request as are specified in a written

request given within [***] after receipt of such written notice from the Company; provided, however, that the Company shall not be obligated to effect any such registration, qualification or compliance, pursuant to this Section 2.3:

(i) if Form S-3 is not available for such offering by the Holders;

(ii) if the Holders, together with the holders of any other securities of the Company entitled to inclusion in such registration, propose to sell Registrable Securities and such other securities (if any) at an aggregate price to the public (net of any underwriters' discounts or commissions) of less than [***];

(iii) if the Company shall furnish to all Holders requesting a registration statement pursuant to this Section 2.3 a certificate signed by the Company's Chief Executive Officer or Chairman of the Board stating that in the good faith judgment of the Board, it would be seriously detrimental to the Company and its stockholders for such registration statement to be effected at such time, in which event the Company shall have the right to defer such filing for a period of not more than [***] after receipt of the request of the S-3 Initiating Holders; provided that such right shall be exercised by the Company not more than [***] in any [***] period;

(iv) in any particular jurisdiction in which the Company would be required to qualify to do business or to execute a general consent to service of process in effecting such registration, qualification or compliance;

(v) if the Company, within [***] of receipt of the request of such S-3 Initiating Holders, gives notice of its bona fide intention to effect the filing of a registration statement with the SEC within [***] of receipt of such request (other than a registration effected solely to qualify an employee benefit plan or to effect a business combination pursuant to Rule 145), provided that the Company is actively employing in good faith its commercially reasonable efforts to cause such registration statement to become effective; or

(vi) during the period starting with the date [***] prior to the Company's good faith estimate of the date of the filing of and ending on a date [***] following the effective date of a Company initiated registration subject to Section 2.2 of this Agreement, provided that the Company is actively employing in good faith its commercially reasonable efforts to cause such registration statement to become effective.

(c) If the S-3 Initiating Holders intend to distribute the Registrable Securities covered by their request by means of an underwriting, they shall so advise the Company as a part of their request made pursuant to this Section 2.3 and the Company shall include such information in the written notice referred to in Section 2.3(a). The provisions of Section 2.1(b) of this Agreement shall be applicable to such request (with the substitution of Section 2.3 for references to Section 2.1).

(d) Subject to the foregoing, the Company shall file a registration statement covering the Registrable Securities and other securities so requested to be registered as soon as practicable after receipt of the request or requests of the S-3 Initiating Holders. Registrations effected pursuant to this Section 2.3 shall not be counted as requests for registration effected pursuant to Section 2.1 of this Agreement.

2.4 Obligations of the Company. Whenever required under this Section 2 to effect the registration of any Registrable Securities, the Company shall, as expeditiously as reasonably possible:

(a)

(a) prepare and file with the SEC a registration statement with respect to such Registrable Securities and use its commercially reasonable efforts to cause such registration statement to become effective, and, upon the request of the Holders of [***] of the Registrable Securities registered thereunder, keep such registration statement effective for a period of up to [***] or, if earlier, until the distribution contemplated in the Registration Statement has been completed;

(b) prepare and file with the SEC such amendments and supplements to such registration statement and the prospectus used in connection with such registration statement as may be necessary to comply with the provisions of the Act with respect to the disposition of all securities covered by such registration statement;

(c) furnish to the Holders such number of copies of a prospectus, including a preliminary prospectus and any Free Writing Prospectus, in conformity with the requirements of the Act, and such other documents as they may reasonably request in order to facilitate the disposition of Registrable Securities owned by them;

(d) use its commercially reasonable efforts to register and qualify the securities covered by such registration statement under such other securities or Blue Sky laws of such jurisdictions as shall be reasonably requested by the Holders, provided that the Company shall not be required in connection therewith or as a condition thereto to qualify to do business or to file a general consent to service of process in any such states or jurisdictions;

(e) in the event of any underwritten public offering, enter into and perform its obligations under an underwriting agreement, in usual and customary form, with the managing underwriter of such offering;

(f) notify each Holder of Registrable Securities covered by such registration statement at any time when a prospectus or Free Writing Prospectus (to the extent prepared by or on behalf of the Company) relating thereto is required to be delivered under the Act of the happening of any event as a result of which the prospectus included in such registration statement, as then in effect, includes an untrue statement of a material fact or omits to state a material fact required to be stated therein or necessary to make the statements therein not misleading in the light of the circumstances then existing, and, at the request of any such Holder, the Company will, as soon as reasonably practicable, file and furnish to all such Holders a supplement or amendment to such prospectus or Free Writing Prospectus (to the extent prepared by or on behalf of the Company) so that, as thereafter delivered to the purchasers of such Registrable Securities, such prospectus will not contain an untrue statement of a material fact or omit to state any fact necessary to make the statements therein not misleading in light of the circumstances under which they were made;

(g) cause all such Registrable Securities registered pursuant to this Section 2 to be listed on a national exchange or trading system and on each securities exchange and trading system on which similar securities issued by the Company are then listed;

(h) promptly make available for inspection by the selling Holders, any managing underwriter(s) participating in any disposition pursuant to such registration statement, and any attorney or accountant or other agent retained by any such

underwriter or selected by the selling Holders, all financial and other records, pertinent corporate documents, and properties of the Company, and cause the Company's officers, directors, employees, and independent accountants to supply all information reasonably requested by any such seller, underwriter, attorney, accountant, or agent, in each case, as necessary or advisable to verify the accuracy of the information in such registration statement and to conduct appropriate due diligence in connection therewith; and

(i) provide a transfer agent and registrar for all Registrable Securities registered pursuant to this Agreement and a CUSIP number for all such Registrable Securities, in each case not later than the effective date of such registration.

Notwithstanding the provisions of this Section 2, the Company shall be entitled to postpone or suspend, for a reasonable period of time, the filing, effectiveness or use of, or trading under, any registration statement if the Company shall determine that any such filing or the sale of any securities pursuant to such registration statement would in the good faith judgment of the Board:

(i) materially impede, delay or interfere with any material pending or proposed financing, acquisition, corporate reorganization or other similar transaction involving the Company for which the Board has authorized negotiations;

(ii) materially and adversely impair the consummation of any pending or proposed material offering or sale of any class of securities by the Company; or

(iii) require disclosure of material nonpublic information that, if disclosed at such time, would be materially harmful to the interests of the Company and its stockholders; provided, however, that during any such period all executive officers and directors of the Company are also prohibited from selling securities of the Company (or any security of any of the Company's subsidiaries or affiliates).

In the event of the suspension of effectiveness of any registration statement pursuant to this Section 2.4, the applicable time period during which such registration statement is to remain effective shall be extended by that number of days equal to the number of days the effectiveness of such registration statement was suspended.

2.5 Information from Holder. It shall be a condition precedent to the obligations of the Company to take any action pursuant to this Section 2 with respect to the Registrable Securities of any selling Holder that such Holder shall furnish to the Company such information regarding itself, the Registrable Securities held by it, and the intended method of disposition of such securities as shall be reasonably required to effect the registration of such Holder's Registrable Securities.

2.6 Expenses of Registration. All expenses other than underwriting discounts, stock transfer taxes and commissions incurred in connection with registrations, filings or qualifications pursuant to Sections 2.1, 2.2 and 2.3 of this Agreement, including, without limitation, all registration, filing and qualification fees, printers' and accounting fees, fees and disbursements of counsel for the Company and the reasonable fees and disbursements of one counsel for the selling Holders (not to exceed [***]) shall be borne by the Company. Notwithstanding the foregoing, the Company shall not be required to pay for any expenses of any registration proceeding begun pursuant to Section 2.1 of this Agreement if the registration request is subsequently withdrawn at the request of the Holders of [***] of the Registrable Securities to be registered (in which case all participating Holders shall bear such expenses pro rata based upon the number of Registrable Securities that were to be included in the withdrawn registration); provided, however, that if at the time of such withdrawal, the Holders have learned

of a material adverse change in the condition, business or prospects of the Company from that known to the Holders at the time of their request and have withdrawn the request with reasonable promptness following disclosure by the Company of such material adverse change, then the Holders shall not be required to pay any of such expenses and shall retain their rights pursuant to Section 2.1 of this Agreement.

2.7 Delay of Registration. No Holder shall have any right to obtain or seek an injunction restraining or otherwise delaying any such registration as the result of any controversy that might arise with respect to the interpretation or implementation of this Section 2.

2.8 Indemnification. In the event any Registrable Securities are included in a registration statement under this Section 2:

(a) To the extent permitted by law, the Company will indemnify and hold harmless each Holder, the partners, members, officers, directors and stockholders of each Holder, legal counsel and accountants for each Holder, any underwriter (as defined in the Act) for such Holder and each Person, if any, who controls such Holder or underwriter within the meaning of the Act or the 1934 Act, against any losses, claims, damages or liabilities (joint or several) to which they may become subject under the Act, the 1934 Act, any state securities laws or any rule or regulation promulgated under the Act, the 1934 Act or any state securities laws, insofar as such losses, claims, damages, or liabilities (or actions or proceedings, whether commenced or threatened, in respect thereof) arise out of or are based upon any of the following statements, omissions or violations (collectively, a "Violation"): (i) any untrue or alleged untrue statement of a material fact contained in such registration statement, including any preliminary prospectus, final prospectus, or Free Writing Prospectus contained therein or any amendments or supplements thereto, any issuer information (as defined in Rule 433 of the Act) filed or required to be filed pursuant to Rule 433(d) under the Act or any other document incident to such registration prepared by or on behalf of the Company or used or referred to by the Company, (ii) the omission or alleged omission of a material fact required to be stated in such registration statement, or necessary to make the statements therein not misleading or (iii) any violation or alleged violation by the Company of the Act, the 1934 Act, any state securities laws or any rule or regulation promulgated under the Act, the 1934 Act or any state securities laws, and the Company will reimburse each such Holder, underwriter, controlling Person or other aforementioned Person for any legal or other expenses reasonably incurred by them in connection with investigating or defending any such loss, claim, damage, liability, action or proceeding as such expenses are incurred; provided, however, that the indemnity agreement contained in this Section 2.8(a) shall not apply to amounts paid in settlement of any such loss, claim, damage, liability, action or proceeding if such settlement is effected without the consent of the Company (which consent shall not be unreasonably withheld), nor shall the Company be liable in any such case for any such loss, claim, damage, liability, action or proceeding to the extent that it arises out of or is based upon a Violation that occurs in reliance upon, and in conformity with, written information furnished expressly for use in connection with such registration by such Holder, underwriter, controlling Person or other aforementioned Person.

(b) To the extent permitted by law, each selling Holder, severally and not jointly, will indemnify and hold harmless the Company, each of its directors, each of its officers who has signed the registration statement, each Person, if any, who controls the Company within the meaning of the Act, legal counsel and accountants for the Company, any underwriter, any other Holder selling securities in such registration statement and any controlling Person of any such underwriter or other Holder, against any losses, claims, damages or liabilities (joint or several) to which any of the foregoing Persons may become subject, under the Act, the 1934 Act, any state securities laws or any rule or regulation promulgated under the Act, the 1934

Act or any state securities laws, insofar as such losses, claims, damages or liabilities (or actions or proceedings, whether commenced or threatened, in respect thereof) arise out of or are based upon any Violation, in each case to the extent (and only to the extent) that such Violation occurs in reliance upon and in conformity with written information furnished by such Holder expressly for use in connection with such registration; and each such Holder will reimburse any Person intended to be indemnified pursuant to this Section 2.8(b) for any legal or other expenses reasonably incurred by such Person in connection with investigating or defending any such loss, claim, damage, liability, action or proceeding as such expenses are incurred; provided, however, that the indemnity agreement contained in this Section 2.8(b) shall not apply to amounts paid in settlement of any such loss, claim, damage, liability, action or proceeding if such settlement is effected without the consent of the Holder (which consent shall not be unreasonably withheld), and provided that in no event shall any indemnity under this Section 2.8(b) exceed the gross proceeds from the offering received by such Holder.

(c) Promptly after receipt by an indemnified party under this Section 2.8 of notice of the commencement of any action or proceeding (including any governmental action or proceeding) for which a party may be entitled to indemnification, such indemnified party will, if a claim in respect thereof is to be made against any indemnifying party under this Section 2.8, deliver to the indemnifying party a written notice of the commencement thereof and the indemnifying party shall have the right to participate in and, to the extent the indemnifying party so desires, jointly with any other indemnifying party similarly noticed, to assume the defense thereof with counsel mutually satisfactory to the parties; provided, however, that an indemnified party (together with all other indemnified parties that may be represented without conflict by one counsel) shall have the right to retain one (1) separate counsel, with the fees and expenses to be paid by the indemnifying party, if (i) representation of such indemnified party by the counsel retained by the indemnifying party would be inappropriate due to actual or potential differing interests between such indemnified party and any other party represented by such counsel in such proceeding, (ii) the indemnifying party does not deliver to the indemnified party within sixty (60) days of receipt of notice of such action or proceeding an acknowledgement that, if the facts as alleged by the claimant in such action or proceeding are true, the indemnifying party would have an indemnity obligation for the expenses, losses, claims, damages and liabilities resulting from such action or proceeding as provided hereunder, (iii) the action or proceeding relates to or arises in connection with any criminal proceeding, action, indictment or allegation, (iv) the indemnified party reasonably believes an adverse determination with respect to the action or proceeding would be detrimental to the reputation or future business prospects of the indemnified party or any of its affiliates or (v) the action or proceeding seeks an injunction or equitable relief against the indemnified party or any of its affiliates. The failure to deliver written notice to the indemnifying party within a reasonable time of the commencement of any such action or proceeding, if prejudicial to its ability to defend such action or proceeding, shall relieve such indemnifying party of liability to the indemnified party under this Section 2.8 to the extent of such prejudice, but the omission to so deliver written notice to the indemnifying party will not relieve such indemnifying party of any liability that it may have to any indemnified party otherwise than under this Section 2.8.

(d) If the indemnification provided for in this Section 2.8 is held by a court of competent jurisdiction to be unavailable to an indemnified party with respect to any loss, liability, claim, damage or expense referred to herein, then the indemnifying party, in lieu of indemnifying such indemnified party hereunder, shall contribute to the amount paid or payable by such indemnified party as a result of such loss, liability, claim, damage or expense in such proportion as is appropriate to reflect the relative fault of the indemnifying party on the one hand and the indemnified party on the other hand in connection with the statements or omissions that resulted in such loss, liability, claim, damage or expense, as well as any other relevant equitable considerations; provided, however, that (i) no contribution by any Holder, when combined with any amounts paid by such Holder pursuant to Section 2.8(b), shall exceed the

gross proceeds from the offering received by such Holder and (ii) no Person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Act) will be entitled to contribution from any Person who was not guilty of such fraudulent misrepresentation; and provided further that in no event shall a Holder's liability pursuant to this Section 2.8(d), when combined with the amounts paid or payable by such Holder pursuant to Section 2.8(b), exceed the proceeds from the offering received by such Holder (net of any expenses paid by such Holder). The relative fault of the indemnifying party and the indemnified party shall be determined by reference to, among other things, whether the untrue or alleged untrue statement of a material fact or the omission or alleged omission to state a material fact relates to information supplied by the indemnifying party or by the indemnified party and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such statement or omission.

(e) Notwithstanding the foregoing, to the extent that the provisions on indemnification and contribution contained in the underwriting agreement entered into in connection with the underwritten public offering are in conflict with the foregoing provisions, the provisions in the underwriting agreement shall control.

(f) The obligations of the Company and Holders under this Section 2.8 shall survive the completion of any offering of Registrable Securities in a registration statement under this Section 2 and otherwise.

2.9 Reports Under the 1934 Act. With a view to making available to the Holders the benefits of Rule 144 and any other rule or regulation of the SEC that may at any time permit a Holder to sell securities of the Company to the public without registration or pursuant to a registration on Form S-3, the Company agrees to:

(a)

(b) make and keep public information available, as those terms are understood and defined in Rule 144, at all times after the effective date of the Initial Offering;

(c) file with the SEC in a timely manner all reports and other documents required of the Company under the Act and the 1934 Act; and

(d) furnish to any Holder, so long as the Holder owns any Registrable Securities, forthwith upon request (i) a written statement by the Company that it has complied with the reporting requirements of Rule 144 (at any time after ninety (90) days after the effective date of the first registration statement filed by the Company), the Act and the 1934 Act (at any time after it has become subject to such reporting requirements), or that it qualifies as a registrant whose securities may be resold pursuant to Form S-3 (at any time after it so qualifies), (ii) a copy of the most recent annual or quarterly report of the Company and such other reports and documents so filed by the Company and (iii) such other information as may be reasonably requested to avail any Holder of any rule or regulation of the SEC that permits the selling of any such securities without registration or pursuant to such form.

2.10 Assignment of Registration Rights. The rights to cause the Company to register Registrable Securities pursuant to this Section 2 may be assigned (but only with all related obligations) by a Holder to a transferee or assignee of such securities that after such assignment or transfer, holds at least [***] of Registrable Securities (appropriately adjusted for any stock split, dividend, combination or other recapitalization), provided: (i) the Company is, within a reasonable time after such transfer, furnished with written notice of the name and address of such transferee or assignee and the securities with respect to which such registration rights are being assigned; (ii) such transferee or assignee agrees in writing to be bound by and

subject to the terms and conditions of this Agreement, including, without limitation, the provisions of Section 2.12 of this Agreement; and (iii) such assignment shall be effective only if immediately following such transfer the further disposition of such securities by the transferee or assignee is restricted under the Act.

2.11 Limitations on Subsequent Registration Rights. From and after the date of this Agreement, the Company shall not, without the prior written consent of the Holders holding [***] of the Registrable Securities then held by all Holders, enter into any agreement with any holder or prospective holder of any securities of the Company that would allow such holder or prospective holder (a) to include any of such securities in any registration filed under Section 2.1, Section 2.2 or Section 2.3 of this Agreement, unless under the terms of such agreement, such holder or prospective holder may include such securities in any such registration only to the extent that the inclusion of such securities will not reduce the amount of the Registrable Securities of the Holders that are included or (b) to demand registration of their securities.

2.12 "Market Stand-Off" Agreement. Each Stockholder hereby agrees that he, she or it will not, without the prior written consent of the managing underwriter, during the period commencing on the date of the final prospectus relating to the Initial Offering and ending on the date specified by the Company and the managing underwriter (such period not to exceed [one hundred eighty (***]) (i) lend, offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of Common Stock or any securities convertible into or exercisable or exchangeable for Common Stock held immediately prior to the effectiveness of the registration statement for such offering, or (ii) enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the Common Stock, whether any such transaction described in clause (i) or (ii) above is to be settled by delivery of Common Stock or other securities, in cash or otherwise. The foregoing provisions of this Section 2.12 shall apply only to the Initial Offering, shall not apply to the sale of any shares to an underwriter pursuant to an underwriting agreement, and shall only be applicable to the Holders if all officers, directors and greater than [***] stockholders of the Company enter into similar agreements. Provided that PureTech, as defined below, may dispose of shares of Common Stock during the applicable period only after consultation with its outside counsel and only as it deems necessary in its reasonable judgement to comply with the Investment Company Act of 1940 (the "1940 Act") and provided further that PureTech shall (i) only dispose of so many shares of Common Stock as it deems reasonably necessary in its reasonable judgement to ensure it shall remain compliant with the 1940 Act and (ii) have provided to the lead underwriter in the Initial Offering notice of the intention to make a disposal as contemplated in this Section 2.12 at least two (2) business days prior to such disposal. The underwriters in connection with the Initial Offering are intended third-party beneficiaries of this Section 2.12 and shall have the right, power and authority to enforce the provisions hereof as though they were a party hereto. Each Stockholder further agrees to execute such agreements as may be reasonably requested by the underwriters in the Initial Offering that are consistent with this Section 2.12 or that are necessary to give further effect thereto. Any discretionary waiver or termination of the restrictions of any or all of such agreements by the Company or the underwriters shall apply to all Holders subject to such agreements pro rata based on the number of shares subject to such agreements.

In order to enforce the foregoing covenant, the Company may impose stop-transfer instructions with respect to the securities of each Stockholder (and the shares or securities of every other Person subject to the foregoing restriction) until the end of such period. Notwithstanding the foregoing, if (i) during the last [***] of the [***] restricted period, the Company issues an earnings release or material news or a material event relating to the Company occurs; or (ii) prior to the expiration of the [***] period, the Company announces that it will

release earnings results during the sixteen (16)-day period beginning on the last day of the one hundred eighty (180)-day period, the restrictions imposed by this Section 2.12 shall continue to apply until the expiration of the eighteen (18)-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event).

2.13 Legends. Each Stockholder agrees that a legend reading substantially as follows shall be placed on all certificates representing all securities of each Stockholder (and the shares or securities of every other Person subject to the restrictions contained in Section 2.12), as needed:

(a) "THESE SECURITIES HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED. THEY MAY NOT BE SOLD, OFFERED FOR SALE, PLEDGED OR HYPOTHECATED IN THE ABSENCE OF A REGISTRATION STATEMENT IN EFFECT WITH RESPECT TO THE SECURITIES UNDER SUCH ACT OR AN OPINION OF COUNSEL SATISFACTORY TO THE COMPANY THAT SUCH REGISTRATION IS NOT REQUIRED OR UNLESS SOLD PURSUANT TO RULE 144 OF SUCH ACT."

(b) "THE SECURITIES REPRESENTED BY THIS CERTIFICATE ARE SUBJECT TO A LOCK-UP PERIOD AFTER THE EFFECTIVE DATE OF THE ISSUER'S REGISTRATION STATEMENT FILED UNDER THE SECURITIES ACT OF 1933, AS AMENDED, AS SET FORTH IN AN AGREEMENT BETWEEN THE COMPANY AND THE ORIGINAL HOLDER OF THESE SECURITIES, A COPY OF WHICH MAY BE OBTAINED AT THE ISSUER'S PRINCIPAL OFFICE. SUCH LOCK-UP PERIOD IS BINDING ON TRANSFEREES OF THESE SECURITIES.

(c) Any legend required by applicable state "blue sky" securities laws, rules and regulations.

2.14 Termination of Registration Rights. No Holder shall be entitled to exercise any right provided for in this Section 2: [***]

3. Covenants of the Company.

3.1 Delivery of Financial Statements. The Company shall, upon request, deliver to each Investor (or transferee of an Investor) that holds Preferred Stock:

(a) as soon as practicable, but in any event within [***] after the end of each fiscal year of the Company, an income statement for such fiscal year, a balance sheet of the Company and statement of stockholders' equity as of the end of such year, and a statement of cash flows for such year, such year-end financial reports to be in reasonable detail, prepared in accordance with generally accepted accounting principles ("GAAP") and audited and certified by independent public accountants of nationally recognized standing selected by the Company;

(b) as soon as practicable, but in any event within [***]after the end of each of the first three quarters of each fiscal year of the Company, an income statement and a statement of cash flows for such fiscal quarter and an unaudited balance sheet as of the end of such fiscal quarter, all prepared in accordance with GAAP (except that such financial statements may (i) be subject to normal year-end audit adjustments and (ii) not contain all notes thereto that may be required in accordance with GAAP);

(c) as soon as practicable, but in any event at least [***] prior to the end of each fiscal year, a budget and business plan for the next fiscal year, prepared on a monthly basis, including balance sheets, income statements and statements of cash flows for such

months and, as soon as prepared, any other budgets or revised budgets prepared by the Company; and

(d) such other information relating to the financial condition, business or corporate affairs of the Company as such Investor may from time to time reasonably request, provided, however, that the Company shall not be obligated under this subsection (d) or any other subsection of Section 3.1 to provide information (i) that it deems in good faith to be a trade secret or similar confidential information or (ii) the disclosure of which would adversely affect the attorney-client privilege between the Company and its counsel.

(e) Notwithstanding anything else in this Section 3.1 to the contrary, the Company may cease providing the information set forth in this Section 3.1 during the period starting with the date [***] before the Company's good-faith estimate of the date of filing of a registration statement if it reasonably concludes it must do so to comply with the SEC rules applicable to such registration statement and related offering; provided that the Company's covenants under this Section 3.1 shall be reinstated at such time as the Company is no longer actively employing its commercially reasonable efforts to cause such registration statement to become effective. If, for any period, the Company has any subsidiary whose accounts are consolidated with those of the Company, then in respect of such period the financial statements delivered pursuant to the foregoing sections shall be the consolidated and consolidating financial statements of the Company and all such consolidated subsidiaries.

3.2 Inspection. The Company shall permit each Investor that holds Preferred Stock, at such Investor's expense, to visit and inspect the Company's properties, to examine its books of account and records and to discuss the Company's affairs, finances and accounts with its officers, all at such reasonable times as may be requested by the Investor; provided, however, that the Company shall not be obligated pursuant to this Section 3.2 to provide access to any information that (i) it reasonably considers to be a trade secret or similar confidential information or (ii) the disclosure of which would adversely affect the attorney-client privilege between the Company and its counsel.

3.3 Board Observer. [***]; provided, however, that such representative shall agree to hold in confidence and trust all information so provided; and provided further, that the Company reserves the right to withhold any information and to exclude such representative from any meeting or portion thereof if access to such information or attendance at such meeting could adversely affect the attorney-client privilege between the Company and its counsel or result in disclosure of highly confidential proprietary information or a conflict of interest.

3.4 Termination of Information, Inspection and Board Observer Rights. The covenants set forth in Sections 3.1, 3.2 and 3.3 shall terminate and be of no further force or effect upon the earlier to occur of (a) immediately before the consummation of the Initial Offering or a SPAC merger, (b) when the Company first becomes subject to the periodic reporting requirements of Sections 12(g) or 15(d) of the 1934 Act, or (c) the consummation of a Deemed Liquidation Event, as that term is defined in the Restated Certificate.

3.5 Confidentiality. Each Investor agrees that such Investor will keep confidential and will not disclose, divulge, or use for any purpose (other than to monitor or make decisions with respect to its investment in the Company) any confidential information obtained from the Company (including notice of the Company's intention to file a registration statement), unless such confidential information (a) is known or becomes known to the public in general (other than as a result of a breach of this Section 3.5 by such Investor), (b) is or has been independently developed or conceived by such Investor without use of, or reference to, the Company's confidential information, or (c) is or has been made known or disclosed to such

Investor by a third party without a breach of any obligation of confidentiality such third party may have to the Company; provided, however, that an Investor may disclose confidential information (i) to its attorneys, accountants, consultants, and other professionals to the extent reasonably necessary to obtain their services in connection with monitoring its investment in the Company; (ii) to any prospective purchaser of any Registrable Securities from such Investor, if such prospective purchaser agrees to be bound by the provisions of this Section 3.5; (iii) to any existing Affiliate, partner, member, stockholder, or wholly owned subsidiary of such Investor in the ordinary course of business, provided that such Investor informs such Person that such information is confidential and directs such Person to maintain the confidentiality of such information or such person is bound by agreement to maintain such confidentiality; or (iv) as may otherwise be required by law, regulation, rule, court order or subpoena, provided that such Investor promptly notifies the Company of such disclosure and takes reasonable steps to minimize the extent of any such required disclosure; and provided further, however, that that each Investor shall be responsible to Company for the failure of any person or entity described in clause (i), (ii), or (iii) above to comply with the provisions of this Section 3.5.

3.6 Right of First Offer. Subject to the terms and conditions specified in this Section 3.6, the Company hereby grants to each Investor a right of first offer with respect to future issuances by the Company of its Shares (as hereinafter defined). For purposes of this Section 3.6, the term "Investor" includes any Affiliates of an Investor. An Investor shall be entitled to apportion the right of first offer hereby granted it among itself and its Affiliates in such proportions as it deems appropriate.

Each time the Company proposes to issue any additional Shares ("New Shares"), the Company shall first make an offering of such New Shares to each Investor in accordance with the following provisions:

(a) The Company shall deliver a notice in accordance with Section 5.5 ("Notice") to each Investor stating (i) its bona fide intention to issue such New Shares, (ii) the number of such New Shares to be issued and (iii) the price and terms upon which it proposes to issue such New Shares. If the consideration to be paid by others for the New Shares is not cash, the fair market value of the consideration shall be determined in good faith by the Board and a reasonably detailed explanation of the Board's determination of such value shall be included in the Notice. All Investors electing to participate in the issuance of the New Shares shall pay the cash equivalent thereof as so determined.

(b) By written notification received by the Company within [***] after the giving of Notice, each Investor may elect to purchase, at the price and on the terms specified in the Notice, up to that portion of such New Shares that equals the proportion that the number of shares of Common Stock that are Registrable Securities issued and held by such Investor (assuming full conversion and exercise of all convertible and exercisable securities then held by such Investor) bears to the total number of shares of Common Stock of the Company then outstanding (assuming full conversion and exercise of all convertible and exercisable securities then outstanding). The Company shall promptly, in writing, inform each Investor that elects to purchase all the New Shares available to it (a "Fully-Exercising Investor") of any other Investor's failure to do likewise. During the [***] period commencing after such information is given, each Fully-Exercising Investor may elect to purchase that portion of the New Shares for which Investors were entitled to subscribe, but which were not subscribed for by the Investors, that is equal to the proportion that the number of Registrable Securities issued and held by such Fully-Exercising Investor bears to the total number of Registrable Securities held by all Fully-Exercising Investors desiring to purchase such unsubscribed New Shares.

(c) If all New Shares that Investors are entitled to obtain pursuant to Section 3.6(b) are not elected to be obtained as provided in Section 3.6(b) hereof, the

Company may, during the [***] period following the expiration of the period provided in Section 3.6(b) hereof, offer the remaining unsubscribed portion of such New Shares to any Person or Persons at a price not less than that, and upon terms no more favorable to the offeree than those, specified in the Notice. If the Company does not enter into an agreement for the sale of the New Shares within such period, or if such agreement is not consummated within [***] of the execution thereof, the right provided hereunder shall be deemed to be revived and such New Shares shall not be offered unless first reoffered to the Investors in accordance with this Section 3.6.

(d) The right of first offer in this Section 3.6 shall not be applicable to (i) the issuance of Series D Preferred Stock pursuant to the Series D Agreement, (ii) Exempted Securities (as such term is defined in the Restated Certificate), and (iii) shares of capital stock issued by the Company in connection with the Initial Offering. In addition to the foregoing, the right of first offer in this Section 3.5 shall not be applicable with respect to any Investor in any subsequent offering of New Shares if (i) at the time of such offering, the Investor is not an "accredited investor," as that term is then defined in Rule 501(a) of the Act and (ii) such offering of New Shares is otherwise being offered only to accredited investors.

(e) The rights provided in this Section 3.6 may not be assigned or transferred by any Investor, except as provided in the first paragraph of this Section 3.6; provided, however, that (i) an Investor that is an investment fund may assign or transfer such rights to an affiliated investment fund, [***]

(f) The rights set provided in this Section 3.6 shall terminate and be of no further force or effect (i) immediately before the consummation of the Initial Offering or (ii) upon the consummation of a Deemed Liquidation Event (as such term is defined in the Restated Certificate) or a SPAC merger.

4. Voting Provisions.

4.1 Agreement to Vote. Each Investor, as a holder of Preferred Stock, hereby agrees on behalf of itself and any transferee or assignee of any such shares of Preferred Stock, to hold all of the shares of Preferred Stock registered in its name and any other securities of the Company now held or subsequently acquired by such Investor in the future (and any securities of the Company issued with respect to, upon conversion of, or in exchange or substitution for such shares or other securities) (hereinafter collectively referred to as the "Investor Shares") subject to, and to vote the Investor Shares at a regular or special meeting of stockholders (or by written consent) in accordance with, the provisions of this Agreement. Each Key Holder, as a holder of Common Stock, hereby agrees on behalf of itself and any transferee or assignee of any such shares of Common Stock, to hold all of such shares registered in its name and any other securities of the Company now held or subsequently acquired by such Key Holder in the future (and any securities of the Company issued with respect to, upon conversion of, or in exchange or substitution for such shares or other securities) (hereinafter collectively referred to as the "Key Holder Shares") subject to, and to vote the Key Holder Shares at a regular or special meeting of stockholders (or by written consent) in accordance with, the provisions of this Agreement. The Investor Shares and the Key Holder Shares are hereinafter collectively referred to as the "Voting Shares".

4.2 Board Size. Each Stockholder shall vote, or cause to be voted, at a regular or special meeting of stockholders (or by written consent) all Voting Shares owned by such Stockholder (or as to which such Stockholder has voting power) to ensure that the size of the Board shall be set and remain at nine (9) directors; provided, however, that such Board size may be subsequently increased or decreased pursuant to an amendment of this Agreement in accordance with Section 5.7 hereof.

4.3 Election of Directors.

(a) In any election of directors of the Company, Stockholders holding Voting Shares shall each vote at any regular or special meeting of stockholders (or by written consent) all Voting Shares then owned by them (or as to which they then have voting power) to elect:

(i) one (a) director nominated by PureTech Health LLC ("PureTech" and a "PureTech Director"), so long as PureTech continues to hold not less than 1,129,098 shares of Series A-1 Preferred Stock and Series A-2 Preferred Stock (appropriately adjusted for any stock split, dividend, combination or recapitalization) who shall initially be Bharatt Chowrira;

[***]

(b) In the absence of any nomination from the Persons with the right to nominate a director as specified above, the director or directors previously nominated by such Persons and then serving shall be reelected if still eligible to serve as provided herein.

(c) To the extent that the application of Section 4.3(a) above shall result in the designation of less than all of the authorized directors, then any remaining directors shall be nominated and elected by the stockholders of the Company entitled to vote thereon in accordance with, and pursuant to, the Restated Certificate.

4.4 Removal; Vacancies. Any director of the Company may be removed from the Board in the manner allowed by law and the Restated Certificate and Bylaws, but with respect to any director nominated pursuant to Section 4.3(a) above, only upon the vote or written consent of the Stockholders (or other Persons) entitled to nominate such director. Any vacancy created by the resignation, removal or death of a director elected pursuant to Section 4.3 above shall be filled pursuant to the provisions of Section 4.3.

4.5 Failure to Designate a Board Member. In the absence of any designation from the Persons or groups with the right to designate a director as specified above, the director previously designated by them and then serving shall be reelected if willing to serve unless such individual has been removed as provided herein, and otherwise such Board seat shall remain vacant until otherwise filled as provided above.

4.6 Vote to Increase Authorized Stock. Each Stockholder agrees to vote or cause to be voted all Voting Shares owned by such Stockholder, or over which such Stockholder has voting control, from time to time and at all times, in whatever manner as shall be necessary to increase the number of authorized shares of Common Stock from time to time to ensure that there will be sufficient shares of Common Stock available for conversion of all of the shares of Preferred Stock outstanding at any given time. Without derogating from the foregoing, and in addition thereto, each Stockholder further agrees to vote or cause to be voted all Voting Shares owned by such Stockholder, or over which such Stockholder has voting control, from time to time, upon the reasonable request of the Board, in whatever manner as shall be necessary to increase the number of authorized shares of Series D Preferred Stock to ensure that there will be sufficient shares of Series D Preferred Stock available for the Company to declare and pay the Series D Accruing Dividends (as such term is defined in the Restated Certificate).

4.7 Drag Along Right.

(a) Definitions.

(b) A "Sale of the Company" shall mean either: (a) a transaction or series of related transactions in which a Person, or a group of related Persons, acquires from stockholders of the Company shares representing more than [***] of the outstanding voting power of the Company (a "Stock Sale") or (b) a transaction that qualifies as a "Deemed Liquidation Event" as defined in the Restated Certificate.

(b) Actions to be Taken.

In the event that [***] approve a Sale of the Company, then each Stockholder hereby agrees with respect to all Shares which it own(s) or over which it otherwise exercises voting or dispositive authority:

(i) in the event such transaction is to be brought to a vote at a stockholder meeting, after receiving proper notice of any meeting of stockholders of the Company, to vote on the approval of a Sale of the Company, to be present, in person or by proxy, as a holder of shares of voting securities, at all such meetings and to be counted for the purposes of determining the presence of a quorum at such meetings;

(ii) to vote (in person, by proxy or by action by written consent, as applicable) all Shares in favor of such Sale of the Company and in opposition to any and all other proposals that could reasonably be expected to delay or impair the ability of the Company to consummate such Sale of the Company;

(iii) to waive all dissenters' rights and rights of appraisal under applicable law at any time with respect to such Sale of the Company (in each such case, whether before or after the consummation of the Sale of the Company) and refrain from asserting any claim or commencing any suit (x) challenging the Sale of the Company or this Agreement, or (y) alleging a breach of any fiduciary duty of the Selling Investors or any affiliate or associate thereof (including, without limitation, aiding and abetting breach of fiduciary duty) in connection with the evaluation, negotiation or entry into the Sale of the Company or the consummation of the transactions contemplated thereby;

(iv) to execute and deliver all related documentation and take such other action in support of the Sale of the Company as shall reasonably be requested by the Company or the Requisite Parties (in each such case, whether before or after the consummation of the Sale of the Company);

(v) if the Sale of the Company is structured as a Stock Sale, to sell the same proportion of his, her or its Shares as is being sold by the Requisite Parties;

(vi) not to deposit, and to cause their Affiliates not to deposit, except as provided in this Agreement, any Shares owned by such Stockholder or Affiliate in a voting trust or subject any such Shares to any arrangement or agreement with respect to the voting of such Shares, unless specifically requested to do so by the acquirer in connection with the Sale of the Company;

(vii) if the consideration to be paid in exchange for the Shares pursuant to this Section 4 includes any securities and due receipt thereof by any Stockholder would require under applicable law (i) the registration or qualification of such securities or of any Person as a broker or dealer or agent with respect to such securities or (ii) the provision to any Stockholder of any information other than such information as a prudent issuer would generally furnish in an offering made solely to "accredited investors" as defined in

Regulation D promulgated under the Act, the Company may cause to be paid to any such Stockholder in lieu thereof, against surrender of the Shares which would have otherwise been sold by such Stockholder, an amount in cash equal to the fair value (as determined in good faith by the Company) of the securities which such Stockholder would otherwise receive as of the date of the issuance of such securities in exchange for the Shares; and

(viii) unless, if any portion of the consideration payable to the stockholders of the Company in connection with such transaction consists of securities unlisted on a public stock exchange, then upon receipt from a Stockholder, of written notice that, based on the advice of legal counsel, the payment or distribution of such securities to the Stockholder, would cause the Stockholder to be in violation of any law, regulation, material contractual obligation or written policy of the Stockholder, the Company shall cause the purchase agreement, merger agreement or related transaction documents to provide the Stockholder with certain stockholder rights to the extent necessary to enable the Stockholder to hold such securities without violating such contract or policy, and if the Company is unable to satisfy such requirements, then the Company shall cause to be paid to the Stockholder, in lieu thereof, against surrender of the Company's shares which would have otherwise been sold by the Stockholder an amount in cash equal to the fair value (as determined in good faith by the Company) of the securities which the Stockholder would otherwise receive as of the date of the issuance of such securities in exchange for the capital stock.

(c) Exceptions. Notwithstanding the foregoing, a Stockholder will not be required to comply with Section 4.7(b) above in connection with any proposed Sale of the Company (the "Proposed Sale") unless the Stockholder shall not be liable for the inaccuracy of any representation or warranty made by any other Person in connection with the Proposed Sale, other than the Company (except to the extent that funds may be paid out of an escrow established to cover breach of representations, warranties and covenants of the Company as well as breach by any stockholder of any identical representations, warranties and covenants provided by all stockholders);

(i) the liability for indemnification, if any, of such Stockholder in the Proposed Sale and for the inaccuracy of any representations and warranties made by the Company or its stockholders in connection with such Proposed Sale, is several and not joint with any other Person (except to the extent that funds may be paid out of an escrow established to cover breach of representations, warranties and covenants of the Company as well as breach by any stockholder of any identical representations, warranties and covenants provided by all stockholders);

(ii) liability of such Stockholder shall be limited to the amount of consideration otherwise payable to such Stockholder in connection with such Proposed Sale in accordance with the provisions of the Restated Certificate, except with respect to claims related to fraud by such Stockholder, the liability for which need not be limited as to such Stockholder;

(iii) upon the consummation of the Proposed Sale, (i) each holder of each series of the Company's stock will receive the same form of consideration for their shares of such series as is received by other holders in respect of their shares of such same series of stock, (ii) each holder of a series of Preferred Stock will receive the same amount of consideration per share of such series of Preferred Stock as is received by other holders in respect of their shares of such same series, (iii) each holder of Common Stock will receive the same amount of consideration per share of Common Stock as is received by other holders in respect of their shares of Common Stock, and (iv) the net consideration (i.e. the aggregate consideration less all reductions for purchase price adjustments, indemnification claims and other adjustments) receivable by all holders of the Preferred Stock and Common Stock shall be

allocated among the holders of Preferred Stock and Common Stock on the basis of the relative liquidation preferences to which the holders of each respective series of Preferred Stock and the holders of Common Stock are entitled in a Deemed Liquidation Event (assuming for this purpose that the Proposed Sale is a Deemed Liquidation Event) in accordance with the Restated Certificate in effect immediately prior to the Proposed Sale;

(iv) subject to Section 4.7(c)(iv) above, requiring the same form of consideration to be available to the holders of any single class or series of capital stock, if any holders of a series of Preferred Stock or the holders of Common Stock are given an option as to the form and amount of consideration to be received as a result of the Proposed Sale, all holders of such series of Preferred Stock or the holders of Common Stock will be given the same option; provided, however, that nothing in this Section 4.7(c)(v) shall entitle any holder to receive any form of consideration that such holder would be ineligible to receive as a result of such holder's failure to satisfy any condition, requirement or limitation that is generally applicable to the Company's stockholders;

(v) no Stockholder will be required to agree (unless such Stockholder is an officer or employee of the Company) to any non-competition or non-solicitation agreement; and

(vi) no Stockholder or its Affiliates will be required to amend, extend or terminate any contractual or other relationship with the Company, the acquirer or their respective Affiliates.

4.8 Bad Actor Representations and Covenants. Each Stockholder hereby represents and warrants to the Company that such Stockholder has not been convicted of any of the felonies or misdemeanors or has been subject to any of the orders, judgments, decrees or other conditions set forth in Rule 506(d) of Regulation D promulgated by the SEC. Each Stockholder covenants to provide immediate written notice to the Company in the event such Stockholder is convicted of any felony or misdemeanor or becomes subject to any order, judgment, decree or other condition set forth in Rule 506(d) of Regulation D promulgated by the SEC, as may be amended from time to time. Each Stockholder covenants to provide such information to the Company as the Company may reasonably request in order to comply with the disclosure obligations set forth in Rule 506(e) of Regulation D promulgated by the SEC, as may be amended from time to time.

4.9 Legend on Share Certificates. Each certificate representing any Voting Shares shall be endorsed by the Company with a legend reading substantially as follows:

"THE SHARES EVIDENCED HEREBY ARE SUBJECT TO AN AGREEMENT (A COPY OF WHICH MAY BE OBTAINED UPON WRITTEN REQUEST FROM THE ISSUER) CONTAINING PROVISIONS REGARDING VOTING RIGHTS AND OBLIGATIONS, AND BY ACCEPTING ANY INTEREST IN SUCH SHARES THE PERSON ACCEPTING SUCH INTEREST SHALL BE DEEMED TO AGREE TO AND SHALL BECOME BOUND BY ALL SUCH VOTING PROVISIONS OF SAID AGREEMENT."

4.10 Covenant of the Company. The Company will not, by any voluntary action, avoid or seek to avoid the observance or performance of any of the terms to be performed by the Company under this Section 4.

4.11 No Liability for Election of Recommended Directors. Neither any Party to this Agreement, nor any officer, director, stockholder, partner, employee or agent of any such Party, makes any representation or warranty as to the fitness or competence of the nominee

of any Party hereunder to serve on the Board by virtue of such Party's execution of this Agreement or by the act of such Party in voting for such nominee pursuant to this Agreement.

4.12 Remedies.

(a) Grant of Proxy and Power of Attorney; No Conflicting Agreements. Each Stockholder hereby constitutes and appoints as the proxies of such Stockholder, and hereby grants a power of attorney, to (a) the President of the Company and (b) a stockholder or other Person designated by the Board, and each of them, with full power and substitution, with respect to the matters set forth herein, and hereby authorizes each of them to represent and to vote, if and only if such Stockholder (i) fails to vote or (ii) attempts to vote (whether by proxy, in person or by written consent) in a manner which is inconsistent with the terms of this Agreement, all of such Stockholder's Voting Shares in the manner provided in Section 4 hereof, and hereby authorizes each of them to take any action necessary to give effect to the provisions contained in Section 4 hereof. Each of the proxy and power of attorney granted in this Section 4.12 is given in consideration of the agreements and covenants of the Parties in connection with the transactions contemplated by this Agreement and, as such, each is coupled with an interest and shall be irrevocable until this Agreement terminates pursuant to its terms or this Section 4.12 is amended to remove such grant of proxy and power of attorney in accordance with Section 5.7 hereof. Each Stockholder hereby revokes any and all previous proxies or powers of attorney with respect to such Stockholder's Voting Shares and shall not hereafter, until this Agreement terminates pursuant to its terms or this Section 4.12 is amended to remove this provision in accordance with Section 5.7 hereof, grant, or purport to grant, any other proxy or power of attorney with respect to such Voting Shares, deposit any of such Voting Shares into a voting trust or enter into any agreement (other than this Agreement), arrangement or understanding with any Person, directly or indirectly, to vote, grant any proxy or power of attorney or give instructions with respect to the voting of any of such Voting Shares, in each case, with respect to any of the matters set forth in this Agreement. [***]

(b) Specific Enforcement. It is agreed and understood that monetary damages would not adequately compensate an injured Party for the breach of this Agreement by any other Party, that this Agreement shall be specifically enforceable, and that any breach or threatened breach of this Agreement shall be the proper subject of a temporary or permanent injunction or restraining order. Further, each Party hereto waives any claim or defense that there is an adequate remedy at law for such breach or threatened breach.

(c) Remedies Cumulative. All remedies, either under this Section 3 or by law or otherwise afforded to any Party, shall be cumulative and not alternative.

4.13 Directors' Expenses. The Company shall reimburse the directors on the Board for all reasonable and documented out-of-pocket expenses incurred by them in connection with attendance at all meetings of the Board (including any meetings of committees of the Board) and the board of directors of each of the Company's subsidiaries (including any meetings of committees thereof) or attending to other matters requested by the Company.

4.14 Subsidiary Boards. The Company shall cause the composition of the board of directors of each subsidiary of the Company and of each committee thereof to, where the appropriate individuals are willing to serve, be consistent with the composition of the Board and each corresponding committee thereof.

4.15 Committees. [***]

4.16 Insurance. To the extent not already obtained, the Company and, to the extent applicable, its subsidiaries shall obtain, within [ninety (90) days] of the date hereof,

a general liability and directors' and officers' liability insurance policies, in each case on terms and conditions that are acceptable to the Board. The Company (and its subsidiaries, to the extent that such subsidiaries obtain such policies) shall maintain such policies in full force and effect at all times.

4.17 Stock Sale. No Stockholder shall enter into any transaction or series of related transactions resulting in a Deemed Liquidation Event (as such term is defined in the Restated Certificate) unless the terms of such transaction or transactions provide that the consideration to be paid to the stockholders of the Company is to be allocated in accordance with the preferences and priorities set forth in the Restated Certificate.

4.18 [***]h

4.19 Matters Requiring Investor Director Approval. The Company hereby covenants and agrees with each of the Stockholders that it shall not, without approval of the Board, [***]

4.20 Notice of Board Meetings. [***]

4.21 Termination of Covenants. The covenants set forth in this Section 4 (other than those set forth in Section 4.8 and Section 4.11) shall terminate upon the earliest to occur of: (i) immediately before the consummation of the Initial Offering, (ii) a Sale of the Company or a SPAC merger, provided that the provisions of Section 4.7 and Section 4.12 shall continue after the closing of any Sale of the Company to the extent necessary to enforce the provisions of Section 4.7 with respect to such Sale of the Company, and (iii) termination of this Agreement in accordance with Section 5.7.

5. Miscellaneous.

5.1 Successors and Assigns. Except as otherwise provided herein, the terms and conditions of this Agreement shall inure to the benefit of and be binding upon the respective successors and assigns of the parties (including transferees of any shares of Registrable Securities) provided, however, that (x) the Company is, within a reasonable time after such transfer, furnished with written notice of the name and address of such transferee and the Registrable Securities with respect to which such rights are being transferred; and (y) such transferee agrees in a written instrument delivered to the Company to be bound by and subject to the terms and conditions of this Agreement, including the provisions of Section 2.12. Nothing in this Agreement, express or implied, is intended to confer upon any party other than the parties hereto or their respective successors and assigns any rights, remedies, obligations or liabilities under or by reason of this Agreement, except as expressly provided in this Agreement.

5.2 Governing Law. This Agreement shall be governed by and construed under the laws of the State of Delaware as applied to agreements among Delaware residents entered into and to be performed entirely within Delaware, without regard to its principles of conflicts of laws.

5.3 Counterparts. This Agreement may be executed and delivered by facsimile or electronic signature and in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

5.4 Titles and Subtitles. The titles and subtitles used in this Agreement are used for convenience only and are not to be considered in construing or interpreting this Agreement.

5.5 Notices. All notices and other communications given or made pursuant hereto shall be in writing and shall be deemed effectively given: (i) upon personal delivery to the party to be notified, (ii) when sent by confirmed electronic mail or facsimile if sent during normal business hours of the recipient; if not, then on the next business day, (iii) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (iv) one (1) day after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt. All communications shall be sent to the respective parties at the addresses set forth on the signature pages attached hereto (or at such other addresses as shall be specified by notice given in accordance with this Section 5.5). If notice is sent to the Company, a copy (which shall not constitute notice) shall also be sent to [***].

5.6 Expenses. If any action at law or in equity is necessary to enforce or interpret the terms of this Agreement, the prevailing party shall be entitled to reasonable attorneys' fees, costs and necessary disbursements in addition to any other relief to which such party may be entitled.

5.7 Entire Agreement; Amendments and Waivers. This Agreement (including the Exhibits hereto, if any) constitutes the full and entire understanding and agreement among the parties with regard to the subjects hereof and thereof and supersedes all other agreements of the parties hereto relating to the subject matter hereof and thereof (including, without limitation, the Prior Agreement). Any term of this Agreement may be amended, modified or terminated, and the observance of any term of this Agreement may be waived (either generally or in a particular instance and either retroactively or prospectively) only with the written consent of the Company and the holders of a majority of the outstanding Series D Preferred Stock which majority must include [***]. Notwithstanding the foregoing, [***]. Any amendment, modification, termination or waiver so effected shall be binding upon all the Parties hereto and all Parties' respective successors and permitted assigns, whether or not any such Party, successor or assign entered into or approved such amendment, modification, termination or waiver. Notwithstanding the foregoing, any provision hereof may be waived by the waiving Party on such Party's behalf, without the written consent of any other Party. Notwithstanding the foregoing, (i) this Agreement may not be amended, modified or terminated and the observance of any term hereof may not be waived with respect to any Investor without the written consent of such Investor, unless such amendment, termination, or waiver applies to all Investors in the same fashion, (ii) no amendment or modification to, or waiver or termination of, this Agreement, (by merger, consolidation or otherwise) shall be effective as to any Investor without that Investor's written consent if such amendment, modification, waiver or termination would impose or would reasonably be expected to impose, any non-competition or non-solicitation covenant on such Investor or would otherwise restrict, or would reasonably be expected to otherwise restrict, such Investor from conducting any business or commercial activity [***].

5.8 Severability. Whenever possible, each provision of this Agreement shall be interpreted in such manner as to be effective and valid under applicable law, but if any provision of this Agreement shall be held to be prohibited by or invalid under applicable law, such provision shall be ineffective only to the extent of such prohibition or invalidity, without invalidating the remainder of such provision or the remaining provisions of this Agreement.

5.9 Aggregation of Stock. All Registrable Securities held or acquired by Affiliates (including affiliated venture capital funds) or persons shall be aggregated together for the purpose of determining the availability of any rights under this Agreement.

5.10 Additional Parties.

(a) Notwithstanding Section 5.7 no consent shall be necessary to add additional Investors as signatories to this Agreement, provided that such Investors have purchased Series D Preferred Stock pursuant to the Series D Agreement, as may be amended from time to time, and have signed a counterpart signature page hereto. Schedule A to this Agreement shall be updated without any action of the Investors to reflect such additional Investors.

(b) In the event that after the date of this Agreement, the Company enters into an agreement with any Person to issue shares of capital stock to such Person (other than to a purchaser of Series D Preferred described in Section 5.10(a) above), following which such Person would hold Shares representing [***] or more of the Company's then outstanding capital stock (treating for this purpose all shares of Common Stock issuable upon exercise or conversion of all then outstanding options, warrants or convertible securities (whether or not then exercisable or convertible) as outstanding), then (i) the Company shall cause such Person, as a condition precedent to the issuance of such capital stock, to become a party to this Agreement by executing an adoption agreement agreeing to be bound by and subject to the terms of this Agreement as a Key Holder and Stockholder hereunder and thereafter such Person shall be deemed a Key Holder and Stockholder for all purposes under this Agreement and (ii) notwithstanding Section 5.7, no consent shall be necessary to add such Person as a signatory to this Agreement.

5.11 Effect on Prior Agreement. Upon the effectiveness of this Agreement, the Prior Agreement automatically shall terminate and be of no further force and effect and shall be amended and restated in its entirety as set forth in this Agreement.

5.12 FIRPTA. Upon request of Investor, the Company shall provide (i) a statement (in such form as may be reasonably requested by Investor) conforming to the requirements of Section 1.897-2(h)(1)(i) and 1.1445-2(c)(3)(i) of the Treasury Regulations certifying that interests in the Company do not constitute "United States real property interests" under Section 897(c) of the Internal Revenue Code of 1986, as amended, and (ii) evidence in form and substance satisfactory to Investor that the Company has delivered to the Internal Revenue Service the notification required under Section 1.897-2(h)(2) of the Treasury Regulations.

(*Remainder of page intentionally left blank*)

IN WITNESS WHEREOF, the parties have executed this Third Amended and Restated Investors' Rights Agreement as of the date first above written.

COMPANY:

AKILI INTERACTIVE LABS, INC.

By: /s/ W. Edward Martucci, Ph.D.

Name: W. Edward Martucci, Ph.D.

Title: Chief Executive Officer

Address: 125 Broad Street, 5th Floor

Boston, MA 02110

IN WITNESS WHEREOF, the parties have executed this Third Amended and Restated Investors' Rights Agreement as of the date first above written.

INVESTORS:

[***]

Exhibit 4.25

CERTAIN IDENTIFIED INFORMATION HAS BEEN EXCLUDED (INDICATED BY: [***] FROM THE EXHIBIT BECAUSE IT IS BOTH (I) NOT MATERIAL AND (II) THE TYPE OF INFORMATION THAT THE REGISTRANT CUSTOMARILY AND ACTUALLY TREATS AS PRIVATE OR CONFIDENTIAL.

Execution Version

AKILI INTERACTIVE LABS, INC.
AMENDED AND RESTATED FIRST REFUSAL AND CO-SALE AGREEMENT

This **AMENDED AND RESTATED FIRST REFUSAL AND CO-SALE AGREEMENT** (the "Agreement") is entered into as of the 25th day of May, 2021 by and among **AKILI INTERACTIVE LABS, INC.**, a Delaware corporation (the "Company"), the holders of Common Stock of the Company (the "Common Stock"), or of options to purchase Common Stock, listed on Exhibit A attached hereto (each a "Common Holder" and, together, the "Common Holders") and the holders of Preferred Stock of the Company (the "Preferred Shares") listed on Exhibit B attached hereto (each an "Investor" and together, the "Investors").

RECITALS

WHEREAS, the Company and certain of the Investors are parties to that certain Series D Preferred Stock Purchase Agreement of even date herewith (the "Series D Agreement"), pursuant to which certain of the Investors are purchasing shares of the Company's Series D Preferred Stock;

WHEREAS, each Common Holder is the beneficial owner of the number of shares of Common Stock or options to purchase Common Stock set forth opposite his/her name on Schedule A attached hereto;

WHEREAS, the Company, certain of the Common Holders and certain of the Investors previously entered into a First Refusal and Co-Sale Agreement, dated January 20, 2016 and an Amended and Restated First Refusal and Co-Sale Agreement, dated [***] (the "Prior Agreement");

WHEREAS, the parties to the Prior Agreement desire to amend and restate the Prior Agreement in its entirety and accept the rights and obligations created pursuant to this Agreement in lieu of their rights and obligations under the Prior Agreement;

WHEREAS, the stockholders of the Company signatory hereto hold the requisite shares of capital stock in order to amend and restate the Prior Agreement in accordance with the terms thereof (subject to the execution of this Agreement by the Company); and

WHEREAS, each Common Holder wishes to provide further inducement to the Investors to purchase the Preferred Shares.

NOW, THEREFORE, in consideration of the foregoing premises and certain other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties agree that the Prior Agreement shall be amended and restated in the entirety by this Agreement and further agree as follows:

1. Definitions.

(a) Affiliate. For purposes of this Agreement, the term "Affiliate" shall mean, (i) with respect to any Person, any other Person who or which, directly or indirectly, controls, is controlled by, or is under common control with such specified Person, including, without limitation, any general partner, officer, director or manager of such Person and any venture capital fund now or hereafter existing that is controlled by one or more general partners or managing members of, or is under common investment management with, such Person, (ii) with respect of TLS Beta Pte. Ltd. ("Temasek"), Temasek's ultimate holding company, Temasek Holdings (Private) Limited ("Temasek Holdings"), and Temasek Holdings' direct and indirect wholly owned companies whose boards of directors or equivalent governing bodies comprise solely of nominees or employees of (a) Temasek Holdings; (b) Temasek Pte. Ltd; and/or (c) wholly owned direct or indirect subsidiaries of Temasek Pte. Ltd.; (iii) with respect to Edinburgh Worldwide Investment Trust plc, any person that receives, directly or indirectly, investment management or management advisory services from Baillie Gifford & Co. or Baillie Gifford Overseas Limited or any of their affiliates and (iv) with respect to Neuberger Berman Principal Strategies PRIMA Fund LP ("Neuberger"), any person that receives, directly or indirectly, investment management or management advisory services from Neuberger Berman Investment Advisers LLC and/or NB Alternatives Advisers LLC or any successor or affiliated registered investment advisor of such firms.

(b) Delivery. For purposes of this Agreement, the term "Delivery" shall have the meaning set forth in Section 6 below.

(c) Equity Securities. For purposes of this Agreement, the term "Equity Securities" shall mean any securities now or hereafter owned or held by a Common Holder (or a transferee who receives such securities subject to the rights of the Company and the Holders under Section 2.1 and Section 2.2) having voting rights in the election of the Board of Directors of the Company, or any securities evidencing an ownership interest in the Company, or any securities convertible into, exchangeable for or exercisable for any shares of the foregoing.

(d) Holders. For purposes of this Agreement, the term "Holders" shall mean the Investors or persons who have acquired shares from any of such persons or their transferees or assignees in accordance with the provisions of this Agreement.

(e) Person. For purposes of this Agreement, the term "Person" shall mean any individual, corporation, partnership, trust, limited liability company, association or other entity.

(f) Transfer. For purposes of this Agreement, the term "Transfer" shall include any sale, assignment, encumbrance, hypothecation, pledge, conveyance in trust, gift, transfer by bequest, devise or descent, or other transfer or disposition of any kind, including, without limitation, transfers pursuant to divorce or legal separation, transfers to receivers, levying creditors, trustees or receivers in bankruptcy proceedings or general assignees for the benefit of creditors, whether voluntary, involuntarily or by operation of law, directly or indirectly, of any of the Equity Securities.

2. Agreements Among the Company, the Holders and the Common Holders.

2.1 Rights of Refusal.

(a) Transfer Notice. If at any time a Common Holder proposes to Transfer Equity Securities (a "Selling Common Holder"), then the Selling Common Holder shall promptly give the Company and each Holder written notice of the Selling Common Holder's

intention to make the Transfer (the "Transfer Notice"). The Transfer Notice shall include (i) a description of the Equity Securities to be Transferred (the "Offered Shares"), (ii) the name(s) and address(es) of the prospective transferee(s), (iii) the purchase price and form of consideration proposed to be paid for the Offered Shares and (iv) the other material terms and conditions upon which the proposed Transfer is to be made. The Transfer Notice shall certify that the Selling Common Holder has received a firm offer from the prospective transferee(s) and in good faith believes a binding agreement for the Transfer is obtainable on the terms set forth in the Transfer Notice. The Transfer Notice shall also include a copy of any written proposal, term sheet or letter of intent or other agreement relating to the proposed Transfer. In the event that the transfer is being made pursuant to the provisions of Section 2.4, the Transfer Notice shall state under which specific clause of Section 2.4 the Transfer is being made.

(b) Company's Right of First Refusal. The Company shall have an option for a period of [***] from Delivery of the Transfer Notice to elect to purchase the Offered Shares at the same price and subject to the same material terms and conditions as described in the Transfer Notice. The Company may exercise such purchase option and purchase all or any portion of the Offered Shares by notifying the Selling Common Holder in writing before expiration of such [ten (10) day] period as to the number of such shares that it wishes to purchase. If the Company gives the Selling Common Holder notice that it desires to purchase such shares, then payment for the Offered Shares shall be made by check or wire transfer against delivery of the Offered Shares to be purchased at a time and place agreed upon between the parties, which time shall be no later than [***] after Delivery to the Company of the Transfer Notice, unless the Transfer Notice contemplated a later closing with the prospective third-party transferee(s) or unless the value of the consideration to be paid for the Offered Shares has not yet been established pursuant to Section 2.1(e)(ii). If the Company fails to purchase any or all of the Offered Shares by exercising the option granted in this Section 2.1(b) within the period provided, the remaining Offered Shares shall be subject to the options granted to the Holders pursuant to Section 2.1(c)-(d).

(c) Additional Transfer Notice. Subject to the Company's option set forth in Section 2.1(b), if at any time the Selling Common Holder proposes a Transfer, then, within [***] after the Company has declined to purchase all, or a portion, of the Offered Shares or the Company's option to so purchase the Offered Shares has expired, the Selling Common Holder shall give each Holder an "Additional Transfer Notice" that shall include all of the information and certifications required in a Transfer Notice and shall additionally identify the Offered Shares that the Company has declined to purchase (the "Remaining Shares") and reference the Holders' rights of first refusal and co-sale rights with respect to the proposed Transfer contained in this Agreement.

(d) Holders' Right of First Refusal.

(i) Each Holder shall have an option for a period of [***] from the Delivery of the Additional Transfer Notice from the Selling Common Holder set forth in Section 2.1(c) to elect to purchase its respective pro rata share of the Remaining Shares at the same price and subject to the same material terms and conditions as described in the Additional Transfer Notice. Each Holder may exercise such purchase option and purchase all or any portion of its pro rata share of the Remaining Shares (a "Participating Holder" for the purposes of this Section 2.1(d) and Section 2.1(e)), by notifying the Selling Common Holder and the Company in writing, before expiration of the [***] period as to the number of such shares that it wishes to purchase (the "Participating Holder Notice"). Each Holder's pro rata share of the Remaining Shares shall be a fraction of the Remaining Shares, the numerator of which shall be the number of shares of Common Stock (including shares of Common Stock issuable upon conversion of Preferred Shares) owned by such Holder on the date of the Transfer Notice and denominator of which shall be the total number of shares of Common Stock (including shares of Common Stock

issuable upon conversion of Preferred Shares) held by all Holders on the date of the Transfer Notice.

(ii) In the event any Holder elects not to purchase its pro rata share of the Remaining Shares available pursuant to its option under Section 2.1(d)(i) within the time period set forth therein, then the Selling Common Holder shall promptly give written notice (the "Overallotment Notice") to each Participating Holder that has elected to purchase all of its pro rata share of the Remaining Shares (each a "Fully Participating Holder"), which notice shall set forth the number of Remaining Shares not purchased by the other Holders ("Unsubscribed Shares"), and shall offer the Fully Participating Holders the right to acquire the Unsubscribed Shares. Each Fully Participating Holder shall have [***] after Delivery of the Overallotment Notice to deliver a written notice to the Selling Common Holder (the "Participating Holders Overallotment Notice") of its election to purchase its pro rata share of the Unsubscribed Shares on the same terms and conditions as set forth in the Additional Transfer Notice, which such Participating Holders Overallotment Notice shall also indicate the maximum number of the Unsubscribed Shares that such Fully Participating Holder will purchase in the event that any other Fully Participating Holder elects not to purchase its pro rata share of the Unsubscribed Shares. For the purposes of determining a Fully Participating Holder's pro rata share of the Unsubscribed Shares under this Section 2.1(d)(ii), the numerator shall be the same as that used in Section 2.1(d)(i) above and the denominator shall be the total number of shares of Common Stock (including shares of Common Stock issuable upon conversion of Preferred Shares) owned by all Fully Participating Holders on the date of the Transfer Notice.

(iii) Each Participating Holder shall be entitled to apportion Remaining Shares to be purchased among its partners and Affiliates, provided that such Participating Holder notifies the Selling Common Holder of such allocation.

(e) Payment.

(i) The Participating Holders shall effect the purchase of the Remaining Shares with payment by check or wire transfer against delivery of the Remaining Shares to be purchased at a time and place agreed upon between the parties, which time shall be no later than [***] after Delivery to the Company of the Transfer Notice, unless the Transfer Notice contemplated a later closing with the prospective third-party transferee(s) or unless the value of the consideration to be paid for the Offered Shares has not yet been established pursuant to Section 2.1(e)(ii).

(ii) Should the purchase price specified in the Transfer Notice or Additional Transfer Notice be payable in a form of consideration other than cash or evidences of indebtedness, the Company (and the Participating Holders) shall have the right to pay such purchase price in an amount of cash equal to the fair market value of such consideration. If the Selling Common Holder and the Company (or the Participating Holders) cannot agree on such fair market value within [***] after Delivery to the Company of the Transfer Notice (or the Delivery of the Additional Transfer Notice to the Holders), the valuation shall be made by an appraiser of recognized standing selected by the Selling Common Holder and the Company (or [***] of the Participating Holders) or, if they cannot agree on an appraiser within [***] after Delivery to the Company of the Transfer Notice (or the Delivery of the Additional Transfer Notice to the Holders), each shall select an appraiser of recognized standing and those appraisers shall designate a third appraiser of recognized standing, whose appraisal shall be determinative of such value. The cost of such appraisal shall be shared equally by the Selling Common Holder, on the one hand, and the Company (and, to the extent there are any, the Participating Holders, on the other hand, with that half of the cost to be borne by the Company and the Participating Holders to be apportioned on a pro rata basis based on the number of shares each such party has expressed an interest in purchasing pursuant to this Section 2). If the time for the closing of the

Company's purchase or the Participating Holders' purchase has expired but the determination of the value of the purchase price offered by the prospective transferee(s) has not been finalized, then such closing shall be held on or prior to the [***] after such valuation shall have been made pursuant to this Section 2.1(e)(ii).

2.2 Right of Co-Sale.

(a) To the extent the Company and the Holders do not exercise their respective rights of refusal as to all of the Offered Shares pursuant to Section 2.1, then each Holder (a "Selling Holder" for purposes of this Section 2.2 and Section 2.6) that notifies the Selling Common Holder in writing within [***] after Delivery of the Additional Transfer Notice referred to in Section 2.1(c) shall have the right to participate in such sale of Equity Securities on the same terms and conditions as specified in the Transfer Notice. Such Selling Holder's notice to the Selling Common Holder shall indicate the number of shares of capital stock of the Company that the Selling Holder desires to sell. To the extent one or more Selling Holders exercise such right of participation in accordance with the terms and conditions of this Section 2.2, the number of shares of Equity Securities that the Selling Common Holder may sell in the Transfer shall be correspondingly reduced.

(b) Each Selling Holder may sell all or any part of that number of shares of Common Stock (or capital stock of the Company convertible into such number of shares of Common Stock) equal in the aggregate to the product obtained by multiplying (i) the aggregate number of shares of Equity Securities covered by the Transfer Notice that have not been subscribed for pursuant to Section 2.1 by (ii) a fraction, the numerator of which is the number of shares of Common Stock (including shares of Common Stock issuable upon conversion of Preferred Shares) owned by such Selling Holder on the date of the Transfer Notice and the denominator of which is the total number of shares of Common Stock (including shares of Common Stock issuable upon conversion of Preferred Shares) owned by the Selling Common Holder and all of the Selling Holders on the date of the Transfer Notice.

(c) Each Selling Holder shall effect its participation in the sale by promptly delivering to the Selling Common Holder for transfer to the prospective purchaser one or more certificates, properly endorsed for transfer, which represent:

(i) the number of shares of Common Stock that such Selling Holder elects to sell; or

(ii) that number of shares of capital stock of the Company that are at such time convertible into the number of shares of Common Stock that such Selling Holder elects to sell; provided, however, that if the prospective third-party purchaser objects to the delivery of shares of capital stock of the Company other than Common Stock, such Selling Holder shall convert such shares of capital stock of the Company into Common Stock and deliver Common Stock as provided in this Section 2.2. The Company agrees to make any such conversion concurrent with the actual transfer of such shares to the purchaser and contingent on such transfer.

(d) The stock certificate or certificates that each Selling Holder delivers to the Selling Common Holder pursuant to Section 2.2(c) shall be transferred to the prospective purchaser in consummation of the sale of the Equity Securities pursuant to the terms and conditions specified in the Transfer Notice, and such Selling Common Holder shall concurrently therewith remit to such Selling Holder that portion of the sale proceeds to which such Selling Holder is entitled by reason of its participation in such sale. To the extent that any prospective purchaser or purchasers prohibits such assignment or otherwise refuses to purchase shares or other securities from a Selling Holder exercising its rights of co-sale hereunder, the

Selling Common Holder shall not sell to such prospective purchaser or purchasers any Equity Securities unless and until, simultaneously with such sale, the Selling Common Holder shall purchase such shares or other securities from such Selling Holder for the same consideration and on the same terms and conditions as the proposed transfer described in the Transfer Notice.

2.3 Non-Exercise of Rights. To the extent that the Company and the Holders have not exercised their rights to purchase the Offered Shares or the Remaining Shares within the time periods specified in Section 2.1 and the Holders have not exercised their rights to participate in the sale of the Remaining Shares within the time periods specified in Section 2.2, the Selling Common Holder shall have a period of [***] from the expiration of such rights in which to sell the Offered Shares or the Remaining Shares, as the case may be, upon terms and conditions (including the purchase price) no more favorable than those specified in the Transfer Notice, to the third-party transferee(s) identified in the Transfer Notice. The Company's first refusal rights and the Holders' first refusal rights and co-sale rights shall continue to be applicable to any subsequent disposition of the Offered Shares or the Remaining Shares acquired by the third-party transferee(s) until such rights lapse in accordance with the terms of this Agreement. In the event the Selling Common Holder does not consummate the sale or disposition of the Offered Shares and Remaining Shares within the [***] period from the expiration of these rights, the Company's first refusal rights and the Holders' first refusal rights and co-sale rights shall continue to be applicable to any subsequent disposition of the Offered Shares or the Remaining Shares by the Selling Common Holder until such rights lapse in accordance with the terms of this Agreement. Furthermore, the exercise or non-exercise of the rights of the Company and the Holders under this Section 2 to purchase Equity Securities from the Selling Common Holder or participate in sales of Equity Securities by the Selling Common Holder shall not adversely affect their rights to make subsequent purchases from the Selling Common Holder of Equity Securities or subsequently participate in sales of Equity Securities by the Selling Common Holder.

2.4 Limitations to Rights of Refusal and Co-Sale. Notwithstanding the provisions of Sections 2.1 and 2.2 of this Agreement, the first refusal rights of the Company and first refusal and co-sale rights of the Holders shall not apply to (i) the Transfer of Equity Securities by a Common Holder for estate planning purposes, either during such Common Holder's lifetime or on death by will or intestacy to such Common Holder's spouse or other member of a Common Holder's immediate family, or to a custodian, trustee (including a trustee of a voting trust), executor or other fiduciary for the account of the Common Holder's spouse or members of the Common Holder's immediate family, or to a trust for the Common Holder's own self, or a charitable remainder trust, (ii) a repurchase of Equity Securities from a Common Holder by the Company at cost and pursuant to an agreement containing vesting and/or repurchase provisions, (iii) any sale of Equity Securities pursuant to the exercise of the bring-along right set forth in Section 4.6 of that certain Second Amended and Restated Investors' Rights Agreement of even date herewith by and among the Company and the other parties thereto, as may be amended from time to time, (iv) any sale of Equity Securities to the public pursuant to a registration statement filed with, and declared effective by, the Securities and Exchange Commission under the Securities Act of 1933, as amended, (v) any pledge of Equity Securities held by a Common Holder made pursuant to a bona fide loan transaction that creates a mere security interest or (vi) any bona fide gift to any charitable organization described in Section 501(c)(3) of the Internal Revenue Code; provided, however, that in the event of any transfer made pursuant to one of the exemptions provided by clause(s) (i) or (vi), (A) the Common Holder shall inform the Holders of such Transfer prior to effecting it and (B) each such transferee or assignee, prior to the completion of the Transfer, shall have executed documents assuming the obligations of Common Holder under this Agreement with respect to the transferred Equity Securities. Such transferred Equity Securities shall remain "Equity Securities" hereunder, and such pledgee, transferee or donee shall be treated as a "Common Holder" for purposes of this Agreement.

2.5 Prohibited Transfers.

(a) Except as otherwise provided in this Agreement, each Common Holder will not sell, assign, transfer, pledge, hypothecate or otherwise encumber or dispose of in any way, all of, any part of or any interest in such Common Holder's Equity Securities. Any sale, assignment, transfer, pledge, hypothecation or other encumbrance or disposition of Equity Securities not made in conformance with this Agreement shall be null and void, shall not be recorded on the books of the Company and shall not be recognized by the Company.

(b) In the event a Common Holder should sell any Equity Securities in contravention of the co-sale rights of the Holders under Section 2.2 (a "Prohibited Transfer"), the Holders, in addition to such other remedies as may be available at law, in equity or hereunder, shall have the put option provided below under Section 2.5(c), and such Common Holder shall be bound by the applicable provisions of such option.

(c) In the event of a Prohibited Transfer, each Holder shall have the right to sell to the Common Holder making such Prohibited Transfer the type and number of shares of Equity Securities equal to the number of shares each Holder would have been entitled to transfer to the third-party transferee(s) under Section 2.2 hereof had the Prohibited Transfer been effected pursuant to and in compliance with the terms hereof. Such sale shall be made on the following terms and conditions:

(i) The price per share at which the shares are to be sold to the Common Holder shall be equal to the price per share paid by the third-party transferee(s) to the Common Holder in the Prohibited Transfer. The Common Holder shall also reimburse each Holder for any and all fees and expenses, including legal fees and expenses, incurred pursuant to the exercise or the attempted exercise of the Holder's rights under Section 2.2.

(ii) Within [***] after the later of (A) the date on which the Holder receives notice of the Prohibited Transfer and (B) the date on which the Holder otherwise becomes aware of the Prohibited Transfer, each Holder shall, if exercising the option created hereby, deliver to the Common Holder the certificate or certificates representing shares to be sold, each certificate to be properly endorsed for transfer.

(iii) The Common Holder shall, upon receipt of the certificate or certificates for the shares to be sold by a Holder pursuant to this Section 2.5, pay the aggregate purchase price therefor and the amount of fees and expenses reimbursable under Section 2.5(c)(i) in cash or by other means acceptable to the Holder.

2.6 Violation of First Refusal Right. If any Common Holder becomes obligated to sell any Equity Securities to the Company or any Holder under this Agreement and fails to deliver such Equity Securities in accordance with the terms of this Agreement, the Company and/or such Holder may, at its option, in addition to all other remedies it may have, send to such Common Holder the purchase price for such Equity Securities as is herein specified and transfer to the name of the Company or such Holder (or request that the Company effect such transfer in the name of a Holder) on the Company's books the certificate or certificates representing the Equity Securities to be sold.

2.7 Status of Shares. Holders that have exercised their rights to purchase the Offered Shares and/or the Remaining Shares pursuant to Section 2.1 shall acquire the Offered Shares and/or the Remaining Shares free and clear of subsequent rights of first refusal and co-sale rights under this Agreement.

3. Assignments and Transfers; No Third-Party Beneficiaries.

3.1 Assignment of Rights. This Agreement and the rights and obligations of the parties hereunder shall inure to the benefit of, and be binding upon, their respective successors, assigns and legal representatives, but shall not otherwise be for the benefit of any third party.

3.2 Condition to Transfer. Any successor or permitted assignee of any Common Holder, including any prospective transferee who purchases any Equity Securities in accordance with the terms hereof, shall deliver to the Company and the Holders, as a condition to any transfer or assignment, a counterpart signature page hereto pursuant to which such successor or permitted assignee shall confirm their agreement to be subject to and bound by all of the provisions set forth in this Agreement that were applicable to the predecessor or assignor of such successor or permitted assignee.

3.3 Restrictions on Assignment. The rights of the Holders hereunder are only assignable (a) to any other Holder, (b) to a partner, member or Affiliate of such Holder or (c) to an assignee or transferee who acquires all of the Equity Securities held by a particular Holder or at least [***] shares of Common Stock (including shares of Common Stock issuable upon conversion of Preferred Shares) (as adjusted for stock splits, combinations, dividends, recapitalizations and the like); provided, that any such assignment shall be subject to and conditioned upon any such assignee's delivery to the Company a counterpart signature page hereto pursuant to which such assignee shall confirm his, her or its agreement to be subject to and bound by all of the provisions set forth in this Agreement that were applicable to the assignor of such assignee. Notwithstanding Section 10 of this Agreement, no consent shall be necessary to update Schedule B to add any such assignee as an "Investor" hereunder.

4. Legend. Each existing or replacement certificate for shares now owned or hereafter acquired by a Common Holder shall bear the following legend upon its face:

"THE SALE, PLEDGE, HYPOTHECATION, ASSIGNMENT OR TRANSFER OF THE SECURITIES REPRESENTED BY THIS CERTIFICATE IS SUBJECT TO THE TERMS AND CONDITIONS OF A CERTAIN AMENDED AND RESTATED FIRST REFUSAL AND CO-SALE AGREEMENT BY AND BETWEEN THE STOCKHOLDER, THE CORPORATION AND CERTAIN HOLDERS OF STOCK OF THE CORPORATION, AS MAY BE AMENDED AND/OR RESTATED FROM TIME TO TIME. COPIES OF SUCH AGREEMENT MAY BE OBTAINED UPON WRITTEN REQUEST TO THE SECRETARY OF THE CORPORATION."

5. Effect of Change in Company's Capital Structure. If, from time to time, the Company pays a stock dividend or effects a stock split or other change in the character or amount of any of the outstanding stock of the Company, then in such event any and all new, substituted or additional securities to which a Common Holder is entitled by reason of such Common Holder's ownership of Equity Securities shall be immediately subject to the rights and obligations set forth in this Agreement with the same force and effect as the stock subject to such rights immediately before such event.

6. Notices. All notices and other communications given or made pursuant hereto shall be in writing and shall be deemed effectively given: (a) upon personal delivery to the party to be notified, (b) when sent by confirmed electronic mail or facsimile if sent during normal business hours of the recipient; if not, then on the next business day, (c) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (d) one (1) day after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt. The occurrence of the events set forth in clauses (a) through (d) above shall constitute "Delivery" of notice. All notices and other communications

shall be sent to the Company at and to the other parties at the addresses set forth on the signature pages and/or Schedule A or Schedule B hereto, as applicable (or at such other addresses as shall be specified by notice given in accordance with this Section 6).

7. Further Instruments and Actions. The parties agree to execute such further instruments and to take such further action as may reasonably be necessary to carry out the intent of this Agreement. Each Common Holder agrees to cooperate affirmatively with the Company, the Investors and the Holders to enforce rights and obligations pursuant hereto.

8. Term. This Agreement shall terminate and be of no further force or effect upon [***]

9. Entire Agreement. This Agreement contains the entire understanding of the parties hereto with respect to the subject matter hereof and supersedes all other agreements between or among any of the parties with respect to the subject matter hereof, including without limitation the Prior Agreement. This Agreement shall be interpreted under the laws of the State of Delaware without reference to Delaware conflicts of law provisions.

10. Amendments and Waivers. Any term of this Agreement may be amended and the observance of any term of this Agreement may be waived (either generally or in a particular instance and either retroactively or prospectively) only with the written consent of [***] Notwithstanding the foregoing, (i) this Agreement may not be amended or terminated and the observance of any term hereof may not be waived with respect to any Holder without the written consent of such Holder, unless such amendment, termination, or waiver applies to all Holders in the same fashion. [***].

11. Severability. If one or more provisions of this Agreement is held to be unenforceable under applicable law, such provision shall be excluded from this Agreement and the balance of the Agreement shall be interpreted as if such provision were so excluded and shall be enforceable in accordance with its terms.

12. Attorneys' Fees. In the event that any dispute among the parties to this Agreement should result in litigation, the prevailing party in such dispute shall be entitled to recover from the losing party all fees, costs and expenses of enforcing any right of such prevailing party under or with respect to this Agreement, including, without limitation, such reasonable fees and expenses of attorneys and accountants, which shall include, without limitation, all fees, costs and expenses of appeals.

13. Aggregation of Stock. For the purposes of determining the availability of any rights under this Agreement, the holdings of any transferee and assignee of an individual or a partnership who is a spouse, ancestor, lineal descendant or siblings of such individual or partners or retired partners of such partnership or Affiliates of such partnership (including spouses and ancestors, lineal descendants and siblings of such partners or spouses who acquire Common Stock by gift, will or intestate succession) shall be aggregated together with the individual or partnership, as the case may be, for the purpose of exercising any rights or taking any action under this Agreement.

14. Conflict with Other Rights of First Refusal. Each Common Holder has entered into a stock purchase agreement or stock restriction agreement with the Company on the Company's standard form (together with any additional stock purchase agreements, stock restriction agreements or option agreements that a Common Holder may enter into with the Company, the "Purchase Agreements"), which agreement contains a right of first refusal provision in favor of the Company. For so long as this Agreement remains in existence, the right of first refusal provisions contained in this Agreement shall supersede the right of first refusal

provisions contained in the Common Holder's Purchase Agreements; provided, however, that the other provisions of the Common Holder's Purchase Agreements shall remain in full force and effect. If, however, this Agreement shall terminate, the right of first refusal provisions contained in the Common Holder's Purchase Agreements shall be in full force and effect in accordance with its terms.

15. Additional Investors. Notwithstanding Section 10 of this Agreement, no consent shall be necessary to add additional Investors as signatories to this Agreement and to update Schedule B accordingly, provided that such Investors have purchased Series D Preferred Stock pursuant to the Series D Agreement.

16. Specific Performance. In addition to any and all other remedies that may be available at law in the event of any breach of this Agreement, each Holder shall be entitled to specific performance of the agreements and obligations of the Company, the Common Holder and the other Holders hereunder and to such other injunction or other equitable relief as may be granted by a court of competent jurisdiction.

17. Counterparts. This Agreement may be executed in two (2) or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. Counterparts may be delivered by facsimile, electronic mail (including pdf) or other transmission method and any counterpart so delivered shall be deemed to have been duly and validly delivered and be valid and effective for all purposes.

18. Additional Common Holders. In the event that after the date of this Agreement, the Company issues shares of Common Stock to any officer of the Company or to any other individual, which shares would collectively constitute with respect to such individual (taking into account all shares of Common Stock, options and other purchase rights held by such individual) [***] or more of the Company's then outstanding Common Stock (treating for this purpose all shares of Common Stock issuable upon exercise of or conversion of outstanding options, warrants or convertible securities, as if exercised or converted), the Company shall, as a condition to such issuance, cause such officer of the Company or such other individual to execute a counterpart signature page hereto as a Common Holder, and such person shall thereby be bound by, and subject to, all the terms and provisions of this Agreement applicable to a Common Holder. Notwithstanding Section 10 of this Agreement, no consent shall be necessary to add such additional Common Holders as signatories to this Agreement and update Schedule A accordingly.

19. Effect on Prior Agreement. Upon the effectiveness of this Agreement, the Prior Agreement automatically shall terminate and be of no further force and effect and shall be amended and restated in its entirety as set forth in this Agreement.

[*Remainder of page intentionally left blank*]

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the date first written above.

COMPANY:

AKILI INTERACTIVE LABS, INC.

By: /s/ W. Edward Martucci

Name: W. Edward Martucci, Ph.D.

Title: Chief Executive Officer

Address: 125 Broad Street, 5th Floor

Boston, MA 02110

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the date first written above.

INVESTORS:

[***]

Exhibit 4.26

CERTAIN IDENTIFIED INFORMATION HAS BEEN EXCLUDED (INDICATED BY: [***]) FROM THE EXHIBIT BECAUSE IT IS BOTH (I) NOT MATERIAL AND (II) THE TYPE OF INFORMATION THAT THE REGISTRANT CUSTOMARILY AND ACTUALLY TREATS AS PRIVATE OR CONFIDENTIAL.

AMENDED AND RESTATED
INVESTORS' RIGHTS AGREEMENT

TABLE OF CONTENTS

AMENDED AND RESTATED
INVESTORS' RIGHTS AGREEMENT

THIS AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT (this "**Agreement**"), is made as of the 15th day of July, 2021, by and among Vedanta Biosciences, Inc., a Delaware corporation (the "**Company**") and each of the investors listed on Schedule A hereto, each of which is referred to in this Agreement as an "**Investor**".

RECITALS

WHEREAS, certain of the Investors (the "**Existing Investors**") hold shares of the Company's Series A-1 Preferred Stock, Series B Preferred Stock, Series C Preferred Stock and/or Series C-2 Preferred Stock and possess certain rights to cause the Company to register shares of Common Stock issuable to the Investors, to receive certain information from the Company, to participate in future equity offerings by the Company, and certain other rights pursuant to that certain Amended and Restated Investors' Rights Agreement, dated as of [***], as such was amended, by and among the Company and such Existing Investors (the "**Prior Agreement**");

WHEREAS, Existing Investors holding at least [***] of the Preferred Stock outstanding as of the date hereof required to amend the Prior Agreement desire to amend and restate the Prior Agreement in its entirety and to accept the rights created pursuant to this Agreement in lieu of the rights granted under the Prior Agreement;

WHEREAS, the Company and certain of the Investors are parties to that certain Series D Preferred Stock Purchase Agreement of even date herewith (the "**Purchase Agreement**"), and it is a condition to the closing of the sale of the Series D Preferred Stock that such Investors and the Company execute and deliver this Agreement.

NOW, THEREFORE, in consideration of the mutual promises and covenants set forth herein, and other consideration, the receipt and adequacy of which is hereby acknowledged, the Existing Investors hereby agree that the Prior Agreement shall be amended and restated and the parties to this Agreement further agree as follows:

1. Definitions. For purposes of this Agreement:

(i) "**Affiliate**" means with respect to any specified Person, any other Person who, directly or indirectly, controls, is controlled by, or is under common control with such Person, including without limitation any general partner, managing member, officer or director of such Person or any venture capital or investment fund now or hereafter existing that is controlled by one or more general partners or managing members of, or shares the same management company with, such Person.

(ii) "**Code**" means the U.S. Internal Revenue Code of 1986, as amended.

(iii) "**Common Stock**" means shares of the Company's common stock, par value $0.0001 per share.

(iv) "**Competitor**" means [***]

(v) "**Damages**" means any loss, damage, claim or liability (joint or several) to which a party hereto may become subject under the Securities Act, the Exchange Act, or other federal or state law, insofar as such loss, damage, claim or liability (or any action in respect thereof) arises out of or is based upon: (i) any untrue statement or alleged

untrue statement of a material fact contained in any registration statement of the Company, including any preliminary prospectus or final prospectus contained therein or any amendments or supplements thereto; (ii) an omission or alleged omission to state therein a material fact required to be stated therein, or necessary to make the statements therein not misleading; or (iii) any violation or alleged violation by the indemnifying party (or any of its agents or Affiliates) of the Securities Act, the Exchange Act, any state securities law, or any rule or regulation promulgated under the Securities Act, the Exchange Act, or any state securities law.

(vi) "**Derivative Securities**" means any securities or rights convertible into, or exercisable or exchangeable for (in each case, directly or indirectly)**,** Common Stock, including options and warrants.

(vii) "**Exchange Act**" means the Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder.

(viii) "**Excluded Registration**" means (i) a registration relating to the sale of securities to employees of the Company or a subsidiary pursuant to a stock option, stock purchase, or similar plan; (ii) a registration relating to an SEC Rule 145 transaction; (iii) a registration on any form that does not include substantially the same information as would be required to be included in a registration statement covering the sale of the Registrable Securities; or (iv) a registration in which the only Common Stock being registered is Common Stock issuable upon conversion of debt securities that are also being registered.

(ix) "**FOIA Party**" means a Person that, in the reasonable determination of the Board of Directors, may be subject to, and thereby required to disclose nonpublic information furnished by or relating to the Company under, the Freedom of Information Act, 6 U.S.C. 552 ("**FOIA**"), any state public records access law, any state or other jurisdiction's laws similar in intent or effect to FOIA, or any other similar statutory or regulatory requirement.

(x) "**Form S-1**" means such form under the Securities Act as in effect on the date hereof or any successor registration form under the Securities Act subsequently adopted by the SEC.

(xi) "**Form S-3**" means such form under the Securities Act as in effect on the date hereof or any registration form under the Securities Act subsequently adopted by the SEC that permits incorporation of substantial information by reference to other documents filed by the Company with the SEC.

(xii) "**GAAP**" means generally accepted accounting principles in the United States.

(xiii) [***]

(xiv) [***]

(xv) "**Holder**" means any holder of Registrable Securities who is a party to this Agreement.

(xvi) "**Immediate Family Member**" means a child, stepchild, grandchild, parent, stepparent, grandparent, spouse, sibling, mother-in-law, father-in-law, son-in-law, daughter-in-law, brother-in-law, or sister-in-law, including, adoptive relationships, of a natural person referred to herein.

(xvii) "**Initiating Holders**" means collectively, Holders who properly initiate a registration request under this Agreement.

(xviii) "**IPO**" means (1) the Company's first underwritten public offering of its Common Stock under the Securities Act or (2) a SPAC Transaction (as defined in the Company's Certificate of Incorporation).

(xix) "**Key Employee**" means [***]

(xx) [***]

(xxi) "**New Securities**" means collectively, equity securities of the Company, whether or not currently authorized, as well as rights, options, or warrants to purchase such equity securities, or securities of any type whatsoever that are, or may become, convertible or exchangeable into or exercisable for such equity securities.

(xxii) "**Permitted Transferee**" means (i) with respect to any Holder that is a discretionary managed fund or its nominee: (A) any partner, member, trustee, manager, beneficiary, shareholder, investor or other participant in such fund which is or whose nominee is the transferor (but only in connection with the dissolution of such fund or any distribution of assets of the fund pursuant to the operation of the fund in the ordinary course), (B) any other fund whose business is managed or advised by the same investment manager as manages or advises the fund which is or whose nominee is the transferor or another investment manager in the same group of companies as such first investment manager, (C) the investment manager who manages the business of the fund which is or whose nominee is the transferor , (D) any directors or employees of such Holder or any of the foregoing or any trust or carried interest or similar partnership in which they or any of them participate and/or (E) any nominee or custodian of the foregoing; (ii) with respect to any Holder that is an investment manager or its nominee: (A) any partner, member, trustee, manager, beneficiary, shareholder, investor or other participant in any investment fund in respect of which the shares to be transferred are held (but only in connection with the dissolution of such investment fund or any distribution of assets of the investment fund pursuant to the operation of the investment fund in the ordinary course), (B) any investment fund whose business is managed by the investment manager who is or whose nominee is the transferor, (C) any other investment manager who manages the business of the investment fund in respect of which the shares are held, (D) any directors or employees of such Holder or any of the foregoing or any trust or carried interest or similar partnership in which they or any of them participate and/or (E) any nominee or custodian of the foregoing; (iii) with respect to the Gates Foundation (A) any successor charitable organization of the Gates Foundation from time to time that is a tax-exempt organization as described in Section 501(c)(3) of the Code, or (b) any tax-exempt organization as described in Section 501(c)(3) of the Code controlled by one or more trustees of the Gates Foundation and (iv) with respect to the Magnetar Group: (A) any partner, member, trustee, manager, beneficiary, shareholder, investor or other participant in such entity which is or whose nominee is the transferor (but only in connection with the dissolution of such entity or any distribution of assets of the entity pursuant to the operation of such entity in the ordinary course), (B) any other entity whose business is managed or advised by the same investment manager as manages or advises such entity which is or whose nominee is the transferor or another investment manager in the same group of companies as such first investment manager, (C) the investment manager who manages the business of such entity which is or whose nominee is the transferor, (D) any directors, managers or employees of such Holder or any of the foregoing or any trust or carried interest or similar partnership in which they or any of them participate and/or (E) any nominee or custodian of the foregoing.

(xxiii) "**Person**" means any individual, corporation, partnership, trust, limited liability company, association or other entity.

(xxiv) "**Preferred Stock**" means collectively, shares of the Company's Series A-1 Preferred Stock, Series B Preferred Stock, Series C Preferred Stock, Series C-2 Preferred Stock and Series D Preferred Stock.

(xxv) "**Qualified Public Offering**" means the closing of the sale of shares of Common Stock to the public at a price of at least [***] per share (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Common Stock), in a firm-commitment underwritten public offering pursuant to an effective registration statement under the Securities Act, resulting in at least [***] of gross proceeds to the Company.

(xxvi) "**Registrable Securities**" means (i) Common Stock issuable or issued upon conversion of the Preferred Stock and (ii) any Common Stock issued as (or issuable upon the conversion or exercise of any warrant, right, or other security that is issued as) a dividend or other distribution with respect to, or in exchange for or in replacement of, the shares referenced in clause (i) above; excluding in all cases, however, any Registrable Securities sold by a Person in a transaction in which the applicable rights under this Agreement are not assigned pursuant to Subsection 7.1, and excluding for purposes of Section 2 any shares for which registration rights have terminated pursuant to Subsection 2.13 of this Agreement.

(xxvii) "**Registrable Securities then outstanding**" means the number of shares determined by adding the number of shares of outstanding Common Stock that are Registrable Securities and the number of shares of Common Stock issuable (directly or indirectly) pursuant to then exercisable and/or convertible securities that are Registrable Securities.

(xxviii)"**Restricted Securities**" means the securities of the Company required to be notated with the legend set forth in Subsection 2.12(b) hereof.

(xxix) "**Rock Springs**" means Rock Springs Capital Master Fund LP, Four Pines Master Fund LP, and their Affiliates.

(xxx) "**SEC**" means the Securities and Exchange Commission.

(xxxi) "**SEC Rule 144**" means Rule 144 promulgated by the SEC under the Securities Act.

(xxxii) "**SEC Rule 145**" means Rule 145 promulgated by the SEC under the Securities Act.

(xxxiii)"**Securities Act**" means the Securities Act of 1933, as amended, and the rules and regulations promulgated thereunder.

(xxxiv)"**Selling Expenses**" means all underwriting discounts, selling commissions, and stock transfer taxes applicable to the sale of Registrable Securities, and fees and disbursements of counsel for any Holder, except for the fees and disbursements of the Selling Holder Counsel borne and paid by the Company as provided in Subsection 2.6.

(xxxv) [***]

(xxxvi)[***]

(xxxvii) "**Series A-1 Preferred Stock**" means shares of the Company's Series A-1 Preferred Stock, par value $0.0001 per share.

(xxxviii) "**Series B Preferred Stock**" means shares of the Company's Series B Preferred Stock, par value $0.0001 per share.

(xxxix)"**Series C Preferred Stock**" means shares of the Company's Series C Preferred Stock, par value $0.0001 per share.

(xl) [***]

(xli) "**Series D Preferred Stock**" means shares of the Company's Series D Preferred Stock, par value $0.0001 per share.

(xlii) [***]

(xliii) "**Stockholder**" means a holder of outstanding capital stock of the Company.

2. Registration Rights. The Company covenants and agrees as follows:

1.1 Demand Registration.

(a) Form S-1 Demand. If at any time after the earlier of (i) [***] after the date of this Agreement or (ii) [***] after the effective date of the registration statement for the IPO, the Company receives a request from Holders of at least [***] of the Registrable Securities then outstanding that the Company file a Form S-1 registration statement with respect to at least [***] of the Registrable Securities then outstanding (or a lesser percent if the anticipated aggregate offering price, net of Selling Expenses, would exceed [***]), then the Company shall (x) within [***] after the date such request is given, give notice thereof (the "**Demand Notice**") to all Holders other than the Initiating Holders; and (y) as soon as practicable, and in any event within [***] after the date such request is given by the Initiating Holders, file a Form S-1 registration statement under the Securities Act covering all Registrable Securities that the Initiating Holders requested to be registered and any additional Registrable Securities requested to be included in such registration by any other Holders, as specified by notice given by each such Holder to the Company within [***] of the date the Demand Notice is given, and in each case, subject to the limitations of Subsections 2.1(c) and 2.3.

(b) Form S-3 Demand. If at any time when it is eligible to use a Form S-3 registration statement, the Company receives a request from Holders of at least [***] of the Registrable Securities then outstanding that the Company file a Form S-3 registration statement with respect to outstanding Registrable Securities of such Holders having an anticipated aggregate offering price, net of Selling Expenses, of at least [***], then the Company shall (i) within [***] after the date such request is given, give a Demand Notice to all Holders other than the Initiating Holders; and (ii) as soon as practicable, and in any event within [***] after the date such request is given by the Initiating Holders, file a Form S-3 registration statement under the Securities Act covering all Registrable Securities requested to be included in such registration by any other Holders, as specified by notice given by each such Holder to the Company within [***] of the date the Demand Notice is given, and in each case, subject to the limitations of Subsections 2.1(c) and 2.3.

(c) Notwithstanding the foregoing obligations, if the Company furnishes to Holders requesting a registration pursuant to this Subsection 2.1 a certificate signed by the Company's chief executive officer stating that in the good faith judgment of the Company's Board of Directors it would be materially detrimental to the Company and its stockholders for such registration statement to either become effective or remain effective for as long as such registration statement otherwise would be required to remain effective, because

such action would (i) materially interfere with a significant acquisition, corporate reorganization, or other similar transaction involving the Company; (ii) require premature disclosure of material information that the Company has a bona fide business purpose for preserving as confidential; or (iii) render the Company unable to comply with requirements under the Securities Act or Exchange Act, then the Company shall have the right to defer taking action with respect to such filing, and any time periods with respect to filing or effectiveness thereof shall be tolled correspondingly, for a period of not more than [***] after the request of the Initiating Holders is given; provided, however, that the Company may not invoke this right more than [***] in any [***] period; and provided further that the Company shall not register any securities for its own account or that of any other stockholder during such [***] period other than an Excluded Registration.

(d) The Company shall not be obligated to effect, or to take any action to effect, any registration pursuant to Subsection 2.1(a) (i) during the period that is [***] before the Company's good faith estimate of the date of filing of, and ending on a date that is [***] after the effective date of, a Company-initiated registration, provided that the Company is actively employing in good faith commercially reasonable efforts to cause such registration statement to become effective; (ii) after the Company has effected [***] registrations pursuant to Subsection 2.1(a); or (iii) if the Initiating Holders propose to dispose of shares of Registrable Securities that may be immediately registered on Form S-3 pursuant to a request made pursuant to Subsection 2.1(b). The Company shall not be obligated to effect, or to take any action to effect, any registration pursuant to Subsection 2.1(b) (i) during the period that is [***] before the Company's good faith estimate of the date of filing of, and ending on a date that is [***] after the effective date of, a Company-initiated registration, provided that the Company is actively employing in good faith commercially reasonable efforts to cause such registration statement to become effective; or (ii) if the Company has effected two registrations pursuant to Subsection 2.1(b) within the [***] period immediately preceding the date of such request. A registration shall not be counted as "effected" for purposes of this Subsection 2.1(d) until such time as the applicable registration statement has been declared effective by the SEC, unless the Initiating Holders withdraw their request for such registration, elect not to pay the registration expenses therefor, and forfeit their right to one demand registration statement pursuant to Subsection 2.6, in which case such withdrawn registration statement shall be counted as "effected" for purposes of this Subsection 2.1(d).

1.2 Company Registration. If the Company proposes to register (including, for this purpose, a registration effected by the Company for stockholders other than the Holders) any of its Common Stock under the Securities Act in connection with the public offering of such securities solely for cash (other than in an Excluded Registration), the Company shall, at such time, promptly give each Holder notice of such registration. Upon the request of each Holder given within [***] after such notice is given by the Company, the Company shall, subject to the provisions of Subsection 2.3, cause to be registered all of the Registrable Securities that each such Holder has requested to be included in such registration. The Company shall have the right to terminate or withdraw any registration initiated by it under this Subsection 2.2 before the effective date of such registration, whether or not any Holder has elected to include Registrable Securities in such registration. The expenses (other than Selling Expenses) of such withdrawn registration shall be borne by the Company in accordance with Subsection 2.6.

1.3 Underwriting Requirements.

(a) If, pursuant to Subsection 2.1, the Initiating Holders intend to distribute the Registrable Securities covered by their request by means of an underwriting, they shall so advise the Company as a part of their request made pursuant to Subsection 2.1, and the Company shall include such information in the Demand Notice. The underwriter(s) will be selected by the Company and shall be reasonably acceptable to a majority in interest of the

Initiating Holders. In such event, the right of any Holder to include such Holder's Registrable Securities in such registration shall be conditioned upon such Holder's participation in such underwriting and the inclusion of such Holder's Registrable Securities in the underwriting to the extent provided herein. All Holders proposing to distribute their securities through such underwriting shall (together with the Company as provided in Subsection 2.4(e)) enter into an underwriting agreement in customary form with the underwriter(s) selected for such underwriting. Notwithstanding any other provision of this Subsection 2.3, if the managing underwriter advises the Initiating Holders in writing that marketing factors require a limitation on the number of shares to be underwritten, then the Initiating Holders shall so advise all Holders of Registrable Securities that otherwise would be underwritten pursuant hereto, and the number of Registrable Securities that may be included in the underwriting shall be allocated among such Holders of Registrable Securities, including the Initiating Holders, in proportion (as nearly as practicable) to the number of Registrable Securities owned by each Holder or in such other proportion as shall mutually be agreed to by all such selling Holders; provided, however, that the number of Registrable Securities held by the Holders to be included in such underwriting shall not be reduced unless all other securities are first entirely excluded from the underwriting. To facilitate the allocation of shares in accordance with the above provisions, the Company or the underwriters may round the number of shares allocated to any Holder to the nearest one hundred (100) shares.

(b) In connection with any offering involving an underwriting of shares of the Company's capital stock pursuant to Subsection 2.2, the Company shall not be required to include any of the Holders' Registrable Securities in such underwriting unless the Holders accept the terms of the underwriting as agreed upon between the Company and its underwriters, and then only in such quantity as the underwriters in their sole discretion determine in good faith will not jeopardize the success of the offering by the Company. If the total number of securities, including Registrable Securities, requested by stockholders to be included in such offering exceeds the number of securities to be sold (other than by the Company) that the underwriters in their reasonable discretion determine is compatible with the success of the offering, then the Company shall be required to include in the offering only that number of such securities, including Registrable Securities, which the underwriters and the Company in their sole discretion determine will not jeopardize the success of the offering. If the underwriters determine in good faith that less than all of the Registrable Securities requested to be registered can be included in such offering, then the Registrable Securities that are included in such offering shall be allocated among the selling Holders in proportion (as nearly as practicable to) the number of Registrable Securities owned by each selling Holder or in such other proportions as shall mutually be agreed to by all such selling Holders. To facilitate the allocation of shares in accordance with the above provisions, the Company or the underwriters may round the number of shares allocated to any Holder to the nearest one hundred (100) shares. Notwithstanding the foregoing, in no event shall (i) the number of Registrable Securities included in the offering be reduced unless all other securities (other than securities to be sold by the Company) are first entirely excluded from the offering, or (ii) the number of Registrable Securities included in the offering be reduced below [***] of the total number of securities included in such offering, unless such offering is the IPO, in which case the selling Holders may be excluded further if the underwriters make the determination described above and no other stockholder's securities are included in such offering. For purposes of the provision in this Subsection 2.3(b) concerning apportionment, for any selling Holder that is a partnership, limited liability company, or corporation, the partners, members, retired partners, retired members, stockholders, and Affiliates of such Holder, or the estates and Immediate Family Members of any such partners, retired partners, members, and retired members and any trusts for the benefit of any of the foregoing Persons, shall be deemed to be a single "selling Holder," and any pro rata reduction with respect to such "selling Holder" shall be based upon the aggregate number of Registrable Securities owned by all Persons included in such "selling Holder," as defined in this sentence.

1.4 Obligations of the Company. Whenever required under this Section 2 to effect the registration of any Registrable Securities, the Company shall, as expeditiously as reasonably possible:

(a) prepare and file with the SEC a registration statement with respect to such Registrable Securities and use its commercially reasonable efforts to cause such registration statement to become effective and, upon the request of the Holders of a majority of the Registrable Securities registered thereunder, keep such registration statement effective for a period of up to [***] or, if earlier, until the distribution contemplated in the registration statement has been completed; provided, however, that (i) such [***] shall be extended for a period of time equal to the period the Holder refrains, at the request of an underwriter of Common Stock (or other securities) of the Company, from selling any securities included in such registration, and (ii) in the case of any registration of Registrable Securities on Form S-3 that are intended to be offered on a continuous or delayed basis, subject to compliance with applicable SEC rules, such [***] period shall be extended for up to [***], if necessary, to keep the registration statement effective until all such Registrable Securities are sold;

(b) prepare and file with the SEC such amendments and supplements to such registration statement, and the prospectus used in connection with such registration statement, as may be necessary to comply with the Securities Act in order to enable the disposition of all securities covered by such registration statement;

(c) furnish to the selling Holders such numbers of copies of a prospectus, including a preliminary prospectus, as required by the Securities Act, and such other documents as the Holders may reasonably request in order to facilitate their disposition of their Registrable Securities;

(d) use its commercially reasonable efforts to register and qualify the securities covered by such registration statement under such other securities or blue-sky laws of such jurisdictions as shall be reasonably requested by the selling Holders; provided that the Company shall not be required to qualify to do business or to file a general consent to service of process in any such states or jurisdictions, unless the Company is already subject to service in such jurisdiction and except as may be required by the Securities Act;

(e) in the event of any underwritten public offering, enter into and perform its obligations under an underwriting agreement, in usual and customary form, with the underwriter(s) of such offering;

(f) use its commercially reasonable efforts to cause all such Registrable Securities covered by such registration statement to be listed on a national securities exchange or trading system and each securities exchange and trading system (if any) on which similar securities issued by the Company are then listed;

(g) provide a transfer agent and registrar for all Registrable Securities registered pursuant to this Agreement and provide a CUSIP number for all such Registrable Securities, in each case not later than the effective date of such registration;

(h) promptly make available for inspection by the selling Holders, any managing underwriter participating in any disposition pursuant to such registration statement, and any attorney or accountant or other agent retained by any such underwriter or selected by the selling Holders, all financial and other records, pertinent corporate documents, and properties of the Company, and cause the Company's officers, directors, employees, and independent accountants to supply all information reasonably requested by any such seller, underwriter, attorney, accountant, or agent, in each case, as necessary or advisable to verify the accuracy of

the information in such registration statement and to conduct appropriate due diligence in connection therewith;

(i) notify each selling Holder, promptly after the Company receives notice thereof, of the time when such registration statement has been declared effective or a supplement to any prospectus forming a part of such registration statement has been filed; and

(j) after such registration statement becomes effective, notify each selling Holder of any request by the SEC that the Company amend or supplement such registration statement or prospectus.

In addition, the Company shall ensure that, at all times after any registration statement covering a public offering of securities of the Company under the Securities Act shall have become effective, its insider trading policy shall provide that the Company's directors may implement a trading program under Rule 10b5-1 of the Exchange Act.

1.5 Furnish Information. It shall be a condition precedent to the obligations of the Company to take any action pursuant to this Section 2 with respect to the Registrable Securities of any selling Holder that such Holder shall furnish to the Company such information regarding itself, the Registrable Securities held by it, and the intended method of disposition of such securities as is reasonably required to effect the registration of such Holder's Registrable Securities.

1.6 Expenses of Registration. All expenses (other than Selling Expenses) incurred in connection with registrations, filings, or qualifications pursuant to Section 2, including all registration, filing, and qualification fees; printers' and accounting fees; fees and disbursements of counsel for the Company; and the reasonable fees and disbursements of one counsel for the selling Holders ("Selling Holder Counsel"), shall be borne and paid by the Company; provided, however, that the Company shall not be required to pay for any expenses of any registration proceeding begun pursuant to Subsection 2.1 if the registration request is subsequently withdrawn at the request of the Holders of a majority of the Registrable Securities to be registered (in which case all selling Holders shall bear such expenses pro rata based upon the number of Registrable Securities that were to be included in the withdrawn registration), unless the Holders of a majority of the Registrable Securities agree to forfeit their right to one registration pursuant to Subsections 2.1(a) or 2.1(b), as the case may be. All Selling Expenses relating to Registrable Securities registered pursuant to this Section 2 shall be borne and paid by the Holders pro rata on the basis of the number of Registrable Securities registered on their behalf.

1.7 Delay of Registration. No Holder shall have any right to obtain or seek an injunction restraining or otherwise delaying any registration pursuant to this Agreement as the result of any controversy that might arise with respect to the interpretation or implementation of this Section 2.

1.8 Indemnification. If any Registrable Securities are included in a registration statement under this Section 2:

(a) To the extent permitted by law, the Company will indemnify and hold harmless each selling Holder, and the partners, members, officers, directors, and stockholders of each such Holder; legal counsel and accountants for each such Holder; any underwriter (as defined in the Securities Act) for each such Holder; and each Person, if any, who controls such Holder or underwriter within the meaning of the Securities Act or the Exchange Act, against any Damages, and the Company will pay to each such Holder, underwriter, controlling Person, or other aforementioned Person any legal or other expenses reasonably

incurred thereby in connection with investigating or defending any claim or proceeding from which Damages may result, as such expenses are incurred; provided, however, that the indemnity agreement contained in this Subsection 2.8(a) shall not apply to amounts paid in settlement of any such claim or proceeding if such settlement is effected without the consent of the Company, which consent shall not be unreasonably withheld, nor shall the Company be liable for any Damages to the extent that they arise out of or are based upon actions or omissions made in reliance upon and in conformity with written information furnished by or on behalf of any such Holder, underwriter, controlling Person, or other aforementioned Person expressly for use in connection with such registration.

(b) To the extent permitted by law, each selling Holder, severally and not jointly, will indemnify and hold harmless the Company, and each of its directors, each of its officers who has signed the registration statement, each Person (if any), who controls the Company within the meaning of the Securities Act, legal counsel and accountants for the Company, any underwriter (as defined in the Securities Act), any other Holder selling securities in such registration statement, and any controlling Person of any such underwriter or other Holder, against any Damages, in each case only to the extent that such Damages arise out of or are based upon actions or omissions made in reliance upon and in conformity with written information furnished by or on behalf of such selling Holder expressly for use in connection with such registration; and each such selling Holder will pay to the Company and each other aforementioned Person any legal or other expenses reasonably incurred thereby in connection with investigating or defending any claim or proceeding from which Damages may result, as such expenses are incurred; provided, however, that the indemnity agreement contained in this Subsection 2.8(b) shall not apply to amounts paid in settlement of any such claim or proceeding if such settlement is effected without the consent of the Holder, which consent shall not be unreasonably withheld; and provided further that in no event shall the aggregate amounts payable by any Holder by way of indemnity or contribution under Subsections 2.8(b) and (d) exceed the proceeds from the offering received by such Holder (net of any Selling Expenses paid by such Holder), except in the case of fraud or willful misconduct by such Holder.

(c) Promptly after receipt by an indemnified party under this Subsection 2.8 of notice of the commencement of any action (including any governmental action) for which a party may be entitled to indemnification hereunder, such indemnified party will, if a claim in respect thereof is to be made against any indemnifying party under this Subsection 2.8, give the indemnifying party notice of the commencement thereof. The indemnifying party shall have the right to participate in such action and, to the extent the indemnifying party so desires, participate jointly with any other indemnifying party to which notice has been given, and to assume the defense thereof with counsel mutually satisfactory to the parties; provided, however, that an indemnified party (together with all other indemnified parties that may be represented without conflict by one counsel) shall have the right to retain one separate counsel, with the fees and expenses to be paid by the indemnifying party, if representation of such indemnified party by the counsel retained by the indemnifying party would be inappropriate due to actual or potential differing interests between such indemnified party and any other party represented by such counsel in such action. The failure to give notice to the indemnifying party within a reasonable time of the commencement of any such action shall relieve such indemnifying party of any liability to the indemnified party under this Subsection 2.8, to the extent that such failure materially prejudices the indemnifying party's ability to defend such action. The failure to give notice to the indemnifying party will not relieve it of any liability that it may have to any indemnified party otherwise than under this Subsection 2.8.

(d) To provide for just and equitable contribution to joint liability under the Securities Act in any case in which either: (i) any party otherwise entitled to indemnification hereunder makes a claim for indemnification pursuant to this Subsection 2.8 but

it is judicially determined (by the entry of a final judgment or decree by a court of competent jurisdiction and the expiration of time to appeal or the denial of the last right of appeal) that such indemnification may not be enforced in such case, notwithstanding the fact that this Subsection 2.8 provides for indemnification in such case, or (ii) contribution under the Securities Act may be required on the part of any party hereto for which indemnification is provided under this Subsection 2.8, then, and in each such case, such parties will contribute to the aggregate losses, claims, damages, liabilities, or expenses to which they may be subject (after contribution from others) in such proportion as is appropriate to reflect the relative fault of each of the indemnifying party and the indemnified party in connection with the statements, omissions, or other actions that resulted in such loss, claim, damage, liability, or expense, as well as to reflect any other relevant equitable considerations. The relative fault of the indemnifying party and of the indemnified party shall be determined by reference to, among other things, whether the untrue or allegedly untrue statement of a material fact, or the omission or alleged omission of a material fact, relates to information supplied by the indemnifying party or by the indemnified party and the parties' relative intent, knowledge, access to information, and opportunity to correct or prevent such statement or omission; provided, however, that, in any such case (x) no Holder will be required to contribute any amount in excess of the public offering price of all such Registrable Securities offered and sold by such Holder pursuant to such registration statement, and (y) no Person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Securities Act) will be entitled to contribution from any Person who was not guilty of such fraudulent misrepresentation; and provided further that in no event shall a Holder's liability pursuant to this Subsection 2.8(d), when combined with the amounts paid or payable by such Holder pursuant to Subsection 2.8(b), exceed the proceeds from the offering received by such Holder (net of any Selling Expenses paid by such Holder), except in the case of willful misconduct or fraud by such Holder.

(e) Notwithstanding the foregoing, to the extent that the provisions on indemnification and contribution contained in the underwriting agreement entered into in connection with the underwritten public offering are in conflict with the foregoing provisions, the provisions in the underwriting agreement shall control.

(f) Unless otherwise superseded by an underwriting agreement entered into in connection with the underwritten public offering, the obligations of the Company and Holders under this Subsection 2.8 shall survive the completion of any offering of Registrable Securities in a registration under this Section 2, and otherwise shall survive the termination of this Agreement.

1.9 Reports Under Exchange Act. With a view to making available to the Holders the benefits of SEC Rule 144 and any other rule or regulation of the SEC that may at any time permit a Holder to sell securities of the Company to the public without registration or pursuant to a registration on Form S-3, the Company shall:

(a) make and keep available adequate current public information, as those terms are understood and defined in SEC Rule 144, at all times after the effective date of the registration statement filed by the Company for the IPO;

(b) use commercially reasonable efforts to file with the SEC in a timely manner all reports and other documents required of the Company under the Securities Act and the Exchange Act (at any time after the Company has become subject to such reporting requirements); and

(c) furnish to any Holder, so long as the Holder owns any Registrable Securities, forthwith upon request (i) to the extent accurate, a written statement by the Company that it has complied with the reporting requirements of SEC Rule 144 (at any time after ninety

(90) days after the effective date of the registration statement filed by the Company for the IPO), the Securities Act, and the Exchange Act (at any time after the Company has become subject to such reporting requirements), or that it qualifies as a registrant whose securities may be resold pursuant to Form S-3 (at any time after the Company so qualifies); (ii) a copy of the most recent annual or quarterly report of the Company and such other reports and documents so filed by the Company; and (iii) such other information as may be reasonably requested in availing any Holder of any rule or regulation of the SEC that permits the selling of any such securities without registration (at any time after the Company has become subject to the reporting requirements under the Exchange Act) or pursuant to Form S-3 (at any time after the Company so qualifies to use such form).

1.10 Limitations on Subsequent Registration Rights. From and after the date of this Agreement, the Company shall not, without the prior written consent of the Holders of [***] of the Registrable Securities then outstanding, enter into any agreement with any holder or prospective holder of any securities of the Company that would allow such holder or prospective holder to include such securities in any registration unless, under the terms of such agreement, such holder or prospective holder may include such securities in any such registration only to the extent that the inclusion of such securities will not reduce the number of the Registrable Securities of the Holders that are included; provided that this limitation shall not apply to any additional Investor who becomes a party to this Agreement in accordance with Subsection 7.9 [***].

1.11 "Market Stand-off" Agreement. Subject to the provisions of Subsection 7.1, each Holder, to the extent permitted by applicable laws and regulations, hereby agrees that it will not, without the prior written consent of the managing underwriter (any such consent received, a "**Lock-Up Waiver**"), during the period commencing on the date of the final prospectus relating to the registration by the Company for its own behalf of shares of its Common Stock or any other equity securities under the Securities Act on a registration statement on Form S-1 or Form S-3, and ending on the date specified by the Company and the managing underwriter (such period not to exceed [***] in the case of the IPO, or such other period as may be requested by the Company or an underwriter to accommodate regulatory restrictions on (1) the publication or other distribution of research reports, and (2) analyst recommendations and opinions, including, but not limited to, the restrictions contained in FINRA Rule 2241 or NYSE Rule 472(f)(4), or any successor provisions or amendments thereto), or such other period as may be requested by the Company or an underwriter to accommodate regulatory restrictions on (1) the publication or other distribution of research reports and (2) analyst recommendations and opinions, including, but not limited to, the restrictions contained in FINRA Rule 2241 or NYSE Rule 472(f)(4), or any successor provisions or amendments thereto), (i) lend; offer; pledge; sell; contract to sell; sell any option or contract to purchase; purchase any option or contract to sell; grant any option, right, or warrant to purchase; or otherwise transfer or dispose of, directly or indirectly, any shares of Common Stock or any securities convertible into or exercisable or exchangeable (directly or indirectly) for Common Stock held immediately before the effective date of the registration statement for such offering or (ii) enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of such securities, whether any such transaction described in clause (i) or (ii) above is to be settled by delivery of Common Stock or other securities, in cash, or otherwise; *provided* that the obligations described in this Subsection 2.11 shall not apply to any transfer that such Holder is required to make in order to comply with laws or regulations applicable to it (including those that have been established in accordance with the UCITS (Undertakings for Collective Investment in Transferable Securities) Directive). [***] The foregoing provisions of this Subsection 2.11 shall not apply to (i) the sale of any shares to an underwriter pursuant to an underwriting agreement, (ii) shares acquired by any Holder in an IPO or subsequent to an IPO in the open market, (iii) the transfer of any shares to any Affiliate of a Holder, provided that such transferee agrees to be bound in writing by the restrictions set forth herein or (iv) the transfer of

any shares to any trust for the direct or indirect benefit of the Holder or the immediate family of the Holder, provided that the trustee of the trust agrees to be bound in writing by the restrictions set forth herein, and provided further that any such transfer shall not involve a disposition for value, and shall be applicable to the Holders only if all officers and directors are subject to the same restrictions and the Company uses commercially reasonable efforts to obtain a similar agreement from all stockholders individually owning more than [***] of the Company's outstanding Common Stock (after giving effect to conversion into Common Stock of all outstanding Preferred Stock). The Company and PureTech hereby agree, and all of the Investors hereby acknowledge, that PureTech shall, without in any way limiting the obligations of any Investor other than PureTech under this Subsection 2.11, be granted additional exceptions to the application of this Subsection 2.11, as agreed upon in good faith by the Company and PureTech, to the extent reasonably necessary for PureTech to maintain exemption from registration under the Investment Company Act of 1940. The underwriters in connection with such registration are intended third-party beneficiaries of this Subsection 2.11 and shall have the right, power and authority to enforce the provisions hereof as though they were a party hereto. Each Holder further agrees to execute such agreements as may be reasonably requested by the underwriters in connection with such registration that are consistent with this Subsection 2.11 or that are necessary to give further effect thereto.

1.12 Restrictions on Transfer.

(a) The Preferred Stock and the Registrable Securities shall not be sold, pledged, or otherwise transferred, and the Company shall not recognize and shall issue stop-transfer instructions to its transfer agent with respect to any such sale, pledge, or transfer, except upon the conditions specified in this Agreement, which conditions are intended to ensure compliance with the provisions of the Securities Act. A transferring Holder will cause any proposed purchaser, pledgee, or transferee of the Preferred Stock and the Registrable Securities held by such Holder to agree to take and hold such securities subject to the provisions and upon the conditions specified in this Agreement.

(b) Each certificate, instrument, or book entry representing (i) the Preferred Stock, (ii) the Registrable Securities, and (iii) any other securities issued in respect of the securities referenced in clauses (i) and (ii), upon any stock split, stock dividend, recapitalization, merger, consolidation, or similar event, shall (unless otherwise permitted by the provisions of Subsection 2.12(c)) be notated with a legend substantially in the following form:

THE SECURITIES REPRESENTED HEREBY HAVE BEEN ACQUIRED FOR INVESTMENT AND HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933. SUCH SHARES MAY NOT BE SOLD, PLEDGED, OR TRANSFERRED IN THE ABSENCE OF SUCH REGISTRATION OR A VALID EXEMPTION FROM THE REGISTRATION AND PROSPECTUS DELIVERY REQUIREMENTS OF SAID ACT.

THE SECURITIES REPRESENTED HEREBY MAY BE TRANSFERRED ONLY IN ACCORDANCE WITH THE TERMS OF AN AGREEMENT BETWEEN THE COMPANY AND THE STOCKHOLDER, A COPY OF WHICH IS ON FILE WITH THE SECRETARY OF THE COMPANY.

The Holders consent to the Company making a notation in its records and giving instructions to any transfer agent of the Restricted Securities in order to implement the restrictions on transfer set forth in this Subsection 2.12.

(c) The holder of such Restricted Securities, by acceptance of ownership thereof, agrees to comply in all respects with the provisions of this Section 2. Before

any proposed sale, pledge, or transfer of any Restricted Securities, unless there is in effect a registration statement under the Securities Act covering the proposed transaction, the Holder thereof shall give notice to the Company of such Holder's intention to effect such sale, pledge, or transfer. Each such notice shall describe the manner and circumstances of the proposed sale, pledge, or transfer in sufficient detail and, if reasonably requested by the Company, shall be accompanied at such Holder's expense by either (i) a written opinion of legal counsel who shall, and whose legal opinion shall, be reasonably satisfactory to the Company, addressed to the Company, to the effect that the proposed transaction may be effected without registration under the Securities Act; (ii) a "no action" letter from the SEC to the effect that the proposed sale, pledge, or transfer of such Restricted Securities without registration will not result in a recommendation by the staff of the SEC that action be taken with respect thereto; or (iii) any other evidence reasonably satisfactory to counsel to the Company to the effect that the proposed sale, pledge, or transfer of the Restricted Securities may be effected without registration under the Securities Act, whereupon the Holder of such Restricted Securities shall be entitled to sell, pledge, or transfer such Restricted Securities in accordance with the terms of the notice given by the Holder to the Company. The Company will not require such a legal opinion or "no action" letter (x) in any transaction in compliance with SEC Rule 144; or (y) in any transaction in which such Holder distributes Restricted Securities to an Affiliate of such Holder for no consideration; provided that each transferee agrees in writing to be subject to the terms of this Subsection 2.12. Each certificate, instrument, or book entry representing the Restricted Securities transferred as above provided shall be notated with, except if such transfer is made pursuant to SEC Rule 144, the appropriate restrictive legend set forth in Subsection 2.12(b), except that such certificate instrument, or book entry shall not be notated with such restrictive legend if, in the opinion of counsel for such Holder and the Company, such legend is not required in order to establish compliance with any provisions of the Securities Act.

1.13 Termination of Registration Rights. The right of any Holder to request registration or inclusion of Registrable Securities in any registration pursuant to Subsections 2.1 or 2.2 shall terminate upon the earliest to occur of:

[***]

3. Voting Provisions Regarding Board of Directors.

1.1 Size of the Board. Each Stockholder agrees to vote, or cause to be voted, all Shares (as defined below) owned by such Stockholder, or over which such Stockholder has voting control, from time to time and at all times, in whatever manner as shall be necessary to ensure that the size of the Board shall be set and remain at eight (8) directors and so long as at least [***]of the Preferred Stock outstanding as of the date hereof remain outstanding, may be increased only with the written consent of Investors holding a majority of the Preferred Stock then outstanding. For purposes of this Section 3, the term "Shares" shall mean and include any securities of the Company the holders of which are entitled to vote for members of the Board, including without limitation, all shares of Common Stock, Series A-1 Preferred Stock, Series B Preferred Stock, Series C Preferred Stock, Series C-2 Preferred Stock and Series D Preferred Stock, by whatever name called, now owned or subsequently acquired by a Stockholder, however acquired, whether through stock splits, stock dividends, reclassifications, recapitalizations, similar events or otherwise.

1.2 Board Composition. Each Stockholder agrees to vote, or cause to be voted, all Shares owned by such Stockholder, or over which such Stockholder has voting control, from time to time and at all times, in whatever manner as shall be necessary to ensure that at each annual or special meeting of stockholders at which an election of directors is held or pursuant to any written consent of the stockholders, the following persons shall be elected to the Board:

(a) Two persons designated by a majority of the holders of the Series A-1 Preferred Stock then outstanding, which individuals shall initially be Christopher Viehbacher and Bennett Shapiro (the "**Series A-1 Designees**"), for so long as such Stockholders and their Affiliates continue to own beneficially any shares of Series A-1 Preferred Stock.

(b) Two persons designated by a majority of the holders of the Series B Preferred Stock then outstanding, which individuals shall initially be John LaMattina and Bharatt Chowrira (the "**Series B Designees**"), for so long as such Stockholders and their Affiliates continue to own beneficially any shares of Series B Preferred Stock.

(c) [***]

(d) [***]

(e) [***]

(f) [***]

To the extent that any of clauses (a) through (f) above shall not be applicable, any member of the Board who would otherwise have been designated in accordance with the terms thereof shall instead be voted upon by all the stockholders of the Company entitled to vote thereon in accordance with, and pursuant to, the Company's Certificate of Incorporation.

1.3 Failure to Designate a Board Member. In the absence of any designation from the Persons or groups with the right to designate a director as specified above, the director previously designated by them and then serving shall be reelected if still eligible to serve as provided herein.

1.4 Removal of Board Members. Each Stockholder also agrees to vote, or cause to be voted, all Shares owned by such Stockholder, or over which such Stockholder has voting control, from time to time and at all times, in whatever manner as shall be necessary to ensure that:

(a) no director elected pursuant to Subsections 3.2 or 3.3 of this Agreement may be removed from office other than for cause unless (i) such removal is directed or approved by the affirmative vote of the Person, or of the holders of a majority of the shares of stock, entitled under Subsections 3.2 to designate that director; or (ii) the Person(s) originally entitled to designate or approve such director pursuant to Subsections 3.2 is no longer so entitled to designate or approve such director;

(b) any vacancies created by the resignation, removal or death of a director elected pursuant to Subsections 3.2 or 3.3 shall be filled pursuant to the provisions of this Section 3; and

(c) upon the request of any party entitled to designate a director as provided in Subsection 3.2 to remove such director, such director shall be removed.

All Stockholders agree to execute any written consents required to perform the obligations of this Agreement, and the Company agrees at the request of any party entitled to designate directors to call a special meeting of stockholders for the purpose of electing directors.

1.5 No Liability for Election of Recommended Directors. No Stockholder, nor any Affiliate of any Stockholder, shall have any liability as a result of designating a person for election as a director for any act or omission by such designated person in his or her capacity

as a director of the Company, nor shall any Stockholder have any liability as a result of voting for any such designee in accordance with the provisions of this Agreement.

1.6 No "Bad Actor" Designees. Each Person with the right to designate or participate in the designation of a director as specified above hereby represents and warrants to the Company that, to such Person's knowledge, none of the "bad actor" disqualifying events described in Rule 506(d)(1)(i)-(viii) promulgated under the Securities Act (each, a "**Disqualification Event**"), is applicable to such Person's initial designee named above except, if applicable, for a Disqualification Event as to which Rule 506(d)(2)(ii) or (iii) or (d)(3) is applicable. Any director designee to whom any Disqualification Event is applicable, except for a Disqualification Event as to which Rule 506(d)(2)(ii) or (iii) or (d)(3) is applicable, is hereinafter referred to as a "**Disqualified Designee**". Each Person with the right to designate or participate in the designation of a director as specified above hereby covenants and agrees (A) not to designate or participate in the designation of any director designee who, to such Person's knowledge, is a Disqualified Designee and (B) that in the event such Person becomes aware that any individual previously designated by any such Person is or has become a Disqualified Designee, such Person shall as promptly as practicable take such actions as are necessary to remove such Disqualified Designee from the Board and designate a replacement designee who is not a Disqualified Designee.

4. Information.

1.1 Delivery of Financial Statements. The Company shall deliver to each Investor who so requests, provided that the Board of Directors has not reasonably determined that such Investor is a Competitor of the Company:

(a) as soon as practicable, but in any event within [***] after the end of each fiscal year of the Company (i) a balance sheet as of the end of such year, (ii) statements of income and of cash flows for such year and (iii) a statement of stockholders' equity as of the end of such year, all such financial statements audited and certified by independent public accountants selected by the Company;

(b) as soon as practicable, but in any event within [***] after the end of each of the first three (3) quarters of each fiscal year of the Company, unaudited statements of income and cash flows for such fiscal quarter, and an unaudited balance sheet and a statement of stockholders' equity as of the end of such fiscal quarter;

(c) such other information relating to the financial condition, annual budget, business, prospects, or corporate affairs of the Company as any Investor may from time to time reasonably request; provided, however, that the Company shall not be obligated under this Subsection 4.1 to provide information (i) that the Company reasonably determines in good faith to be a trade secret or confidential information (unless covered by an enforceable confidentiality agreement, in a form acceptable to the Company); or (ii) the disclosure of which would adversely affect the attorney-client privilege between the Company and its counsel; and

(d) as soon as practicable, but in any event [***] before the end of each fiscal year and a budget for the next fiscal year (collectively, the "**Budget**"), approved by the Board of Directors and prepared on a [***] basis, including balance sheets, income statements, and statements of cash flow for such [***] and, promptly after prepared, any other budgets or revised budgets prepared by the Company.

If, for any period, the Company has any subsidiary whose accounts are consolidated with those of the Company, then in respect of such period, the financial statements delivered pursuant to the

foregoing sections shall be the consolidated and consolidating financial statements of the Company and all such consolidated subsidiaries.

Notwithstanding anything else in this Subsection 4.1 to the contrary, the Company may cease providing the information set forth in this Subsection 4.1 during the period starting with the date [***] before the Company's good-faith estimate of the date of filing of a registration statement if it reasonably concludes it must do so to comply with the SEC rules applicable to such registration statement and related offering; provided that the Company's covenants under this Subsection 4.1 shall be reinstated at such time as the Company is no longer actively employing its commercially reasonable efforts to cause such registration statement to become effective.

1.2 Inspection Rights. The Company shall permit each Investor who so requests, provided that the Board of Directors has not reasonably determined that such Investor is a Competitor of the Company, at such Investor's expense, to visit and inspect the Company's properties; examine its books of account and records; and discuss the Company's affairs, finances, and accounts with its officers, during normal business hours of the Company as may be reasonably requested by the Investor; provided, however, that the Company shall not be obligated pursuant to this Subsection 4.2 to provide access to any information that it reasonably and in good faith considers to be a trade secret or confidential information (unless covered by an enforceable confidentiality agreement, in form acceptable to the Company) or the disclosure of which would adversely affect the attorney-client privilege between the Company and its counsel.

1.3 Observer Rights.

[***]

1.4 Termination of Information Rights. The covenants set forth in Subsections 4.1, 4.2 and 4.3 shall terminate and be of no further force or effect [***]

1.5 Confidentiality. Each Investor agrees that such Investor will keep confidential and will not disclose, divulge, or use for any purpose (other than to monitor its investment in the Company) any confidential information obtained from the Company pursuant to the terms of this Agreement (including notice of the Company's intention to file a registration statement), unless such confidential information (a) is known or becomes known to the public in general (other than as a result of a breach of this Subsection 4.5 by such Investor), (b) is or has been independently developed or conceived by the Investor without use of the Company's confidential information, or (c) is or has been made known or disclosed to the Investor by a third party without a breach of any obligation of confidentiality such third party may have to the Company; provided, however, that an Investor may disclose confidential information (i) to its attorneys, accountants, consultants, and other professionals to the extent necessary to obtain their services in connection with monitoring its investment in the Company; (ii) to any prospective purchaser of any Registrable Securities from such Investor, if such prospective purchaser agrees to be bound by the provisions of this Subsection 4.5; (iii) to any Affiliate, partner, member, stockholder, or wholly owned subsidiary of such Investor in the ordinary course of business, provided that such Investor informs such Person that such information is confidential and directs such Person to maintain the confidentiality of such information; or (iv) as may otherwise be required by law, provided that the Investor promptly notifies the Company of such disclosure and takes reasonable steps to minimize the extent of any such required disclosure.

5. Rights to Future Stock Issuances.

1.1 Right of First Offer. Subject to the terms and conditions of this Subsection 5.1 and applicable securities laws, if the Company proposes to offer or sell any New Securities, the Company shall first offer such New Securities to each Investor. An Investor shall

be entitled to apportion the right of first offer hereby granted to it, in such proportions as it deems appropriate, among (i) itself, (ii) its Affiliates and (iii) its beneficial interest holders, such as limited partners, members or any other Person having "beneficial ownership," as such term is defined in Rule 13d-3 promulgated under the Exchange Act, of such Investor ("**Investor Beneficial Owners**"); provided that each such Affiliate or Investor Beneficial Owner (x) is not a Competitor or FOIA Party, unless such party's purchase of New Securities is otherwise consented to by the Board of Directors, (y) agrees to enter into this Agreement (provided that any Competitor or FOIA Party shall not be entitled to any rights as an Investor under Subsections 4.1, 4.2 and 5.1 hereof), and (z) agrees to purchase at least such number of New Securities as are allocable hereunder to the Investor holding the fewest number of Preferred Stock and any other Derivative Securities.

(a) The Company shall give notice (the "**Offer Notice**") to each Investor, stating (i) its bona fide intention to offer such New Securities, (ii) the number of such New Securities to be offered, and (iii) the price and terms, if any, upon which it proposes to offer such New Securities.

(b) By notification to the Company within [***] after the Offer Notice is given, each Investor may elect to purchase or otherwise acquire, at the price and on the terms specified in the Offer Notice, up to that portion of such New Securities which equals the proportion that the Common Stock then held by such Investor (including all shares of Common Stock then issuable (directly or indirectly) upon conversion and/or exercise, as applicable, of the Preferred Stock and any other Derivative Securities then held by such Investor) bears to the total Common Stock of the Company then outstanding (assuming full conversion and/or exercise, as applicable, of all Preferred Stock and other Derivative Securities). At the expiration of such [***] period, the Company shall promptly notify each Investor that elects to purchase or acquire all the shares available to it (each, a "**Fully Exercising Investor**") of any other Investor's failure to do likewise. During the [***] period commencing after the Company has given such notice, each Fully Exercising Investor may, by giving notice to the Company, elect to purchase or acquire, in addition to the number of shares specified above, up to that portion of the New Securities for which Investors were entitled to subscribe but that were not subscribed for by the Investors which is equal to the proportion that the Common Stock issued and held, or issuable (directly or indirectly) upon conversion and/or exercise, as applicable, of Preferred Stock and any other Derivative Securities then held, by such Fully Exercising Investor bears to the Common Stock issued and held, or issuable (directly or indirectly) upon conversion and/or exercise, as applicable, of the Preferred Stock and any other Derivative Securities then held, by all Fully Exercising Investors who wish to purchase such unsubscribed shares. The closing of any sale pursuant to this Subsection 5.1(b) shall occur within the later of [***] of the date that the Offer Notice is given and the date of initial sale of New Securities pursuant to Subsection 5.1(c).

(c) If all New Securities referred to in the Offer Notice are not elected to be purchased or acquired as provided in Subsection 5.1(b), the Company may, during the [***] period following the expiration of the periods provided in Subsection 5.1(b), offer and sell the remaining unsubscribed portion of such New Securities to any Person or Persons at a price not less than, and upon terms no more favorable to the offeree than, those specified in the Offer Notice. If the Company does not enter into an agreement for the sale of the New Securities within such period, or if such agreement is not consummated within [***] of the execution thereof, the right provided hereunder shall be deemed to be revived and such New Securities shall not be offered unless first reoffered to the Investors in accordance with this Subsection 5.1.

(d) The right of first offer in this Subsection 5.1 shall not be applicable to (i) Exempted Securities (as defined in the Company's Certificate of Incorporation); (ii) shares of Common Stock issued in the IPO; and (iii) the issuance of shares of Series D Preferred Stock to Additional Purchasers pursuant to Section 1.2(c) of the Purchase Agreement.

1.2 Termination. The covenants set forth in Subsection 5.1 shall terminate and be of no further force or effect (i) immediately before the consummation of the IPO, (ii) when the Company first becomes subject to the periodic reporting requirements of Section 12(g) or 15(d) of the Exchange Act, or (iii) upon a distribution of the proceeds of a Deemed Liquidation Event, as such term is defined in the Company's Certificate of Incorporation, whichever event occurs first.

6. Additional Covenants.

1.1 Insurance. If the Board of Directors deems it appropriate, the Company shall use its commercially reasonable efforts to maintain, from financially sound and reputable insurers, Directors and Officers liability insurance and term "key-person" insurance on [***], in an amount and on terms and conditions satisfactory to the Board of Directors, until such time as the Board of Directors determines that such insurance should be discontinued. The key-person policy shall name the Company as loss payee, and neither policy shall be cancelable by the Company without prior approval by the Board of Directors. [***]

1.2 Employee Agreements. The Company will cause each person now or hereafter employed by it or by any subsidiary (or engaged by the Company or any subsidiary as a consultant/independent contractor) with access to confidential information and/or trade secrets to enter into a nondisclosure and proprietary rights assignment agreement in the form attached hereto as Exhibit A. The Company shall cause each grant of equity securities to its employees to be subject to vesting over four years from the date of the grant, subject to acceleration provisions and/or alternative vesting schedules approved by the Board of Directors.

1.3 Successor Indemnification. If the Company or any of its successors or assignees consolidates with or merges into any other Person and is not the continuing or surviving corporation or entity of such consolidation or merger, then to the extent necessary, proper provision shall be made so that the successors and assignees of the Company assume the obligations of the Company with respect to indemnification of members of the Board of Directors as in effect immediately before such transaction, whether such obligations are contained in the Company's Bylaws, its Certificate of Incorporation, or elsewhere, as the case may be.

1.4 Right to Conduct Activities. [***]

1.5 FCPA. The Company represents that it shall not (and shall not permit any of its subsidiaries or affiliates or any of its or their respective directors, officers, managers, employees, independent contractors, representatives or agents to) promise, authorize or make any payment to, or otherwise contribute any item of value to, directly or indirectly, to any third party, including any Non-U.S. Official (as such term is defined in the U.S. Foreign Corrupt Practices Act of 1977, as amended (the "**FCPA**")), in each case, in violation of the FCPA, the U.K. Bribery Act, or any other applicable anti-bribery or anti-corruption law. The Company further represents that it shall (and shall cause each of its subsidiaries and affiliates to) cease all of its or their respective activities, as well as remediate any actions taken by the Company, its subsidiaries or affiliates, or any of their respective directors, officers, managers, employees, independent contractors, representatives or agents in violation of the FCPA, the U.K. Bribery Act, or any other applicable anti-bribery or anti-corruption law. Upon request, the Company agrees to provide responsive information and/or certifications concerning its compliance with applicable anti-corruption laws. The Company shall promptly notify each Investor if the Company becomes aware of any Enforcement Action (as defined in the Purchase Agreement). The Company shall, and shall cause any direct or indirect subsidiary or entity controlled by it, whether now in existence or formed in the future, to comply with the FCPA.

1.6 Termination of Covenants. The covenants set forth in this Section 6, except for Subsection 6.3 and 6.4, shall terminate and be of no further force or effect (i) immediately before the consummation of the IPO, (ii) when the Company first becomes subject to the periodic reporting requirements of Section 12(g) or 15(d) of the Exchange Act, or (iii) upon a distribution of the proceeds of a Deemed Liquidation Event, as such term is defined in the Company's Certificate of Incorporation, whichever event occurs first.

7. Miscellaneous.

1.1 Successors and Assigns. The rights under this Agreement may be assigned (but only with all related obligations) by a Holder to a transferee of Registrable Securities that (i) is an Affiliate of a Holder; (ii) is a Holder's Immediate Family Member or trust for the benefit of an individual Holder or one or more of such Holder's Immediate Family Members; (iii) after such transfer, holds at least 100,000 shares of Registrable Securities (subject to appropriate adjustment for stock splits, stock dividends, combinations, and other recapitalizations); or (iv) is a Permitted Transferee; provided, however, that (x) the Company is, within a reasonable time after such transfer, furnished with written notice of the name and address of such transferee and the Registrable Securities with respect to which such rights are being transferred; and (y) such transferee agrees in a written instrument delivered to the Company to be bound by and subject to the terms and conditions of this Agreement, including the provisions of Subsection 2.11. For the purposes of determining the number of shares of Registrable Securities held by a transferee, the holdings of a transferee (1) that is an Affiliate or stockholder of a Holder; (2) who is a Holder's Immediate Family Member; or (3) that is a trust for the benefit of an individual Holder or such Holder's Immediate Family Member shall be aggregated together and with those of the transferring Holder; provided further that all transferees who would not qualify individually for assignment of rights shall have a single attorney-in-fact for the purpose of exercising any rights, receiving notices, or taking any action under this Agreement. The terms and conditions of this Agreement inure to the benefit of and are binding upon the respective successors and permitted assignees of the parties. Nothing in this Agreement, express or implied, is intended to confer upon any party other than the parties hereto or their respective successors and permitted assignees any rights, remedies, obligations or liabilities under or by reason of this Agreement, except as expressly provided herein. Notwithstanding anything in the contrary contained in this Subsection 7.1, a Holder shall be permitted to make any such transfer that is required in order for such Holder to comply with laws or regulations applicable to it (including those that have been established in accordance with the UCITS (Undertakings for Collective Investment in Transferable Securities) Directive).

1.2 Governing Law. This Agreement shall be governed by the internal law of the State of Delaware, regardless of the laws that might otherwise govern under applicable principles of conflicts of law.

1.3 Counterparts. This Agreement may be executed in two (2) or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. Counterparts may be delivered via facsimile, electronic mail (including pdf or any electronic signature complying with the U.S. federal ESIGN Act of 2000, *e.g.*, www.docusign.com) or other transmission method and any counterpart so delivered shall be deemed to have been duly and validly delivered and be valid and effective for all purposes.

1.4 Titles and Subtitles. The titles and subtitles used in this Agreement are for convenience only and are not to be considered in construing or interpreting this Agreement.

1.5 Notices. All notices and other communications given or made pursuant to this Agreement shall be in writing and shall be deemed effectively given upon the earlier of actual receipt or (i) personal delivery to the party to be notified; (ii) when sent, if sent by

electronic mail or facsimile during the recipient's normal business hours, and if not sent during normal business hours, then on the recipient's next business day; (iii) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid; or (iv) one (1) business day after the business day of deposit with a nationally recognized overnight courier, freight prepaid, specifying next-day delivery, with written verification of receipt. All communications shall be sent to the respective parties at their addresses as set forth on Schedule A hereto, or to the principal office of the Company and to the attention of the Chief Executive Officer, in the case of the Company, or to such email address, facsimile number, or address as subsequently modified by written notice given in accordance with this Subsection 7.5. If notice is given to the Company, a copy shall also be sent to [***].

1.6 Amendments and Waivers. Any term of this Agreement may be amended and the observance of any term of this Agreement may be waived (either generally or in a particular instance, and either retroactively or prospectively) only with the written consent of the Company and the holders of a [***] of the Preferred Stock, voting together as a single class on an as converted basis, then outstanding; [***] (x) the Company may in its sole discretion waive compliance with Subsection 2.12(c) (and the Company's failure to object promptly in writing after notification of a proposed assignment allegedly in violation of Subsection 2.12(c) shall be deemed to be a waiver); and (xi) any provision hereof may be waived by any waiving party on such party's own behalf, without the consent of any other party. Notwithstanding the foregoing, this Agreement may not be amended or terminated and the observance of any term hereof may not be waived with respect to any Investor without the written consent of such Investor, unless such amendment, termination, or waiver applies to all Investors in the same fashion (it being agreed that a waiver of the provisions of Section 5 with respect to a particular transaction shall be deemed to apply to all Investors in the same fashion if such waiver does so by its terms, notwithstanding the fact that certain Investors may nonetheless, by agreement with the Company, purchase securities in such transaction). The Company shall give prompt notice of any amendment or termination hereof or waiver hereunder to any party hereto that did not consent in writing to such amendment, termination, or waiver. Any amendment, termination, or waiver effected in accordance with this Subsection 7.6 shall be binding on all parties hereto, regardless of whether any such party has consented thereto. No waivers of or exceptions to any term, condition, or provision of this Agreement, in any one or more instances, shall be deemed to be or construed as a further or continuing waiver of any such term, condition, or provision.

1.7 Severability. In case any one or more of the provisions contained in this Agreement is for any reason held to be invalid, illegal or unenforceable in any respect, such invalidity, illegality, or unenforceability shall not affect any other provision of this Agreement, and such invalid, illegal, or unenforceable provision shall be reformed and construed so that it will be valid, legal, and enforceable to the maximum extent permitted by law.

1.8 Aggregation of Stock. All shares of Registrable Securities held or acquired by Affiliates shall be aggregated together for the purpose of determining the availability of any rights under this Agreement and such Affiliated persons may apportion such rights as among themselves in any manner they deem appropriate.

1.9 Additional Investors. Notwithstanding anything to the contrary contained herein, if the Company issues additional shares of the Company's Series D Preferred Stock after the date hereof, any purchaser of such shares of Series D Preferred Stock may become a party to this Agreement by executing and delivering an additional counterpart signature page to this Agreement, and thereafter shall be deemed an "Investor" for all purposes hereunder. No action or consent by the Investors shall be required for such joinder to this Agreement by such additional Investor, so long as such additional Investor has agreed in writing to be bound by all of the obligations as an "Investor" hereunder.

1.10 Entire Agreement. This Agreement (including any Schedules and Exhibits hereto) constitutes the full and entire understanding and agreement among the parties with respect to the subject matter hereof, and any other written or oral agreement relating to the subject matter hereof existing between the parties is expressly canceled.

1.11 Dispute Resolution. The parties (a) hereby irrevocably and unconditionally submit to the jurisdiction of the state courts of Delaware and to the jurisdiction of the United States District Court for the District of Delaware for the purpose of any suit, action or other proceeding arising out of or based upon this Agreement, (b) agree not to commence any suit, action or other proceeding arising out of or based upon this Agreement except in the state courts of Delaware or the United States District Court for the District of Delaware, and (c) hereby waive, and agree not to assert, by way of motion, as a defense, or otherwise, in any such suit, action or proceeding, any claim that it is not subject personally to the jurisdiction of the above-named courts, that its property is exempt or immune from attachment or execution, that the suit, action or proceeding is brought in an inconvenient forum, that the venue of the suit, action or proceeding is improper or that this Agreement or the subject matter hereof may not be enforced in or by such court.

Each party will bear its own costs in respect of any disputes arising under this Agreement. Each of the parties to this Agreement consents to personal jurisdiction for any equitable action sought in the U.S. District Court for the District of Delaware or any court of the State of Delaware having subject matter jurisdiction.

1.12 Delays or Omissions. No delay or omission to exercise any right, power, or remedy accruing to any party under this Agreement, upon any breach or default of any other party under this Agreement, shall impair any such right, power, or remedy of such nonbreaching or nondefaulting party, nor shall it be construed to be a waiver of or acquiescence to any such breach or default, or to any similar breach or default thereafter occurring, nor shall any waiver of any single breach or default be deemed a waiver of any other breach or default theretofore or thereafter occurring. All remedies, whether under this Agreement or by law or otherwise afforded to any party, shall be cumulative and not alternative.

7.13 Acknowledgement [***]

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date first written above

VEDANTA BIOSCIENCES, INC.

[***]

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date first written above.

INVESTORS:

[***]

Exhibit 12.1

Certification by the Principal Executive Officer pursuant to
Securities Exchange Act Rules 13a-14(a) and 15d-14(a)
as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Daphne Zohar, certify that:

1. I have reviewed this annual report on Form 20-F of PureTech Health plc;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the company as of, and for, the periods presented in this report;

4. The company's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the company and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with UK-adopted International Financial Reporting Standards;

   (c) Evaluated the effectiveness of the company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the company's internal control over financial reporting; and

5. The company's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the company's auditors and the audit committee of the company's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the company's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the company's internal control over financial reporting.

April 25, 2022

/s/ Daphne Zohar

Daphne Zohar
Chief Executive Officer
(Principal Executive Officer)

Exhibit 12.2

Certification by the Principal Executive Officer pursuant to
Securities Exchange Act Rules 13a-14(a) and 15d-14(a)
as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, George Farmer, certify that:

1. I have reviewed this annual report on Form 20-F of PureTech Health plc;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the company as of, and for, the periods presented in this report;

4. The company's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the company and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with UK-adopted International Financial Reporting Standards;

   (c) Evaluated the effectiveness of the company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the company's internal control over financial reporting; and

5. The company's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the company's auditors and the audit committee of the company's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the company's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the company's internal control over financial reporting.

April 25, 2022

/s/ George Farmer

George Farmer
Chief Financial Officer
(Principal Financial Officer)

Exhibit 13.1

CERTIFICATION OF CHIEF EXECUTIVE OFFICER PURSUANT
TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 20-F of PureTech Health plc (the "Company") for the fiscal year ended December 31, 2021 (the "Report"), I, Daphne Zohar, Chief Executive Officer of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

April 25, 2022

/s/ Daphne Zohar
Daphne Zohar
Chief Executive Officer
(Principal Executive Officer)

Exhibit 13.2

CERTIFICATION OF CHIEF FINANCIAL OFFICER PURSUANT
TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 20-F of PureTech Health plc (the "Company") for the fiscal year ended December 31, 2021 (the "Report"), I, George Farmer, Chief Financial Officer of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

April 25, 2022

/s/ George Farmer
George Farmer
Chief Financial Officer
(Principal Financial Officer)

Exhibit 15.1

PURETECH

GIVING LIFE TO SCIENCE®

PURETECH HEALTH PLC – ANNUAL REPORT AND ACCOUNTS 2021

Giving Life to Science

PureTech Health plc ("PureTech Health", "PureTech" or "the Company") is a clinical-stage biotherapeutics company dedicated to discovering, developing and commercializing highly differentiated medicines for devastating diseases, including inflammatory, fibrotic and immunological conditions, intractable cancers, lymphatic and gastrointestinal diseases and neurological and neuropsychological disorders, among others. We discover and develop new therapies for serious diseases where limited or no treatment options currently exist for patients. The common theme underlying all of our programs has been to start with a tremendous patient need. In many cases, these programs are identified based on some previous human efficacy and clinically validated biology, which has enabled us to advance therapeutic candidates with substantially de-risked profiles and robust development rationales, resulting in differentiated treatment candidates for patients that improve on key challenges of existing therapeutics, such as poor safety, tolerability, oral bioavailability or dosing. We do this often by building upon underlying mechanisms from well-established science that have been validated in clinical testing, while applying unique innovative insight or technology that generates new medicines that can unleash the full potential of the therapeutic. We have created a broad and deep pipeline through the expertise of our experienced research and development team and our extensive network of scientists, clinicians and industry leaders. Our pipeline, which is being advanced both internally and through our Founded Entities[1], is comprised of 27 therapeutics and therapeutic candidates, including two that have received both U.S. Food and Drug Administration (FDA) clearance and European marketing authorization. All of the underlying programs and platforms that resulted in this pipeline of therapeutic candidates were initially identified or discovered and then advanced by our team through key validation points based on unique insights in immunology and drug development.

PureTech is led by a proven and seasoned management team of industry leaders with significant experience in discovering and developing important new medicines, delivering them to market and maximizing shareholder value.

Headquarters	Nasdaq	LSE
Boston, MA	PRTC	PRTC

1 Our Founded Entities are comprised of our Controlled Founded Entities and our Non-Controlled Founded Entities. References in this report to our "Controlled Founded Entities" refer to Follica, Incorporated, Vedanta Biosciences, Inc., Sonde Health, Inc. and Entrega, Inc. References in this report to our "Non-Controlled Founded Entities" refer to Gelesis Holdings, Inc., Akili Interactive Labs, Inc., Karuna Therapeutics, Inc. and Vor Bio Inc., and, for all periods prior to December 18, 2019, resTORbio, Inc. We formed each of our Founded Entities and have been involved in development efforts in varying degrees. In the case of each of our Controlled Founded Entities, we continue to maintain majority voting control. With respect to our Non-Controlled Founded Entities, we may benefit from appreciation in our minority equity investment as a shareholder of such companies.

Highlights of the Year – 2021

PureTech Level Cash and Cash Equivalents as of Year End

$418.9m[2]

2020: $349.4m
2019: $120.6m
2018: $177.7m
2017: $126.7m

Consolidated Cash and Cash Equivalents as of Year End

$465.7m[2]

Includes cash held at the PureTech level and at Controlled Founded Entities (Follica, Entrega, Vedanta, and Sonde)

2020: $403.9m
2019: $162.4m
2018: $250.9m
2017: $188.7m

Amount of funding secured for Founded Entities

$731.9m[3,4]

$709.3m (96.9%) came from third parties

2020: $247.8m
2019: $666.8m
2018: $274.0m
2017: $102.9m

Wholly Owned Programs

Our team, network and insights and expertise in immunology and therapeutic development have enabled the rapid advancement and growth of our Wholly Owned Programs[5]. Focused on immunological, fibrotic and lymphatic system disorders, our Wholly Owned Pipeline builds upon validated biologic pathways and proven pharmacology, and currently consists of seven therapeutic candidates, including LYT-100 (deupirfenidone), a clinical therapeutic candidate that we are pursuing for the potential treatment of a range of conditions involving inflammation and fibrosis and disorders of lymphatic flow, LYT-200, a clinical immuno-oncology fully human monoclonal antibody candidate targeting a foundational immunosuppressive protein, galectin-9, that we are developing for the potential treatment of difficult-to-treat solid tumors, LYT-210, a preclinical immuno-oncology therapeutic candidate targeting immunomodulatory gamma delta-1 T cells that we are developing for a range of cancer indications, LYT-300 (oral allopregnanolone), a clinical therapeutic candidate that we are developing for a range of neurological and neuropsychological conditions, which was generated from our Glyph™ lymphatic targeting platform, and three therapeutic candidates generated from Alivio™, our technology platform that enables targeting of therapeutics locally to the sites of inflammation while minimizing systemic exposure, for the potential treatment of a range of chronic and acute inflammatory disorders: LYT-510 (oral immunosuppressant molecule), in development for the potential treatment of inflammatory bowel disease (IBD) and chronic pouchitis, LYT-500 (oral combination of two therapeutic agents), in development for the potential treatment of mucosal barrier damage in people with IBD, and LYT-503/IMB-150, which is a partnered program being advanced as a potential non-opioid treatment for interstitial cystitis or bladder pain syndrome (IC/BPS). In addition to these programs, we are advancing Orasome™ and other Technology Platforms for the oral administration of therapeutics. Finally, we are pursuing our meningeal lymphatics research program to develop potential treatments for neurodegenerative and neuroinflammatory diseases. In addition to programs originating from these innovative platforms to fuel our pipeline, we also continually identify external clinical-stage programs that are highly differentiated and complementary to the immuno-modulation focus of our Wholly Owned Pipeline.

2 For more information in relation to the PureTech Level Cash and Cash Equivalents and Consolidated Cash and Cash Equivalents measures used in this Annual Report, please see pages 97 and 98 of the Financial Review. At prior comparative periods from 2016 to 2019, balances included cash, cash equivalents and short-term investments. For more information in relation to the PureTech Level Cash Reserves and Consolidated Cash Reserves measures, please also see pages 97 and 98 of the Financial Review.

3 Funding figure includes private equity financings, loans and promissory notes, public offerings or grant awards. Funding figure excludes future milestone considerations received in conjunction with partnerships and collaborations. Funding figure does not include Gelesis' gross proceeds of approximately $105.0 million from its January 2022 post-period SPAC merger.

4 Number represents figure for the relevant fiscal year only and is not cumulative.

5 References in this report to "Wholly Owned Programs" refer to the Company's seven therapeutic candidates (LYT-100, LYT-200, LYT-210, LYT-300, LYT-510, LYT-500 and LYT-503/IMB-150), four lymphatic and inflammation platforms and potential future therapeutic candidates and platforms that the Company may develop or obtain. References to "Wholly Owned Pipeline" refer to LYT-100, LYT-200, LYT-210, LYT-300, LYT-510, LYT-500 and LYT-503/IMB-150. On July 23, 2021, Imbrium Therapeutics exercised its option to license LYT-503/IMB-150 pursuant to which it is responsible for all future development activities and funding for LYT-503/IMB-150.

Clinical trial initiations[4,6]

11

2020: 6
2019: 6

Clinical trial readouts[4,7]

6

2020: 5
2019: 5

Key developments and progress across PureTech's Wholly Owned Programs include:

- In the January 2022 post-period, we were pleased to announce results from a randomized, double-blind crossover study in healthy older adults demonstrating that approximately 50% fewer subjects treated with LYT-100 (deupirfenidone) experienced gastrointestinal (GI)-related adverse events (AE) compared to subjects treated with pirfenidone (17.4% vs. 34.0%). Based on these results, discussions with our Clinical Advisory Board that includes many of the world's leading experts in idiopathic pulmonary fibrosis (IPF) clinical development, additional data generated from our robust LYT-100 clinical program as well as recent regulatory feedback, we intend to advance LYT-100 into late-stage clinical development for the treatment of IPF, beginning with a dose-ranging study evaluating six months of treatment with LYT-100 with topline results expected by the end of 2023.
- In 2021, we progressed two Phase 2 clinical trials of LYT-100 including 1) a global, randomized, double-blind, placebo-controlled Phase 2 trial to evaluate the efficacy, safety and tolerability of LYT-100-COV in adults with Long COVID[8] respiratory complications and related sequelae and 2) a Phase 2a proof-of-concept study of LYT-100-LYMPH in patients with breast cancer-related, upper limb secondary lymphedema. Topline results from the LYT-100-COV trial are expected in the first half of 2022, and topline results from the LYT-100-LYMPH trial are expected in 2022.
- In 2021, we also initiated a three-month, open-label extension of the LYT-100-COV Phase 2 trial in adults with Long COVID respiratory complications and related sequelae who completed the first portion of the trial. The primary endpoint of the extension trial will measure change in distance walked on the six-minute walk test (6MWT), with secondary endpoints to assess the longer-term safety and tolerability of LYT-100-COV up to 182 days of treatment.
- In 2021, we initiated additional clinical studies to further evaluate the pharmacokinetic (PK), dosing and tolerability of LYT-100 in healthy volunteers and healthy older adults to inform the clinical development of LYT-100 across multiple indications. Results from these studies demonstrated that LYT-100 was well-tolerated at 824mg TID dosing with low rates of GI AEs that were comparable to placebo. These results will further inform our dose-ranging study design in treatment-naïve IPF patients.
- In 2021, we continued to build our clinical development team by bringing together seasoned experts focused on tackling diseases with significant unmet medical needs. Julie Krop, M.D., was appointed as Chief Medical Officer. Dr. Krop oversees all clinical development, regulatory, CMC and medical affairs for advancing our Wholly Owned Pipeline. Other additions to our team included Paul Ford, M.D., Ph.D., SVP of Clinical Development who is primarily overseeing the overall LYT-100 development program, including for IPF. We also formed a Clinical Advisory Board for IPF and other progressive fibrosing interstitial lung diseases (PF-ILDs). These physicians and researchers with deep expertise in the clinical development of novel therapies in PF-ILDs include Bill Bradford, M.D., Ph.D., biopharma advisor with broad expertise in drug development; Vincent Cottin, M.D., Professor of Respiratory Medicine at Université Claude Bernard Lyon and Coordinator of the National Coordinating Reference Center for Rare Pulmonary Diseases at Louis Pradel Hospital, Hospices Civils de Lyon, Lyon, France; Kevin Flaherty, M.D., Professor at the University of Michigan specializing in IPF and other ILDs; Toby Maher, M.D., Ph.D., Professor of Clinical Medicine and Director of Interstitial Lung Disease at Keck School of Medicine of the University of Southern California; Paul Noble, M.D., Chair of the Department of Medicine at Cedars-Sinai Medical Center and a noted researcher in lung inflammation and fibrosis; and Marlies Wijsenbeek, M.D., Ph.D., pulmonary physician at the Erasmus Medical Center.
- In the March 2022 post-period, we appointed Sharon Barber-Lui to our board of directors as a non-executive director and as a member of the Audit Committee. She previously led U.S. Oncology Portfolio Strategy, Operations and Business Analytics at Merck & Co. Inc. Ms. Barber-Lui brings extensive experience in finance, operations, portfolio management and commercialization to our board of industry, business and academic leaders.

6 PureTech initiated five clinical trials, Karuna initiated four clinical trials, Vor Bio initiated one clinical trial and Akili initiated one clinical trial in 2021.
7 PureTech (two), Karuna (one), Gelesis (one), and Vedanta (two) reported clinical results from across their pipelines in 2021.
8 Long COVID is a term being used to describe the emerging and persistent complications following the resolution of COVID-19 infection, also known as post-acute COVID-19 syndrome (PACS).

- In August 2021, we presented the results of the Phase 1 multiple ascending dose and food effect study of LYT-100 at the virtual European Respiratory Society (ERS) International Congress. The results from the study were subsequently published in the journal *Clinical Pharmacology in Drug Development* in November 2021.
- In 2021, we progressed the first stage of an adaptive Phase 1/2 clinical trial evaluating LYT-200 (anti-galectin-9 fully human monoclonal antibody) as a single agent for the potential treatment of difficult-to-treat solid tumors. In November 2021, we presented a scientific poster describing the trial at the Society for Immunotherapy of Cancer (SITC) 36th annual meeting. Topline results from the Phase 1 portion of the study are expected in the first half of 2022. Pending these results, we intend to initiate the Phase 2 expansion cohort portion of the trial, which is designed to evaluate LYT-200 both as a single agent and/or in combination with BeiGene's tislelizumab, an anti-PD-1 monoclonal antibody, or chemotherapy. The Phase 2 portion of the study is currently planned to enroll patients with a range of solid tumor types, including pancreatic cancer and other GI solid tumors. Under the terms of the clinical trial and supply agreement we entered into with an affiliate of BeiGene, Ltd. in July 2021, we will maintain control of the LYT-200 program, including global R&D and commercial rights, and BeiGene has agreed to supply tislelizumab for use in combination with LYT-200 for the planned Phase 2 study cohorts.
- In November 2021, the FDA granted orphan drug designation to LYT-200 for the treatment of pancreatic cancer. The FDA grants orphan drug designation to novel drug and biologic products for the treatment, diagnosis or prevention of conditions affecting fewer than 200,000 persons in the U.S. Orphan drug designation qualifies PureTech for incentives under the Orphan Drug Act, including tax credits for some clinical trials and eligibility for seven years of market exclusivity in the U.S. if the drug is approved, in addition to our broad intellectual property coverage which can extend the exclusivity into 2038.
- In April 2021, we presented a scientific poster detailing additional promising preclinical results for LYT-210 (anti-gamma-delta-1 fully human monoclonal antibody) at the 2021 American Association for Cancer Research (AACR) Annual Virtual Meeting. The research demonstrated that LYT-210 is both highly specific and highly potent, rapidly inducing cell death of immunomodulatory gamma delta-1 (γδ1) T cells, while sparing other T cells, such as cytotoxic gamma delta T cells, that play important roles in a healthy immune response.
- In December 2021, we initiated a Phase 1 clinical study of LYT-300 (oral allopregnanolone), the first therapeutic candidate generated from our Glyph platform, for the potential treatment of neurological and neuropsychological conditions. The Phase 1 study of LYT-300 involves multiple parts, including the evaluation of a single ascending dose, multiple ascending doses and the effect of food in healthy volunteers. Safety, tolerability and PK will be assessed. Given the $GABA_A$ receptor modulating activity of allopregnanolone, the study will also explore the impact of LYT-300 on beta-EEG, a marker of $GABA_A$ target engagement, thus potentially providing early insights into the mechanistic effects of LYT-300. Results from the study are expected in the second half of 2022 and will be used to inform the design of possible future studies evaluating LYT-300 in indications that could include depression, anxiety, sleep disorders, fragile X tremor-associated syndrome, essential tremor and epileptic disorders, among others.
- In June 2021, we announced the acquisition of the remaining 22% of outstanding shares in our Founded Entity, Alivio Therapeutics ('Alivio'). Alivio's therapeutic candidates, in development for inflammatory disorders including IBD, have been integrated into our Wholly Owned Pipeline, and the underlying Alivio technology platform has been added to our lymphatic and inflammation platforms. The Alivio technology platform has generated three therapeutic candidates, including LYT-510, an orally-administered therapeutic candidate for the potential treatment of IBD and chronic pouchitis, LYT-500, an oral therapeutic candidate that we are developing for the potential treatment of mucosal barrier damage in people with IBD, and LYT-503/IMB-150 for the potential treatment of IC/BPS (being developed as a partnered program). We expect preclinical proof-of-concept data for LYT-500 in the first half of 2022. We intend to file for regulatory approval to initiate first-in-human studies at year end 2022 and initiate a clinical study evaluating LYT-510 as a single agent for the potential treatment of IBD and chronic pouchitis in early 2023. An IND application for LYT-503/IMB-150 is expected to be filed in 2022.
- In September 2021, preclinical proof-of-concept research supporting the Glyph technology platform, which showed for the first time that restoring normal function of the mesenteric lymphatics may reverse insulin resistance and modify obesity-associated metabolic disease, was published in *Nature Metabolism*. Preclinical proof-of-concept work published in the *Journal of Controlled Release* in February 2021 also supported the platform's ability to directly target the lymphatic system.
- In April 2021, preclinical work supporting our meningeal lymphatics research program was published in *Nature*. The research suggests that restoring lymphatic flow in the brain, either alone or in combination with passive immunotherapies such as antibodies directed at amyloid beta, has the potential to address a range of neurodegenerative diseases, including Alzheimer's and Parkinson's diseases and the associated neuroinflammation. The work also uncovered a link between dysfunctional meningeal lymphatics and damaging microglia activation in Alzheimer's disease, which potentially impairs the efficacy of passive immunotherapies such as amyloid-beta-targeting antibodies. This suggests another route by which restoring healthy drainage patterns could improve clinical outcomes.
- In 2021, we also progressed versatile and programmable oral biotherapeutics approaches, such as our Orasome platform, which is a novel programmable and scalable approach for the oral administration of nucleic acids and other biologics. We established preclinical proof-of-concept supporting the platform's potential to achieve therapeutic levels of proteins in circulation following the oral administration of therapeutic protein expression systems. We expect to generate additional preclinical data, with Orasomes and other technologies, in 2022.

Founded Entities[9]

PureTech's Founded Entities have made significant progress advancing 20 therapeutics and therapeutic candidates, of which two have been cleared for marketing by the FDA and granted marketing authorization in the European Economic Area and 13 are clinical stage. Key developments included the following:

KARUNA THERAPEUTICS

Karuna Therapeutics, Inc. (PureTech ownership: 5.6%; We also are eligible to receive payments under our license agreement, including sublicense payments and royalties on net sales)

- In November 2021, Karuna announced further updates to the EMERGENT program's four ongoing Phase 3 trials, including that topline data from EMERGENT-2, a five-week inpatient trial evaluating the efficacy and safety of KarXT compared to placebo in 246 adults with schizophrenia in the U.S., are expected in mid-2022. EMERGENT-3, a five-week inpatient trial evaluating the efficacy and safety of KarXT compared to placebo in 246 adults with schizophrenia in the U.S. and Ukraine, is underway. EMERGENT-4, a 52-week outpatient, open-label extension trial evaluating the long-term safety and tolerability of KarXT in 350 adults with schizophrenia who completed EMERGENT-2 or EMERGENT-3, and EMERGENT-5, a 52-week outpatient, open-label trial evaluating the long-term safety and tolerability of KarXT in adults with schizophrenia who were not enrolled in EMERGENT-2 or EMERGENT-3, are also underway.
- In 2021, Karuna initiated the Phase 3 ARISE trial evaluating the safety and efficacy of KarXT compared to placebo as an adjunctive treatment in adults with schizophrenia who experience an inadequate response to current standard of care.
- In June 2021, Karuna announced data from its completed Phase 1b trial evaluating the safety and tolerability of KarXT in healthy elderly volunteers, which followed a preliminary analysis of data from the first two cohorts in the trial announced earlier this year. The results suggest that KarXT can be administered to elderly volunteers at doses which achieve xanomeline blood levels similar to those reported in the Phase 2 EMERGENT-1 trial in adults with schizophrenia while maintaining a favorable tolerability profile. Data from the trial also suggest that a lower dose ratio of trospium to xanomeline, compared to the ratios used in Phase 1 trials in healthy adult volunteers and in the Phase 2 EMERGENT-1 trial evaluating KarXT in adults with schizophrenia, was better tolerated by healthy elderly volunteers.
- In November 2021, Karuna announced the evaluation of KarXT for the treatment of dementia-related psychosis (DRP) will initially focus on psychosis in Alzheimer's disease, the most common subtype of DRP. The initial focus on the Alzheimer's disease dementia subtype reflects various strategic development, regulatory and commercial considerations, and Karuna remains interested in exploring KarXT in other dementia subtypes in future development programs. Karuna plans to initiate a Phase 3 program in mid-2022.
- In late 2021, Karuna initiated a Phase 1 trial of an advanced formulation of KarXT as it continued to advance its earlier pipeline of muscarinic receptor targeted programs and novel formulations of KarXT. Karuna is also advancing its artificial intelligence-based target agnostic discovery program for treating psychiatric and neurological conditions.
- In November 2021, Karuna announced its entry into an exclusive license agreement with Zai Lab for the development, manufacturing and commercialization of KarXT in Greater China, including mainland China, Hong Kong, Macau and Taiwan. Under the terms of the agreement, Karuna received a $35.0 million upfront payment and is eligible to receive certain development and regulatory milestone and sales milestone payments, as well as royalties based on annual net sales of KarXT in Greater China.
- In February 2021, Karuna announced that results from the EMERGENT-1 Phase 2 clinical trial evaluating KarXT for the treatment of schizophrenia were published in the *New England Journal of Medicine* (NEJM).
- In March 2021, Karuna completed a follow-on public offering of its common stock, from which it received net proceeds of $270.0 million.
- In 2021, PureTech sold 1,750,000 shares of Karuna common stock for a cash consideration of approximately $218 million in two separate transactions in February and November.

9 While PureTech maintains ownership of equity interests in its Founded Entities, the Company does not, in all cases, maintain control over these entities (by virtue of (i) majority voting control and (ii) the right to elect representation to the entities' board of directors) or direct the management and development efforts for these entities. Consequently, not all such entities are consolidated in the financial statements. Where PureTech maintains control, the entity is referred to as a Controlled Founded Entity in this report and is consolidated in the financial statements. Where PureTech does not maintain control, the entity is referred to as a Non-Controlled Founded Entity in this report and is not consolidated in the financial statements. As of December 31, 2021, Controlled Founded Entities include Follica Incorporated, Vedanta Biosciences, Inc., Sonde Health, Inc. and Entrega, Inc., and Non-Controlled Founded Entities include Gelesis Holdings, Inc., Karuna Therapeutics, Inc., Akili Interactive Labs, Inc., Vor Bio Inc.

Akili Interactive Labs, Inc. (PureTech ownership: 22.3%)

- In the January 2022 post-period, Akili entered into a definitive agreement to become publicly traded via a merger with Social Capital Suvretta Holdings Corp. I ("SCS") (Nasdaq: DNAA), a special purpose acquisition company. The transaction is expected to close in mid-2022, after which Akili will be listed on the Nasdaq stock market under the new ticker symbol "AKLI". The transaction implies a post-money equity value of the combined company of up to approximately $1 billion and is expected to deliver up to $412 million in gross cash proceeds to Akili, including the contribution of up to $250 million of cash held in SCS's trust account and $162 million from PIPE investors at $10 per share.
- In May 2021, Akili announced the closing of a $160 million combined equity and debt financing. With the completion of the oversubscribed Series D financing, the funding is expected to accelerate commercialization of EndeavorRx®[10], enable expansion of core technologies to treat acute and chronic cognitive disorders and drive further research and development of potential new digital therapeutics.
- In March 2021, the full data from a multi-site open-label study (the STARS Adjunct study) evaluating the impact of EndeavorRx (AKL-T01) on symptoms and functional impairments in children with attention-deficit/hyperactivity disorder (ADHD) was published in *Nature Digital Medicine*. Statistically significant improvement was demonstrated in all predetermined endpoints of the study, which included parent and clinician ratings of children's ADHD symptoms and related impairments in daily life.
- In the February 2022 post-period, Akili announced the publication of full data in the medical journal *PLOS ONE* from a single arm, unblinded study conducted by Dr. Elysa Marco at Cortica Healthcare and Drs. Joaquin Anguera and Courtney Gallen at the University of California, San Francisco. The study measured electroencephalography (EEG) data alongside behavioral and clinical metrics of attention in children with ADHD using AKL-T01 (EndeavorRx). Data from the study show that EndeavorRx treatment resulted in increased brain activity related to attention function, as measured by EEG, which correlated with improvements in objective behavioral measures of attention.
- In September 2021, Akili announced topline results of a Phase 2 study of SDT-001 (Japanese version of AKL-T01), a digital therapeutic designed to improve measures of attention in children diagnosed with attention-deficit/hyperactivity disorder (ADHD). The study, conducted by Akili partner Shionogi & Co., Ltd., was designed to evaluate the feasibility, safety and efficacy of the digital therapeutic in children with ADHD and to inform the design of a potential pivotal study. Results showed the treatment was well-received by patients and demonstrated improvements in ADHD inattention symptoms consistent with those seen across previous studies of AKL-T01.
- In the March 2022 post-period, Akili announced it had been named to *Fast Company*'s prestigious list of the World's Most Innovative Companies for 2022. This list honors businesses that are making the biggest impacts on their industries and culture as a whole and thriving in today's ever-changing world.
- In July 2021, Akili introduced new gaming features and functionalities to its EndeavorRx treatment. Akili is releasing these new gameplay features as it expands its pre-launch activities to bring EndeavorRx to families and healthcare professionals.
- In April 2021, Akili announced collaborations with Weill Cornell Medicine, New York-Presbyterian Hospital and Vanderbilt University Medical Center to evaluate Akili digital therapeutic AKL-T01 as a treatment for patients with cognitive dysfunction following COVID-19 (also known as "COVID fog"). Under each collaboration, Akili will work with research teams at each institution to conduct two separate randomized, controlled clinical studies evaluating AKL-T01's ability to target and improve cognitive functioning in COVID-19 survivors who have exhibited a deficit in cognition. Akili expects data from the studies in COVID fog in the second half of 2022.
- In August 2021, Akili and Australian digital health company TALi® (ASX:TD1), completed an agreement for Akili to license TALi's technology designed to address early childhood attention impairments. The companies plan to work together to execute clinical trials of the TALi technology in pediatric ADHD in the U.S. and pursue FDA regulatory clearance. Under the terms of the agreement, Akili will lead potential U.S. commercialization and roll-out.
- In the March 2022 post-period, Akili appointed Jon David as Chief Product Officer. A 20-year veteran of the games industry, Mr. David joins Akili to develop and execute the strategic vision of Akili's future product pipeline after serving as Vice President and General Manager at Glu Mobile, acquired in 2021 by Electronic Arts, where he led the development of both new IP and hit franchises including *Covet Fashion* and *Diner Dash Adventures*. Mr. David also guided the success of fan-favorite franchises and the launches of hit titles including *Plants vs. Zombies 2* and *Plants vs. Zombies Garden Warfare*.

10 EndeavorRx® is a digital therapeutic indicated to improve attention function as measured by computer-based testing in children ages 8-12 years old with primarily inattentive or combined-type ADHD, who have a demonstrated attention issue. Patients who engage with EndeavorRx demonstrate improvements in a digitally assessed measure, Test of Variables of Attention (TOVA®) of sustained and selective attention and may not display benefits in typical behavioral symptoms, such as hyperactivity. EndeavorRx should be considered for use as part of a therapeutic program that may include clinician-directed therapy, medication, and/or educational programs, which further address symptoms of the disorder. There were no serious adverse events; 9.3% of subjects experienced side effects, including frustration, headache, dizziness, emotional reaction, nausea or aggression. EndeavorRx is only available to your patients through a prescription, and is not intended as a stand-alone therapeutic or a substitute for your patient's medication.

GELESIS

Gelesis Holdings, Inc. (PureTech ownership: 23.5%; We also are eligible to receive payments under our license agreement, including sublicense payments and royalties on net sales)

- In December 2021, Gelesis announced that Plenity®[11] is now broadly available across the U.S. to adults who meet the prescription criteria.
- In the January 2022 post-period, Gelesis announced the completion of its business combination with Capstar Special Purpose Acquisition Corp. (NYSE: CPSR) ("Capstar"). Gelesis Holdings, Inc. began trading on the New York Stock Exchange under the ticker symbol "GLS" on January 14, 2022.
- In January 2022 post-period, Gelesis launched the "Who Said?" marketing campaign across the U.S., which challenges many long-held cultural and societal assumptions around weight loss. Plenity's multichannel campaign encompasses TV, digital, social and Out of Home (OOH) to grow awareness of Plenity's novel approach to weight management.
- In the March 2022 post-period, Gelesis announced preliminary results from its broad awareness media campaign, noting that within the first three weeks, the company saw a 3-fold increase in web traffic and 3.5-fold increase in the number of individuals seeking a new prescription compared to previous months when supply was limited.
- In November 2021, Gelesis' first commercial-scale manufacturing line was completed and validated, and the company announced that it had received a $30 million fully paid pre-order, in addition to the $10 million pre-order received in January 2021, for its first commercial product for weight management, Plenity, from Ro, a leading U.S. direct-to-patient healthcare company.
- In late 2021, both primary endpoints were achieved in the Gelesis LIGHT-UP study of GS200 in adults with overweight or obesity who also have prediabetes or type 2 diabetes.
- In November 2021, Gelesis announced a publication in *Nature's Scientific Reports* describing the genesis of the underlying technology and engineering process for Gelesis' non-systemic superabsorbent hydrogels. These new materials were designed to replicate compositional and mechanical properties of raw vegetables, and the paper describes their therapeutic approach for weight management as well as possible future solutions for other gut-related conditions.
- In May 2021, Gelesis presented a scientific poster at the American Association of Clinical Endocrinology (AACE) 2021 Annual Virtual Meeting. The post-hoc analysis showed that treatment for weight management with Plenity decreased a marker for liver fibrosis (the NAFLD fibrosis score) compared to placebo.
- In the January 2022 post-period, Gelesis appointed Inogen Co-Founder and former CFO, Ali Bauerlein, to its Board of Directors and Audit Committee. Ms. Bauerlein brings success in scaling to $300M+ revenue in a direct-to-consumer business model and public company execution as Gelesis plans to scale Plenity to meet growing consumer demand.

VOR

Vor Bio Inc. (PureTech ownership: 8.6%)

- In February 2021, Vor Bio announced the pricing of its initial public offering of common stock on the Nasdaq Global Market under the symbol "VOR". The aggregate gross proceeds to Vor Bio from the offering were approximately $203.4 million, before deducting the underwriting discounts and commissions and other offering expenses payable by Vor Bio.
- In the March 2022 post-period, Vor Bio announced VCAR33 is now made up of two programs with different cell sources. The VCAR33 programs are chimeric antigen receptor T (CAR-T) cell therapy candidates designed to target CD33, a clinically-validated target for AML. VCAR33^{AUTO} uses autologous cells from each patient, and is being studied in an ongoing Phase 1/2 clinical trial sponsored by the National Marrow Donor Program (NMDP) in young adult and pediatric patients with relapsed/refractory AML in a bridge-to-transplant study. VCAR33^{ALLO} uses allogeneic healthy donor-derived cells. Vor Bio also announced it plans to collect initial data on VOR33 from the VBP101 clinical trial and initial clinical data from the VCAR33^{ALLO} program prior to IND submission for the Treatment System following ongoing discussions with the FDA and alongside improved scientific understanding of the differences in T-cell sources.
- In September 2021, the FDA granted Fast Track designation to VOR33, Vor Bio's lead engineered hematopoietic stem cell (eHSC) therapeutic candidate for the treatment of acute myeloid leukemia (AML).
- Vor Bio initiated VBP101, a Phase 1/2a clinical trial of VOR33 for AML patients who currently have limited treatment options and expects to report VOR33's initial clinical data in the second half of 2022.
- In November 2021, Vor Bio announced its first multi-targeted treatment system comprising VOR33-CLL1 multiplex-edited eHSC therapy and VCAR33-CLL1 multi-specific CAR-T therapy. Vor Bio continues to make progress on editing multiple antigens with its eHSC platform.
- In June 2021, Vor Bio announced the build-out of an in-house clinical manufacturing facility in Cambridge, Massachusetts in the same premises as Vor Bio's current headquarters, to support flexible manufacturing for the company's eHSC and CAR-T product candidate pipeline for patients with blood cancers. Vor Bio anticipates that the facility will be operational in 2022.
- In July 2021, Vor Bio announced the formation of a collaboration with Janssen Biotech, Inc. (Janssen), one of the Janssen Pharmaceutical Companies of Johnson & Johnson.

11 Important Safety Information about Plenity®: Patients who are pregnant or are allergic to cellulose, citric acid, sodium stearyl fumarate, gelatin, or titanium dioxide should not take Plenity. To avoid impact on the absorption of medications: For all medications that should be taken with food, take them after starting a meal. For all medications that should be taken without food (on an empty stomach), continue taking on an empty stomach or as recommended by your physician. The overall incidence of side effects with Plenity was no different than placebo. The most common side effects were diarrhea, distended abdomen, infrequent bowel movements, and flatulence. Contact a doctor right away if problems occur. If you have a severe allergic reaction, severe stomach pain, or severe diarrhea, stop using Plenity until you can speak to your doctor. Rx Only. For the safe and proper use of Plenity or more information, talk to a healthcare professional, read the Patient Instructions for Use, or call 1-844-PLENITY.

The agreement was facilitated by Johnson & Johnson Innovation. Under the terms of the collaboration, Vor Bio will investigate the combination of these two technologies into a treatment solution, pairing Vor Bio's "invisible" eHSC transplant platform with one of Janssen's bi-specific antibodies in development for AML. The collaboration agreement provides that each company retains all rights and ownership to their respective programs and platforms.

- In June 2021, Vor Bio entered into a multi-year strategic collaboration and license agreement with Abound Bio to research both single- and multi-targeted CAR-T treatments to be used in combination with Vor Bio's eHSC platform, with the goal of generating novel treatment systems for patients fighting AML and other devastating forms of blood cancer.
- In January 2021, Vor Bio announced that the FDA had accepted the company's IND application for VOR33. In May 2021, Vor Bio announced that it received the Canadian clinical trial application clearance for VOR33 from Health Canada.
- In June 2021, Vor Bio announced the appointment of Matthew R. Patterson as Chairman of its Board of Directors. Mr. Patterson brings nearly 30 years of senior leadership experience in the research, development and commercialization of innovative therapeutics, most recently at Audentes Therapeutics, Inc., which he co-founded and led as the company's Chief Executive Officer from its inception in 2012 through its acquisition by Astellas Pharma Inc. in January 2020.

VEDANTA BIOSCIENCES

Vedanta Biosciences, Inc. (PureTech ownership: 41.4%)

- In October 2021, Vedanta announced that its Phase 2 clinical trial of VE303, an orally administered investigational live biotherapeutic product (LBP) in development for the prevention of recurrent *C. difficile* infection (CDI) in high-risk patients, met its primary endpoint of preventing disease recurrence through Week 8. VE303 achieved a 31.7% absolute risk reduction in rate of recurrence when compared with placebo, representing a greater than 80% reduction in the odds of a recurrence. This is believed to be the most advanced clinical trial of an investigational drug based on a rationally defined bacterial consortium, a microbiome-based therapeutic approach that delivers orally administered candidates of precisely known composition that can be manufactured with pharmaceutical-grade consistency. Based on the Phase 2 data, the Biomedical Advanced Research and Development Authority (BARDA) exercised its first contract option for additional funding of $23.8 million, pursuant to its existing 2020 contract with Vedanta, to support a planned Phase 3 clinical trial of VE303.
- In January 2021, Vedanta announced a $25 million investment from Pfizer, as part of the Pfizer Breakthrough Growth Initiative. Vedanta will retain control of all of its programs and has granted Pfizer a right of first negotiation on VE202, Vedanta's 16-strain defined bacterial consortium candidate. As part of the investment, Michael Vincent, M.D., Ph.D., Senior Vice President and Chief Scientific Officer, Inflammation & Immunology Research Unit at Pfizer, joined Vedanta's Scientific Advisory Board.
- In late 2021, Vedanta also completed the build-out of its Phase 3 and commercial launch CGMP manufacturing facility for supply of VE303.
- In June 2021, Vedanta presented additional results from a Phase 1 study in healthy volunteers of VE202, Vedanta's 16-strain defined bacterial consortium candidate for IBD, at the International Human Microbiome Consortium Congress 2021 (IHMC). The data summarized the long-term safety and colonization dynamics of the 16-strain version of VE202 in 31 healthy volunteers. Vedanta plans to initiate a Phase 2 clinical trial of VE202 in mild to moderate ulcerative colitis patients.
- In 2021, Vedanta's ongoing Phase 1/2 clinical trial of VE416 for food allergy continued to progress.
- In July 2021, Vedanta announced results from the Phase 1 study evaluating the safety and initial clinical activity of VE800, and immuno-oncology therapeutic candidate, in combination with Bristol Myers Squibb's Opdivo® (nivolumab) in 54 patients across select types of advanced or metastatic cancers. VE800 demonstrated an acceptable safety and tolerability profile, though the observed response rates did not meet the prespecified criteria to advance into the next stage of the study. Vedanta is analyzing blood, stool and tumor samples from patients in whom response or disease control was observed in order to profile patient subtypes that might benefit from microbiome manipulation. Vedanta plans to present the results at a future medical conference and will continue work to identify cancer settings and patient populations that might benefit from microbiome manipulation with its defined bacterial consortia.
- In July 2021, Vedanta closed a $68 million financing, which included the $25 million investment from Pfizer as part of the Pfizer Breakthrough Growth Initiative announced in January 2021. Vedanta plans to use the proceeds to advance its pipeline of defined bacterial consortia, including progressing VE303 into a Phase 3 clinical trial in patients at high risk for recurrent CDI, initiating a Phase 2 clinical trial of VE202 in mild to moderate ulcerative colitis and continuing to advance programs in additional indications.
- In February 2021, Vedanta appointed Mark Mullikin as Chief Financial Officer. Mr. Mullikin brings 25 years of experience raising and deploying capital for life sciences companies, and most recently held leadership roles in finance and investor relations at publicly-traded companies such as Editas Medicine and Novartis.
- In October 2021, Vedanta announced the appointment of Simona Levi, Ph.D., J.D., as Chief Legal Officer and Corporate Secretary. Dr. Levi brings over 25 years of U.S. and international legal experience with private and public companies across the life sciences industry focusing on complex transactions, intellectual property law and litigation as well as corporate governance.

follica

Follica, Incorporated (PureTech ownership: 76.0%. We also are eligible to receive payments under our license agreement, including sublicense payments and royalties on net sales)

- In January 2021, Follica announced the appointment of two leaders in aesthetic medicine and dermatology to its Board of Directors. Tom Wiggans, former Chief Executive Officer of Dermira, joined as Executive Chairman with over 30 years of experience leading biopharmaceutical companies from the start-up stage to global commercialization, and Michael Davin, former Chief Executive Officer of Cynosure, joined as an Independent Director with over 30 years of experience in the medical device industry.
- Preparations are underway for the registration clinical program in male androgenetic alopecia and initiation is anticipated in 2022.

SONDE

Sonde Health, Inc. (PureTech ownership: 44.6%)

- In October 2021, Sonde launched Sonde Mental Fitness, a voice-enabled mental health detection and monitoring technology that uses a brief voice sample to evaluate mental well-being. Sonde Mental Fitness is currently available through its API platform for integration into third-party apps. It's also available as a standalone app for iOS and Android, mobile devices to serve as a proof-of-concept for health systems, employers and wellness services interested in testing out the API's capabilities.
- In the January 2022 post-period, Sonde announced the signing of a multi-year strategic partnership with GN Group to research and develop commercial vocal biomarkers for mild cognitive impairment. The research will serve as the backbone for new voice-based tools to help at-risk individuals gain timely and accurate health insights using GN Group's device technologies and, ultimately, to enable early detection and management of life-threatening diseases for the millions of people living with hearing loss.
- In July 2021, Sonde announced a strategic collaboration with leading chipmaker Qualcomm Technologies, Inc. (Qualcomm) to embed Sonde's vocal biomarker technology into its flagship and high-tier Qualcomm® Snapdragon™ 888 and 778G 5G Mobile Platforms to help bring native, machine learning-driven vocal biomarker capabilities to mobile and IoT devices globally. The optimization has the potential to unlock several native health screening and monitoring applications on up to the hundreds of millions of mobile devices that use these Snapdragon mobile platforms.

entrega

Entrega, Inc. (PureTech ownership: 74.3%)

- Entrega continued to advance its platform for the oral administration of biologics, vaccines and other drugs that are otherwise not efficiently absorbed when taken orally. As part of its collaboration with Eli Lilly, Entrega has continued to investigate the application of its peptide administration technology to certain Eli Lilly therapeutic candidates. The partnership has been extended into 2022.
- Entrega has also continued advancement of its ENT-100 platform for the oral administration of biologics, vaccines and other drugs that are otherwise not efficiently absorbed when taken orally.

Components of Value

Wholly Owned Pipeline

Our programs[1]	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
LYT-100-ILD Deupirfenidone	Idiopathic pulmonary fibrosis (IPF)					
LYT-100-COV Deupirfenidone	Long COVID[2] respiratory complications and related sequelae					
LYT-100-LYMPH Deupirfenidone	Lymphatic flow disorders, including lymphedema					
LYT-200 Anti-Galectin-9 mAb	Solid tumors					
LYT-210 Anti-Delta-1 mAb	Solid tumors					
LYT-300 Oral Allopregnanolone	Neurological and neuropsychological conditions					
LYT-510 Oral Immunosuppressant	Inflammatory bowel disease (IBD)/ Chronic pouchitis					
LYT-500 Oral IL-22 + Immunosuppressant	Inflammatory bowel disease (IBD)					
LYT-503/IMB-150 (Partnered program) Non-opioid	Interstitial cystitis/bladder pain syndrome (IC/BPS)					

Phase completed | Phase in progress | Registration-enabling studies to begin in 1H2022

Lymphatic and Inflammation Platforms

- Glyph™ Technology Platform (Lymphatic Targeting)
- Orasome™ and Other Technology Platforms (Oral Biotherapeutics)
- Alivio™ Technology Platform (Inflammation Targeting)
- Meningeal Lymphatics Research Program

Cash at PureTech Level

$418.9m PureTech Level Cash and Cash Equivalents as of December 31, 2021[3]

1 The FDA and corresponding regulatory authorities will ultimately review our clinical results and determine whether our wholly-owned therapeutic candidates are safe and effective. No regulatory agency has made any such determination that our wholly-owned therapeutic candidates are safe or effective for use by the general public for any indication.
2 Long COVID is a term being used to describe the emerging and persistent complications following the resolution of COVID-19 infection, also known as post-acute COVID-19 syndrome (PACS).
3 For more information in relation to the PureTech Level Cash and Cash Equivalents and Consolidated Cash and Cash Equivalents measures used in this Annual Report, please see pages 97 and 98 of the Financial Review.

Founded Entities[4]

Advancing transformative medicines for people living with psychiatric and neurological conditions

Interest[5]
5.6% Equity plus Royalties, Milestone Payments & Sublicense Revenues

Stage of Development
Phase 3

Nasdaq
KRTX

Pioneering the development of cognitive treatments through game-changing technologies

Interest[5]
22.3% Equity

Stage of Development
Commercial

Advancing a novel category of treatments for weight management and gut related chronic diseases

Interest[5]
23.5% Equity plus Royalties

Stage of Development
Commercial

NYSE
GLS

Engineering hematopoietic stem cell therapies combined with targeted therapies

Interest[5]
8.6% Equity

Stage of Development
Phase 1/2a

Nasdaq
VOR

Pioneering a new category of oral therapies based on defined bacterial consortia

Interest[5]
41.4% Equity

Stage of Development
Phase 3 Ready

Building a regenerative biology platform for androgenetic alopecia, epithelial aging and other medical indications

Interest[5]
76.0% Equity plus Royalties

Stage of Development
Phase 3 Ready

Developing a voice-based technology platform to detect changes of health conditions

Interest[5]
44.6% Equity

Stage of Development
Commercial Release

Engineering hydrogels to enable the oral administration of biologics

Interest[5]
74.3% Equity

Stage of Development
Preclinical

4 This figure represents the stage of development for each Founded Entity's most advanced therapeutic candidate. For additional information, please see footnote no. 9 on page 5.

5 Relevant ownership interests for Founded Entities contained in this strategic report (pages 2-72) were calculated on a partially diluted basis (as opposed to a voting basis) as of December 31, 2021, including outstanding shares, options and warrants, but excluding unallocated shares authorized to be issued pursuant to equity incentive plans. Vor Bio, Karuna and Gelesis ownerships were calculated on a beneficial ownership basis in accordance with SEC rules as of March 4, 2022 and February 15, 2022 and March 31, 2022, respectively.

Letter from the Chair

"In my experience, very few companies come anywhere close to PureTech's realization of a truly innovative business and development model that has established a foundation for long-term growth."

Christopher Viehbacher,
Chair of the Board of Directors

The past year has been a highly dynamic one for the biotech industry. With vaccines and therapies against COVID-19 taking center stage in the public consciousness, investment in life sciences companies soared and then public companies faced headwinds. The pace of incredible innovation across a wide range of therapeutic modalities and diseases accelerated. The fundamental opportunity we have to bring transformative medicines to people in need has never been larger or more achievable. Research tools grow more powerful at an accelerating pace, and we are steadily building the evidence base for many innovative platforms with the potential to fill pipelines of breakthrough medicines in the years to come.

PureTech represents the most compelling elements of the biotherapeutics industry in a single company. We leverage world-leading expertise in immunology and the brain, immune and gastrointestinal systems to address serious debilitating diseases. We prioritize harnessing validated biology to advance differentiated therapeutic candidates with well-managed risk profiles and robust development rationales from day one. The result is a unique pharmaceutical pioneer with a strong track record of innovation and clinical success, an exciting, diversified pipeline of innovative therapeutic candidates and programs, a strong balance sheet and a clear vision for bringing breakthrough new medicines to the patients.

We are moving steadily towards our vision of a fully integrated biotherapeutics company, creating value organically from internally-driven growth while also sourcing programs that complement our strategy and expertise to build a truly differentiated portfolio of high-value new medicines. In my experience, very few companies come anywhere close to PureTech's realization of a truly innovative business and development model that has delivered such a sustainable foundation for long-term growth.

Across our Wholly Owned Pipeline, all our work is united by a mission to deliver highly differentiated medicines for devastating diseases where there are currently limited or no options available for patients. That internal pipeline now includes seven therapeutic candidates. We advanced three of these through the clinic in 2021, most notably in two Phase 2 trials of LYT-100, a Phase 1/2 trial of LYT-200 and a Phase 1 study of LYT-300.

As a highly versatile therapeutic candidate built on substantial validated biology and clinical data, PureTech's lead therapeutic candidate, LYT-100 (deupirfenidone), is rapidly building a compelling expanded clinical profile to address a range of serious fibrotic and inflammatory diseases. Study data announced in late 2021 and the early 2022 post-period have helped paint a picture of a therapeutic with substantially enhanced tolerability relative to pirfenidone, a drug already approved for IPF, a chronic orphan condition that causes progressive scarring of the lungs and has a median survival of 3-5 years.

This de-risked strategy of leveraging validated biology is employed across several of our Wholly Owned Pipeline candidates. It is enhanced by our novel research platform technologies, each of which can be applied to known therapeutic entities, with clinical validation, to generate novel candidates that not only help grow our Wholly Owned Pipeline organically but have the potential to change the treatment paradigm for a range of serious diseases and generate significant value for the patients and our shareholders.

To complement our innovative R&D engine, our Founded Entities are also maturing well, with three of them now publicly traded and a fourth one soon expected to go public, and they continue to generate value for PureTech through their ongoing, independent activity. In 2021, for example, we monetized a portion of our equity in one of our Founded Entities, Karuna Therapeutics, resulting in approximately $218 million being added to PureTech's balance sheet and bringing the total to approximately $565 million generated to date while still maintaining a significant equity stake as one of the largest shareholders and the right to receive royalties and sublicense revenues from the KarXT programs. Our Founded Entities are a source of value to us through potential M&A transactions, equity stakes, royalties and milestone payments as they continue to deliver on their promise. Monetization of our stakes in the Founded Entities has provided us with important resources to advance our Wholly Owned Pipeline.

Collectively, our eight Founded Entities are now advancing 20 therapeutics and therapeutic candidates, of which two have been cleared for marketing by the FDA and granted marketing authorization in the European Economic Area, and 13 are clinical stage.

The Founded Entities continued to mature over the year, with Akili and Gelesis making major strides towards full commercial launches for their groundbreaking products as well as entering the public equity markets. Vor Bio also entered the clinic and completed its initial public offering on Nasdaq.

In the January 2022 post-period, Gelesis became public, raising capital to fuel its commercialization strategy for Plenity®[1] as a truly novel approach for overweight and obesity. Akili also announced its entry into a definitive agreement to become publicly traded via a merger with Social Capital Suvretta. The transaction is expected to close in mid-2022, after which Akili will be listed on the Nasdaq stock market under the new ticker symbol "AKLI".

Diversifying the ways we can create value for shareholders adds stability to our anticipated growth trajectory and – as we have seen – feeds value back into the core enterprise centered on the Wholly Owned Programs. Those programs have substantial potential opportunities in major markets, while the risk profile of the portfolio is offset by our equity holdings, royalties and other payments from our Founded Entities. The resulting balance of opportunity and risk is rare in the biotherapeutics industry, and we are justifiably proud of the model.

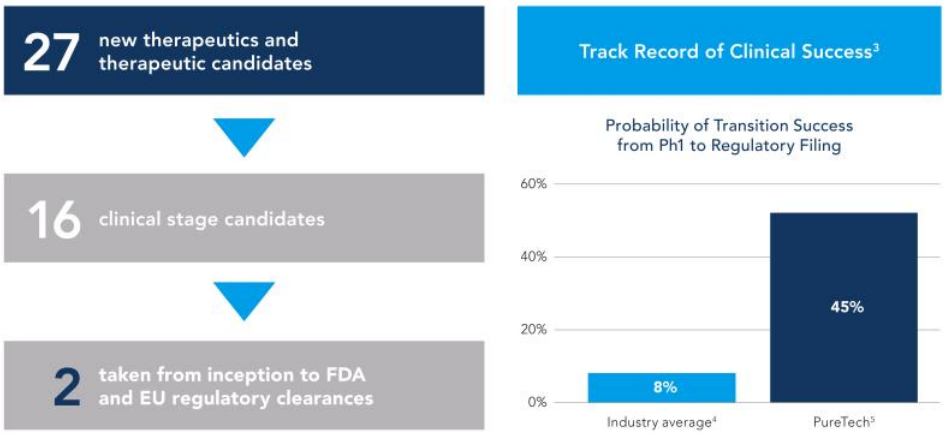
Overall, PureTech delivered substantial growth across the Founded Entities and Wholly Owned Pipeline in 2021. Sustaining this momentum over such an extensive range of projects does not happen without a significant unified effort, and I congratulate the hard work and dedication of the PureTech team and its broader network. It is deeply rewarding to work with such a seasoned Board of Directors and management team who translate the Board's guidance into operational excellence and strong partnerships. The grounding focus of our shared passion for helping people with devastating diseases is palpable in our work, and I am convinced it is integral to PureTech's culture and success.

Thank you to all of our shareholders for continuing to support our work for patients. After another year of PureTech evolving into an exemplar for a truly innovative pharmaceutical enterprise, I am humbled by the opportunity to be part of the team's journey and I look forward to continued success in 2022.

Christopher Viehbacher
Chair

April 25, 2022

PureTech's R&D Engine Has Delivered Results[2]



1 Please see footnote 11 on page 7 for Important Safety Information about Plenity®.

2 PureTech has established the underlying programs and platforms that have resulted in therapeutics and therapeutic candidates that are being advanced within our Wholly Owned Programs or by our Founded Entities. The numbers on this graphic reflects status of those therapeutics and therapeutic candidates as of the date of PureTech's most recently filed Annual Report on Form 20-F.

3 The cumulative percentages are calculated by multiplying the individual phase percentages listed in the following footnotes 4 & 5.

4 Industry average data measures the probability of clinical trial success of therapeutics by calculating the number of programs progressing to the next phase vs. the number progressing and suspended (Phase 1=52%, Phase 2=29%, Phase 3=58%). BIO, PharmaIntelligence, QLS (2021) Clinical Development Success Rates 2011 – 2020. This study did not include therapeutics regulated as devices.

5 The aggregate percentages include all therapeutic candidates advanced through at least Phase 1 by PureTech or its Founded Entities from 2009 onward, using the aforementioned calculation method based on the following individual phase percentages, Phase 1 (n = 6/8; 75%), Phase 2 (n = 10/11; 91%), Phase 3 (n = 2/3; 67%); Phase 2 and Phase 3 percentages include some therapeutic candidates where Phase 1 trials were not conducted by PureTech or its Founded Entities (i) due to the requirements of the medical device regulatory pathway or (ii) because a prior Phase 1 trial was conducted by a third party.

GIVING LIFE TO SCIENCE®

"PureTech is in an enviable position as we build on the momentum of our accomplishments in 2021. Our balance sheet, Founded Entities equity and royalty stakes, and Wholly Owned Programs put us in a stronger position than ever to build value in the current environment and deliver on our mission of bringing breakthrough medicines to patients."

Daphne Zohar,
Founder and Chief Executive Officer

Towards our goal of building value and delivering on our mission of bringing breakthrough medicines to patients, we continue to deliver on the growing value from the hub-and-spoke R&D model that PureTech pioneered for therapeutic development. For years, we developed in-house expertise and a global network of world-class advisors that informed the creation of our Founded Entities (the spokes). The success of several of our Founded Entities as they became independent and are advancing innovative new medicines validated our R&D model and established a strong track record which enables self-sustaining growth, as evidenced by their raising $1.9 billion in aggregate over the last few years. In addition, these Founded Entities are a source of capital to PureTech. To date, we have been able to generate over $560 million in non-dilutive cash while still maintaining strong equity positions. We anticipate further value to us from these entities through events such as M&A transactions or public listings with subsequent value accretion in addition to royalty and milestone payments from commercialized products such as KarXT or Plenity and product candidates in development. We are also structured to potentially receive sublicense revenues from pharma partnerships entered into with certain Founded Entities.

As our balance sheet and track record strengthened, we decided to maintain a group of Wholly Owned Programs to capture more of the value from our core capabilities of identifying and inventing novel medicines and taking them through proof-of-concept. The Wholly Owned Programs and our core areas of expertise around brain, immune and gastrointestinal systems, with a particular focus on immunological disorders, are the hub of our R&D model. In addition, we have consistently demonstrated our ability to harness validated biology and add important innovative steps that enable new medicines to advance. We have been building a differentiated, integrated biopharmaceutical company that develops its own wholly-owned therapeutics as well as benefits from the successes of the now-independent Founded Entities. This gives PureTech a diverse foundation for sustainable growth with a well-managed risk profile.

PureTech's history of building on validated biology has been woven into our strategic framework from our early days. For example, our Founded Entity Karuna's core technology improved upon a clinical compound by addressing tolerability issues and opening up new possibilities in an area of major need where therapeutic innovation has languished – schizophrenia and other serious psychiatric and neurological conditions. This is very similar to our approach to our Wholly Owned Program, LYT-100, in the way of its de-risked clinical profile with a new chemical entity. LYT-100 maintains the pharmacology of pirfenidone with a differentiated PK profile, enabling an improved tolerability profile. We were excited when LYT-100 demonstrated a comparable total exposure to pirfenidone based on PK modeling from prior studies, while improving on the GI-related AEs, as announced in the January 2022 post-period.

Each of our programs is highly innovative and has the potential to change the treatment paradigm for a number of serious diseases. In the same vein as Karuna and LYT-100, LYT-300 from our Glyph™ platform, LYT-510 and LYT-500 from our Alivio™ platform, and Orasome™ programs are reasonably de-risked given they are based on validated biology and pharmacology. We believe that focusing on validated biology therefore offers us an important strategic advantage and confidence as we invest in these programs. I am beyond excited about the progress of our Wholly Owned Programs, especially those that are now in human studies. Our other public Founded Entities, Gelesis and Vor Bio, also harnessed validated biology to create new opportunities for millions of patients as a result of our foundational input.

We are building our Wholly Owned Pipeline based on candidates that emerge from three potentially disruptive technology platforms as well as from thematic sourcing of programs externally.

Our proprietary technology platforms in lymphatics and inflammation are powerful tools for further enabling this strategy. Across our Alivio, Glyph and Orasome and other oral delivery technologies, we have a versatile toolkit for rapidly articulating entirely new target product profiles based on validated biology and pharmacology. An example is LYT-300, an oral allopregnanolone candidate emerging from the Glyph platform. Allopregnanolone is a natural neurosteroid that is approved to treat postpartum depression but is generally poorly orally bioavailable and has to be administered as a 60-hour intravenous infusion. Although efficacious, the intravenous formulation has limited its application. Applying our Glyph technology, we have developed an oral form of natural allopregnanolone (LYT-300) that we are currently evaluating in a first-in-human clinical study. Similarly, we have several molecules with clinically validated biology and pharmacology that we are evaluating

Milestones achieved in 2021

$418.9m PureTech Level Cash and Cash Equivalents as of December 31, 2021[1]

Proven track record of value creation, credibility and transparency

January

Vor Bio announced FDA clearance of IND application for VOR33

February

PureTech generated approximately **$118M** from Founded Entity equity sale[2]

Vor Bio completed **$203.4M** IPO

Karuna's Phase 2 EMERGENT-1 trial of KarXT in schizophrenia published in *NEJM*

PureTech's Glyph preclinical POC study published in *Journal of Controlled Release*

March

Akili's EndeavorRx® clinical study in pediatric ADHD published in *Nature Digital Medicine*

Karuna closed **$270.0M** follow-on public offering

April

Akili announced collaboration with Weill Cornell & Vanderbilt to evaluate AKL-T01 for COVID fog

PureTech's meningeal lymphatics research program published in *Nature*

May

Akili announced the closing of **$160M** Series D

PureTech formed Clinical Advisory Board for IPF and other PF-ILDs

June

PureTech acquired remaining interest in Founded Entity, Alivio Therapeutics

Karuna completed Phase 1b trial of KarXT in healthy volunteers

Vedanta announced presentation of new data from Phase 1 study of VE202 for treatment of IBD

July

Vedanta announced the closing of **$68M** Series D

Gelesis announced SPAC merger with Capstar Special Purpose Acquisition Corp.

Vor Bio announced its collaboration with Janssen Biotech to develop eHSC with a bi-specific antibody therapy for AML

Sonde announced collaboration with Qualcomm Technologies for vocal biomarker technology

PureTech announced clinical trial and supply agreement with BeiGene to evaluate LYT-200 and tislelizumab in solid tumors

August

PureTech appointed Dr. Julie Krop as Chief Medical Officer

Akili announced strategic licensing agreement with TALi

September

Akili announced completion of Shionogi Phase 2 study of SDT-001 in Japan

PureTech's Glyph technology platform published in *Nature Metabolism*

Vor Bio announced FDA granted fast track designation for VOR33

October

Sonde launched Sonde Mental Fitness

Vedanta announced topline Phase 2 data for VE303 and exercise of **$23.8M** option by BARDA

November

Gelesis received **$30M** Plenity® order from Ro

PureTech's LYT-100 Phase 1 results published in the journal *Clinical Pharmacology in Drug Development*

PureTech received orphan drug designation for LYT-200

PureTech generated approximately **$100M** from Founded Entity equity sale[3]

Karuna announced collaboration with Zai Lab for KarXT development, manufacturing, and commercialization of KarXT in Greater China

Gelesis' foundational biomimetic platform published in *Scientific Reports*

December

Gelesis' Plenity® became broadly available in the US

PureTech announced Phase 1 initiation of LYT-300

1 For more information in relation to the PureTech Level Cash and Cash Equivalents and Consolidated Cash and Cash Equivalents measures used in this Annual Report, please see pages 97 and 98 of the Financial Review.
2 Approximately $118 million in proceeds from the February 10, 2021 sale of 1 million Karuna common shares.
3 Approximately $100 million in proceeds from the November 9, 2021 sale of 750,000 Karuna common shares.

utilizing our Glyph, Alivio and Orasome and other oral delivery technologies to breathe new life into these molecules with a highly differentiated profile. We plan to advance one or more of these into clinical development under the Wholly Owned Pipeline.

In addition to the innovation engine of our platforms, we continually identify and seek access to external clinical-stage programs that are highly differentiated and complementary to the immune modulation focus of our Wholly Owned Pipeline.

Looking ahead, we believe our strategy and in-house capabilities strongly position us to build on the value through advancing innovative, differentiated medicines for patients.

The core of our business is advancing innovative medicines, and we believe 2022 will deliver significant growth on that front, with our internal pipeline expecting multiple clinical milestones, new registration-enabling studies, new programs and deepened platform validation.

In addition to research and development excellence, we are executing on a broader strategy to build shareholder value. This includes continuing to strengthen our balance sheet, implementing steps to address the disconnect we believe exists between our valuation and true value and supporting our Founded Entities in their growth and creation. We have also been considering various approaches to drive additional value for our shareholders, including through the implementation of a capital deployment strategy that balances investment in the continued growth of our business with potential returns of capital to shareholders.

Portfolio review

Across the key areas of pipeline development and clinical execution, PureTech continued to deliver. Highlights from the past year include:

Wholly Owned Pipeline

In 2021, our team was proud to welcome Dr. Julie Krop as Chief Medical Officer, who brings deep expertise in regulatory affairs, CMC and clinical development (both as a leader and as a board-certified physician) to oversee the significantly expanded Wholly Owned Pipeline.

- **LYT-100:** In the January 2022 post-period, we were excited to share a successful readout from a Phase 1 trial enrolling a healthy older adult population which demonstrated that 50% fewer subjects experienced GI-related AEs compared to those treated with the FDA-approved drug pirfenidone for IPF. We intend to advance a late-stage clinical program in IPF that will leverage a streamlined 505(b)(2) development path, with topline results from the dose-ranging study expected by the end of 2023. LYT-100 is a selectively deuterated form of pirfenidone that maintains the pharmacology of pirfenidone but has a highly differentiated PK profile that has translated into favorable tolerability, as demonstrated by data from multiple human clinical studies. We have assembled a stellar clinical advisory board of advisors for IPF and related lung disorders to help us advance LYT-100 into registration-enabling studies, and have appointed pulmonary drug development veteran, Paul Ford, M.D., Ph.D., as SVP of Clinical Development to provide additional internal expertise. LYT-100 is also being evaluated in a Phase 2 trial in Long COVID with results expected in the first half of 2022, and a Phase 2a trial in lymphedema with topline results expected in 2022. We are evaluating a range of additional fibrotic conditions for LYT-100, such as radiation induced fibrosis, myocardial fibrosis and other organ system fibrosis.
- **LYT-200/210:** LYT-200 is currently being evaluated as a single agent in the first stage of an adaptive Phase 1/2 trial and we expect to report topline results in the first half of 2022 from this study. Complementing this activity, we entered into a clinical trial and supply agreement with BeiGene to evaluate LYT-200 with BeiGene's tislelizumab, an anti-PD-1 immune checkpoint inhibitor, in patients with difficult-to-treat solid tumors. On the regulatory front, the FDA granted LYT-200 orphan drug designation for pancreatic cancer, which qualifies PureTech for incentives under the Orphan Drug Act, including tax credits for some clinical trials and eligibility for seven years of market exclusivity in the U.S. if the drug is approved. We believe the targeting of a foundational immunosuppressive protein, galectin-9, gives LYT-200 the potential to treat a range of cancers. This year we also presented new research at the American Association for Cancer Research (AACR) Annual Meeting demonstrating that our other fully human monoclonal antibody candidate for cancer, LYT-210, which is both highly specific and highly potent, rapidly inducing cell death of immunomodulatory gamma delta-1 T cells while sparing other T cells that play important roles in a healthy immune response.
- **LYT-300:** We initiated a first-in-human clinical trial of LYT-300, oral allopregnanolone, to evaluate its safety, tolerability and PK profile, as well as its impact on beta-EEG, a marker of $GABA_A$ target engagement, potentially providing early insights into its mechanism. We also presented preclinical proof-of-concept data at the American College of Neuropsychopharmacology (ACNP) Annual Meeting showing that systemic exposure of natural allopregnanolone was achieved after oral administration of LYT-300 in multiple preclinical models. Results from the Phase 1 trial are expected in the second half of 2022 and will be used to inform the design of possible future studies evaluating LYT-300 in indications that could include depression, anxiety, sleep disorders, fragile X tremor-associated syndrome, essential tremor and epileptic disorders, among others.

- On top of the progress of LYT-300 (developed using the Glyph platform), preclinical proof-of-concept work was published in *Nature Metabolism* and the *Journal of Controlled Release* supporting the Glyph technology platform's ability to employ the body's natural lipid absorption and transport process to send oral drugs into the lymphatic system.
- **LYT-510:** LYT-510 is an oral inflammation-targeting formulation of tacrolimus, a potent immunosuppressant drug, in development to treat IBD and chronic pouchitis. In multiple preclinical IBD models, LYT-510 showed significant improvements in several efficacy endpoints compared to untreated controls. Furthermore, the inflammation-targeting properties were shown to result in very low systemic blood levels compared to the current immunosuppressant formulations, which minimizes the potential for systemic side effects. We intend to file for regulatory approval to initiate first-in-human studies at year end 2022 and initiate a clinical study evaluating LYT-510 as a single agent for the potential treatment of IBD and chronic pouchitis in early 2023.
- **LYT-500:** We identified this candidate as a potential therapy for IBD and progressed preclinical evaluation. LYT-500 uses the Alivio platform to combine two active agents (IL-22 and an immunosuppressant drug) into a single therapeutic candidate for IBD that is designed to enhance the treatment of inflamed tissues while having the potential to minimally impact the rest of the body. Proof-of-concept data are expected in the first half of 2022. In addition to the progress of LYT-510 and LYT-500 (developed using the Alivio platform), we are evaluating other potential therapeutic candidates leveraging Alivio to selectively restore immune homeostasis at inflamed sites in the body, while minimalizing impact on the rest of the immune system.
- **LYT-503/IMB-150:** This non-opioid pain candidate being developed as a partnered program for the potential treatment of IC/BPS is expected to be filed for an IND application in 2022.
- **Orasome platform and other technologies for oral administration of biologics:** We have established preclinical proof-of-concept supporting the platform's potential to achieve therapeutic levels of proteins in circulation following oral administration of therapeutic protein expression systems. We intend to generate additional preclinical data in 2022 exploring the potential of Orasomes and other technologies, for a wide array of novel therapeutic protein-based applications.
- **Meningeal lymphatics research program:** We published preclinical research in *Nature* supporting the hypothesis that restoring lymphatic flow in the brain has the potential to address a range of neurodegenerative diseases, such as Alzheimer's and Parkinson's diseases and associated neuroinflammation.

Founded Entities

- **Karuna Therapeutics (Nasdaq: KRTX):** Announced that all four Phase 3 trials in their EMERGENT program, evaluating KarXT for the treatment of psychosis in adults with schizophrenia, are enrolling. They also initiated their Phase 3 ARISE trial of KarXT for the treatment of schizophrenia in adults who experience an inadequate response to current standard of care. Additional clinical milestones include data from Karuna's completed Phase 1b trial of KarXT in healthy elderly volunteers, which Karuna intends to support a Phase 3 program evaluating KarXT for the treatment of psychosis in Alzheimer's disease, initiating in mid-2022. Earlier in 2021, results from the Phase 2 EMERGENT-1 trial evaluating KarXT for the treatment of schizophrenia were published in NEJM. Finally, Karuna announced entry into an exclusive license agreement with Zai Lab for the development, manufacturing and commercialization of KarXT in Greater China, including mainland China, Hong Kong, Macau and Taiwan. Karuna received a $35.0 million upfront payment and is eligible to receive certain development and regulatory milestone and sales milestone payments, as well as royalties based on annual net sales of KarXT in Greater China.
- **Akili:** Delivered strong progress on multiple fronts, including taking a step towards becoming a publicly-traded company. In the January 2022 post-period, Akili entered into a definitive agreement to become publicly traded via a merger with Social Capital Suvretta Holdings Corp. I (Nasdaq: DNAA), a special purpose acquisition company. With a fully committed PIPE of $162 million, transaction is expected to close in mid-2022, after which Akili will be listed on the Nasdaq stock market under the new ticker symbol "AKLI". Akili previously completed a $160 million financing, a new licensing agreement with Australian digital health company, TALi®, and the launch of new gaming features and functionalities for its FDA and European marketing-authorized video game treatment, EndeavorRx®, designed for children with attention deficit hyperactivity disorder (ADHD). Additionally, Akili initiated pilot studies of AKL-T01 for COVID brain fog in collaboration with Weill Cornell Medicine, New York Presbyterian Hospital and Vanderbilt University Medical Center. Akili also published data in *Nature Digital Medicine* from their STARS Adjunct study of EndeavorRx and announced positive results from Japanese partner Shionogi's Phase 2 ADHD study of SDT-001.

- **Gelesis (NYSE: GLS):** Made broad commercialization-focused progress in the U.S. toward the launch of Plenity®, an FDA-cleared weight management approach, for adults meeting prescription criteria. In the January 2022 post-period, Gelesis debuted as a public company following a business combination with Capstar Special Purpose Acquisition Corp., raising approximately $105 million in gross proceeds to support Plenity's launch. Also in the January 2022 post-period, Gelesis launched the "Who Said?" multichannel marketing campaign across the U.S., which challenges many long-held cultural and societal assumptions around weight loss. Other achievements include completing and validating its first commercial-scale manufacturing line, the successful LIGHT-UP study of GS200 in adults who are overweight or obese who also have prediabetes or type 2 diabetes and receipt of $40 million fully paid pre-orders for Plenity® from leading U.S. direct-to-patient healthcare company Ro. Finally, leading nutrition authority, Joy Bauer, MS, RDN, CDN, was appointed Chief Nutrition Officer of Plenity.
- **Vor Bio (Nasdaq: VOR):** Initiated VBP101, a Phase 1/2a clinical trial for VOR33, its eHSC therapy candidate for acute myeloid leukemia, an indication for which FDA granted Fast Track designation. Vor Bio also completed its initial public offering on Nasdaq under the ticker symbol "VOR", with gross proceeds of over $200 million. Additionally, Vor Bio entered into a collaboration with Janssen Biotech to investigate the combination of Vor Bio's "invisible" eHSC transplant platform with one of Janssen's bi-specific antibodies in development for AML.
- **Vedanta Biosciences:** Successfully completed its most advanced clinical study to date, achieving its primary endpoint in a Phase 2 clinical trial of VE303 for the prevention of recurrent CDI in high-risk patients. This triggered the exercise of a $23.8 million option by program partner, the U.S. Biomedical Advanced Research and Development Authority (BARDA), to support a Phase 3 clinical trial of VE303. Vedanta also completed a $68 million financing, including a $25 million investment from Pfizer as part of the Pfizer Breakthrough Growth Initiative.
- **Follica:** Appointed two leaders in aesthetic medicine and dermatology to its Board of Directors. Tom Wiggans, former Chief Executive Officer of Dermira, joined as Executive Chairman with over 30 years of experience leading biopharmaceutical companies from the start-up stage to global commercialization, and Michael Davin, former Chief Executive Officer of Cynosure, joined as an Independent Director with over 30 years of experience in the medical device industry.
- **Sonde:** Launched Sonde Mental Fitness, a voice-enabled mental health detection and monitoring technology that uses a brief voice journal entry to evaluate mental well-being, expanding Sonde beyond respiratory health. This news followed Sonde's collaboration announcement with leading chipmaker, Qualcomm Technologies, to embed Sonde's vocal biomarker technology on the flagship and high-tier Qualcomm® Snapdragon™ mobile platforms. This is intended to help bring native, machine learning-driven vocal biomarker capabilities to mobile and IoT devices globally.
- **Entrega:** Entrega's platform for the oral administration of biologics has continued development including via a partnership with Eli Lilly regarding certain Lilly therapeutic candidates.

We are well-positioned for a new stage of PureTech's development. In the year ahead, our anticipated catalysts continue to grow in scope and maturity, with two commercial entities – Gelesis and Akili – aiming to build launch momentum in addition to a wide range of clinical readouts and clinical pipeline expansion across the broader portfolio.

As always, I am proud of the breadth of activity and momentum PureTech sustains across our deep pipeline & portfolio, and am very grateful for the continued efforts, passion and counsel of our team, our R&D Committee and broader advisory network, as well as our Board and investors. Thank you to all. I am encouraged by the entrepreneurial spirit that is infused in our work and the mission that unites us in striving to bring powerful new medicines to patients.

To the patients and physicians taking part in our clinical trials: Thank you for your sacrifices and your trust in us as we work towards dramatically improving treatment for the conditions that impact your lives and the lives of many others. Advancing medicine is a shared project and we are privileged to partner with you in shaping its future.

Daphne Zohar
Founder, Chief Executive Officer and Director

April 25, 2022

Letter from the Chief Scientific Officer, Chief Medical Officer and Chief Innovation and Strategy Officer

"A year of advances in every aspect of PureTech R&D."

Joseph Bolen, Ph.D.,
Chief Scientific Officer

Julie Krop, M.D.,
Chief Medical Officer

Eric Elenko, Ph.D.,
Chief Innovation and Strategy Officer

2021 was a year of growth for PureTech's internal R&D as we significantly expanded our clinical activity across our Wholly Owned Pipeline while also delivering substantial research advances for our platform technologies. Our R&D strategy continues to support our overarching corporate focus on building a differentiated, integrated biopharmaceutical company focused on developing new therapies for underserved and often devastating diseases with limited or no options available for patients. Our unique innovative research engine is designed to produce new medicines that can be rapidly advanced into the clinic with our experienced fully integrated clinical, regulatory and manufacturing expertise.

Our research process begins by identifying therapeutic products for serious diseases that have a well-established human efficacy, but their usage is significantly limited by challenges, such as poor safety, tolerability, oral bioavailability or dosing.

Second, we apply our innovative research and development expertise and proprietary platform technologies, to these products to generate a novel therapeutic candidate that addresses one or more of the key underlying limitations and potentially unlock the full therapeutic effectiveness of the therapy.

The essential ingredient in our program selection is typically oriented around providing key benefits to the patients, such as substantially improving the tolerability profile of existing therapies that had previously demonstrated robust efficacy or through targeting of existing therapies to certain cells, such as the immune cells and sites of disease, such as inflammation, in order to improve efficacy while reducing systemic side effects.

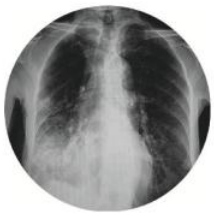
This strategy has helped us provide a solid foundation for PureTech's long-term growth. In addition to the success of our Founded Entity programs, we've also made tremendous strides with our Wholly Owned Pipeline, which is built on three potentially disruptive technology platforms in addition to external programs thematically identified to align with our immune modulation focus. We currently have seven therapeutic candidates in our Wholly Owned Pipeline including one that is being advanced as a partnered program. In 2021, we advanced three clinical-stage wholly-owned therapeutic candidates that have the potential to treat a range of indications including serious lung conditions, solid tumors lymphatic flow disorders and neurological indications. Additionally, we saw continued validation of our lymphatic and inflammation-focused technology platforms, including the advancement of a therapeutic candidate from one of these platforms into human studies and the achievement of preclinical proof-of-concept from another. The highlights of our extensive progress across the portfolio are summarized below:

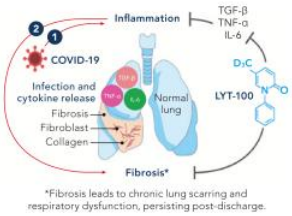
Multi-pronged progress for LYT-100 across a range of indications

LYT-100 (deupirfenidone) is our most advanced wholly-owned therapeutic candidate. It is a selectively deuterated form of pirfenidone, a drug that is approved for treating IPF, a serious and progressive lung disease. Based on prior work with pirfenidone, a substantial amount of preclinical and clinical data support LYT-100's broader potential in inflammatory and fibrotic conditions. These include lung disease (IPF and other respiratory conditions), and disorders of lymphatic flow, such as lymphedema. We are also exploring the potential evaluation of LYT-100 in radiation induced fibrosis, myocardial fibrosis and other organ system fibrosis. Due to LYT-100's broad potential across a range of fibrotic and inflammatory diseases, we expect LYT-100 to have a "pipeline within a product" opportunity which enables rapid clinical development in multiple indications, and so our clinical development strategy has focused on a comprehensive analysis of the potential applicability of

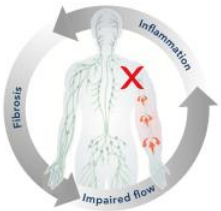
LYT-100 development plan overview

LYT-100-ILD	LYT-100-COV	LYT-100-LYMPH
Initiating registration-enabling studies in IPF in 1H 2022	Topline results expected from Phase 2 in Long COVID[1] in 1H 2022	Topline results expected from Phase 2a POC in lymphedema in 2022





*Fibrosis leads to chronic lung scarring and respiratory dysfunction, persisting post-discharge.



LYT-100 in areas of greatest unmet medical need that map against its known validated biological effects.

Although pirfenidone is one of the standard of care medicines for IPF and has demonstrated efficacy against this progressive, fatal disease, its usage has been greatly limited by the drug's severe tolerability issues – especially with regards to GI side-effects. Approximately half of the IPF patients that start therapy with pirfenidone either discontinue therapy, reduce their dose or switch to other therapies, all of which lead to suboptimal disease management. These issues pushed our team to establish a goal: To demonstrate a favorable tolerability profile of LYT-100 that could improve compliance and potentially lead to improved disease outcomes.

LYT-100's deuterium modification improves the metabolic stability of the molecule and enables its administration at a dosage that can achieve the same level of drug exposure as pirfenidone, but with a lower maximal drug concentration (Cmax). High Cmax is often associated with AEs, therefore by reducing the Cmax while maintaining the comparable exposure to pirfenidone, LYT-100 has the potential to allow the patient to stay on the therapy longer to potentially achieve an optimal therapeutic outcome.

To date, our clinical studies strongly support a substantial tolerability advantage of LYT-100 over pirfenidone. Our study enrolling healthy older adults showed an approximate 50% reduction in the number of healthy older adults treated with LYT-100 that experienced GI-related AEs relative to those treated with pirfenidone. Additionally, our multiple ascending dose study and our healthy older adults crossover study demonstrated that LYT-100 was well-tolerated at all doses studied and that all treatment-related AEs were mild and transient. Results of the Phase 1 multiple ascending dose and food effect study were presented at the virtual European Respiratory Society International Congress and published in the journal *Clinical Pharmacology in Drug Development*.

We attribute this improved tolerability to LYT-100's substantially differentiated PK properties that reduce AEs while preserving exposure and pharmacology. These results are extremely encouraging, and we are advancing LYT-100 into further clinical development for IPF.

Last year, we initiated a LYT-100 Phase 2 clinical study focused on patients who suffer from Long COVID respiratory complications. Since then, the pandemic has affected more than 500 million people around the world. Over 40% of hospitalized COVID-19 patients have lasting dyspnea and up to 33% of severe COVID-19 patients develop lung fibrosis. In the last 12 months, we've progressed the Phase 2 clinical trial of LYT-100 in patients who suffer from Long COVID respiratory complications and related sequelae, and we anticipate topline results in the first half of 2022.

We've also progressed LYT-100 in a Phase 2a proof-of-concept trial in patients with breast cancer-related, upper limb, secondary lymphedema. There are no approved treatments for lymphedema and we believe leveraging our unique insights into the lymphatic system and immunology can provide a role for deupirfenidone to make an impact for patients living with severe unmet medical need with this condition. Our preclinical work supports this hypothesis. In fact, in those studies, LYT-100 showed greater anti-fibrotic and anti-inflammatory activity when compared to pirfenidone. Results from the Phase 2a study are anticipated in 2022.

Anti-cancer programs: LYT-200 targeting galectin-9 and LYT-210 targeting gamma delta-1 T cells

Our anti-cancer programs target emerging, foundational immunosuppressive mechanisms to pursue a differentiated approach to cancer types that currently do not have adequate effective treatments. We see potential for PureTech as a leader against these targets, with both our fully human monoclonal antibody candidates having potential both as single agents and in combination with existing therapies such as checkpoint inhibitors and chemotherapeutics.

We are developing LYT-200 for solid tumors with currently poor survival rates. In 2021, the FDA granted LYT-200 orphan drug designation for the treatment of pancreatic cancer, which qualifies PureTech for incentives under the Orphan Drug Act, including tax credits for some clinical trials and eligibility for seven years of market exclusivity in the U.S. if the drug is approved, in addition to our broad intellectual property coverage which can extend the exclusivity into 2038.

1 Long COVID is a term being used to describe the emerging and persistent complications following the resolution of COVID-19 infection, also known as post-acute COVID-19 syndrome (PACS).

The ongoing Phase 1 portion of its adaptive Phase 1/2 study in solid tumors continues to progress, with a maximum tolerated dose not yet reached, and is expected to read out in the first half of 2022.

In 2021 we also began a clinical relationship with BeiGene to evaluate LYT-200 together with tislelizumab, an anti-PD-1 immune checkpoint inhibitor, in patients with solid tumors. LYT-200 is being evaluated as a single agent in the first phase of the adaptive Phase 1/2 study, which, pending the results, is then designed to investigate LYT-200 in combination with tislelizumab. While we believe that LYT-200 has the potential to have activity on its own, its mechanism for targeting immunosuppression may also lead to increased efficacy when combined with other cancer immunotherapies, such as checkpoint inhibitors or chemotherapeutic drugs, depending on the cancer.

For LYT-210, we presented promising preclinical data at the eminent American Association for Cancer Research (AACR) Annual Meeting. That research demonstrated that LYT-210 is both very specific and exceptionally potent, rapidly inducing cell death of immunomodulatory gamma delta-1 T cells, while sparing other T cells, such as cytotoxic gamma delta T cells, that play important roles in a healthy immune response. Gamma delta T cells are an increasingly well recognized approach for tackling difficult-to-treat cancers.

LYT-300: Harnessing lymphatic targeting through our Glyph™ platform

We were thrilled to initiate first-in-human clinical studies of LYT-300 (oral allopregnanolone) in December 2021. LYT-300 is the first candidate from the Glyph technology platform to enter the clinic, leveraging the platform's ability to enable direct delivery of an oral drug to the lymphatic system.

Given the research supporting the broad potential neurological and neuropsychological effects of allopregnanolone, LYT-300 is being evaluated for the potential treatment of a variety of conditions. The Phase 1 study evaluates multiple aspects of safety, tolerability and PK, and topline results are expected in the second half of 2022.

In early 2021, we presented preclinical proof-of-concept data for LYT-300 at the American College of Neuropsychopharmacology (ACNP) Annual Meeting.

As we advance LYT-300, we see its maturing data set as also being supportive of our Glyph technology platform. The Glyph technology enables us to generate novel prodrugs by reversibly linking small molecule drugs to dietary fat molecules. This linkage is designed to enable the transport of the small molecules directly into systemic circulation via the lymphatic system following oral administration, thereby bypassing first-pass liver metabolism.

We believe our Glyph platform could similarly enhance the potential of natural biologically active molecules or existing therapies that had previously demonstrated robust efficacy but could not be administered orally, by unlocking oral administration including natural neurosteroids or immune modulators that could directly target the mesenteric lymph nodes. Furthermore, preclinical proof-of-concept studies were published in the *Journal of Controlled Release* and *Nature Metabolism* that support the Glyph platform's ability to directly target the lymphatic system.

LYT-510, LYT-500, LYT-503/IMB-150: The integration of Alivio™

In 2021, we completed the acquisition of Alivio Therapeutics and the integration of its targeted anti-inflammatory platform technology and candidates into our Wholly Owned Pipeline. LYT-510, in development for the treatment of IBD and chronic pouchitis, is an oral inflammation-targeting formulation of tacrolimus. Tacrolimus is a potent immunosuppressant drug approved for certain indications, however its approval for IBD and chronic pouchitis has been hampered by systemic toxicities, narrow therapeutic window of activity and opportunistic infections that can arise from systemic immunosuppression. There is clinical data demonstrating that tacrolimus is effective in addressing IBD indications, but AEs have held it back. We believe that LYT-510 can overcome these clinical challenges with targeted drug delivery to the intestines, with the potential to be the first tacrolimus treatment approved for IBD in the U.S. We intend to file for regulatory approval to initiate first-in-human studies at year end 2022 and initiate a clinical study evaluating LYT-510 as a single agent for the potential treatment of IBD and chronic pouchitis in early 2023. LYT-500, an oral therapeutic candidate in development for the potential treatment of mucosal barrier damage in people with IBD, includes two orally dosed active agents (IL-22 and an immunosuppressant drug) designed to selectively act at inflamed intestinal tissues while reducing their impact on normal tissue. We expect preclinical proof-of-concept data for LYT-500 in the first half of 2022. We believe the targeted activation and oral formulation offered by Alivio offers a path to unlocking the full therapeutic potential of tacrolimus and other anti-inflammatory drugs in a way that matches the chronic, variable expression of autoimmune diseases.

The Alivio integration also includes the addition of therapeutic candidate, LYT-503/IMB-150, to our Wholly Owned Pipeline. It is being developed as a partnered program as a potential non-opioid treatment for interstitial cystitis or bladder pain syndrome (IC/BPS). An IND application is expected to be filed for LYT-503/IMB-150 in 2022.

Progressing the Orasome™ platform and other oral delivery technologies, and Meningeal Lymphatics Research Program

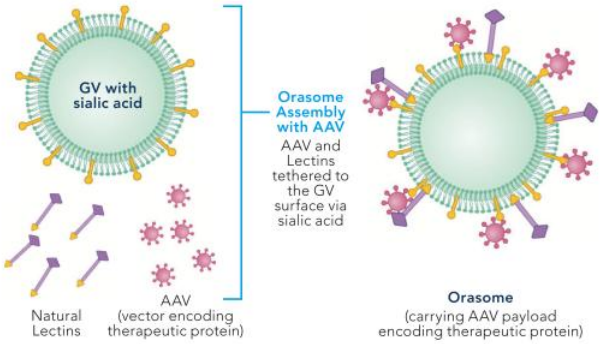
In addition to Glyph and Alivio, we are also making strides with the oral administration of biologics, such as the Orasome platform, and meningeal lymphatics research program. Each of these possesses a huge breadth of potential applications that could offer our pipeline many developmental options as they mature.

In 2021, the Orasome platform achieved preclinical proof-of-concept of its core concept: This technology is designed to promote following oral administration of an expression system, intestinal tract cells to produce virtually any type of therapeutic protein, including monoclonal antibodies, "on command" with transport to the circulatory system. We recently demonstrated in a preclinical model that administration of Orasomes carrying an expression system for a therapeutic protein, to the GI tract of a rodent led to therapeutic protein detection in systemic circulation.

This is a big idea – if we are successful, a patient could swallow a pill and have the body make its own therapeutic protein. We intend to generate additional preclinical data for Orasome and other technologies in 2022.

For our meningeal lymphatics research program, we and our collaborators published notable preclinical work in *Nature* suggesting that restoring lymphatic flow in the brain has the potential to address a range of neurodegenerative diseases, such as Alzheimer's and Parkinson's diseases and associated neuroinflammation. The research also uncovered a link between dysfunctional meningeal lymphatics and damaging microglia activation in Alzheimer's disease, suggesting another route by which restoring healthy (lymphatic) drainage could improve clinical outcomes.

Orasome Construct for oral administration of Therapeutic Proteins



AAV = Adeno Associated Virus; GV = Glycocalyx Vesicles

PureTech advantages: strategy, people and passion

With many teams in the industry advancing single platform technologies, internally we are energized by the opportunity to be advancing a portfolio of programs across multiple promising approaches. They are built on leading research from our scientific collaborators and provide important innovative approaches that leverage validated biology and pharmacology to reduce technology and development risk. This is a key part of our R&D strategy, and we believe we realize synergies from their parallel internal development that potentially enable new medicines to advance.

Our approach gives PureTech multiple opportunities for success and we're proud of our track record, having now generated 27 therapeutics and therapeutic candidates, of which 16 are clinical stage and two have gone from inception through successful FDA and EU regulatory clearances for marketing.

To reach this point, we have collaborated with the world's leading domain experts on disease-specific discovery themes, particularly to leverage our expertise in immunology. All of our Wholly Owned Programs are building upon validated biologic pathways and proven pharmacology of known therapeutics while applying important innovation that enable new medicines to advance. We have proven our ability to utilize cross-disciplinary research and discovery efforts across multiple indications and potential therapeutic area thanks to a team of esteemed collaborators and co-inventors.

We are very proud of our work to advance our Wholly Owned Programs in 2021. Our focus on unmet medical needs in devastating diseases is a clear guiding principle that we believe brings out the best of our team and collaborators – we extend our warmest thanks to both for their efforts and counsel. We are in a transformative phase for PureTech and look forward to sharing our progress with you soon.

Dr. Joseph Bolen
Chief Scientific Officer

Dr. Julie Krop
Chief Medical Officer

Dr. Eric Elenko
Chief Innovation and Strategy Officer

April 25, 2022

How PureTech is building value for investors

"In light of the strong foundation we have built for PureTech's future growth, the Board and senior leadership team are considering various approaches to drive additional value to our shareholders. We are reviewing a capital allocation strategy that will see us prioritize funding the continued development and expansion of our Wholly Owned Pipeline and strategic investment in our Founded Entities in accordance with our strategic plan while we will also look to return certain proceeds we may receive in the future to shareholders through various distribution mechanisms, including share buybacks or special dividends."

We are a clinical-stage biotherapeutics company dedicated to discovering, developing and commercializing highly differentiated medicines for devastating diseases where limited or no treatment options currently exist for patients. We do this by building upon underlying mechanisms from well-established science that have been validated in clinical testing, while applying innovative insight or technology that generates new medicines that can unleash the full potential of the therapeutic. All the activity within our Wholly Owned Pipeline and the foundational activities at our Founded Entities were initiated by our experienced research and development team and our extensive network of scientists, clinicians and industry leaders. We are led by a proven and seasoned management team with significant experience in discovering and developing important new medicines, delivering them to market and maximizing shareholder value. Collectively, the members of our management team have overseen research and development of therapeutics supporting 26 regulatory approvals and have served in the C-suite of companies acquired for more than $14 billion in the aggregate.

Our model leverages collaboration with the world's leading experts in specific diseases, bringing together cross-disciplinary perspectives on new treatment opportunities. We combine these insights with our research and development expertise and proprietary platform technologies to generate novel therapeutic candidates that often are aimed at addressing key limitations with existing treatments that have limited their broad application or adoption. In addition to building on validated biology and clinical pharmacology, we further de-risk programs with key experiments at an early stage to validate the underlying value proposition. This model has enabled our consistent early access to scientific breakthroughs before their peer-reviewed publication and gives us an edge in advancing innovative and substantially differentiated treatment approaches for a range of indications including inflammatory, fibrotic and immunological conditions, intractable cancers, lymphatic and gastrointestinal diseases and neurological and neuropsychological disorders, among others.

Across the entire portfolio, we established the underlying programs and platforms that have resulted in 27 therapeutics and therapeutic candidates that are being advanced within our Wholly Owned Programs or by our Founded Entities. Of these therapeutics and therapeutic candidates, 16 are clinical-stage and two have been cleared for marketing by the FDA and granted marketing authorization in the European Economic Area, or EEA, and in other countries that recognize the CE Mark. Our publicly-listed Founded Entities, Karuna, Vor and Gelesis, are advancing seven of these therapeutic candidates, including two that are currently in Phase 3/Pivotal studies, as well as one FDA-cleared therapeutic. Our privately-held Founded Entities, Akili, Vedanta, Follica, Sonde and Entrega, are advancing 13 other therapeutic candidates, including two that are expected to enter a Phase 3 study. Finally, we are advancing seven therapeutic candidates within our Wholly Owned Pipeline, including one therapeutic candidate that is being as a partnered program, with two Phase 2 and two Phase 1 clinical trials underway. We and our Founded Entities have relationships with several pharmaceutical companies or their investment arms to advance some of the programs and platforms underlying these therapeutics and therapeutic candidates.

This diverse portfolio is a natural result of the innovative R&D model we pioneered for therapeutic development. It adds stability to our anticipated growth trajectory and feeds value back into the core enterprise centered on the Wholly Owned Programs. The basis for our high growth strategy is to build a differentiated, integrated biopharmaceutical company that develops its own therapeutics while also benefiting from the successes of the now-independent Founded Entities. This provides PureTech with a strong foundation for sustainable growth with a well-managed risk profile that helps drive new opportunities for patients as well as shareholder value.

Components of our Value

The table to the right depicts the four components of our value: **(1)** our Wholly Owned Programs, **(2)** Founded Entities, **(3)** our available cash, cash equivalents and short-term investments at the PureTech level and **(4)** our return of capital to shareholders.

We hold majority voting control of or otherwise retain significant influence over our Controlled Founded Entities and continue to play a role in the development of their therapeutic candidates through representation on their boards of directors. Our board designees represent a majority of the members of the board of directors of Follica and Vedanta and a minority of the members of the board of directors of Sonde and Entrega. With respect to our Non-Controlled Founded Entities, we do not hold majority equity ownership and are not responsible for the development or commercialization of their therapeutic candidates and therapeutics. Our Non-Controlled Founded Entities have independent management teams, and we do not control the day-to-day development of their respective therapeutic candidates.

1. **Our Wholly Owned Programs.** We are focused on the advancement of our Wholly Owned Programs and delivering value to our shareholders by driving our Wholly Owned Programs to key clinical and commercial milestones, while continuing cutting-edge research and development efforts to discover and advance new therapeutic candidates. The table to the right includes a summary of our Wholly Owned Programs and their development status.
2. **Our Founded Entities[1].** The table to the right summarizes the therapeutic candidates being developed by our Founded Entities in order of our equity value. We established the underlying programs and platforms that have resulted in the therapeutic candidates noted in the table, each of which targets indications related to one or more of the brain, immune and gastrointestinal systems, and advanced them through key validation points. In certain cases, our interest in the therapeutic candidates of these entities is limited to the potential appreciation of our equity interest in these entities. In other cases, we have an equity interest in these entities and the right to receive royalty payments on product sales and/or sublicense revenues. Any value we realize from these therapeutic candidates will be through the potential growth and realization of equity and royalty stakes, including sublicense payments from pharma partnerships entered into with certain Founded Entities.
3. **Cash and Cash Equivalents.** We had PureTech Level Cash and Cash Equivalents of $418.9 million as of December 31, 2021[2].
4. **Our Return of Capital to Shareholders.** In light of the strong foundation we have built for PureTech's future growth, the Board and senior leadership team are considering various approaches to drive additional value to our shareholders. We are reviewing a capital allocation strategy that will see us prioritize funding the continued development and expansion of our Wholly Owned Pipeline and strategic investment in our Founded Entities in accordance with our strategic plan while we will also look to return certain proceeds we may receive in the future to shareholders through various distribution mechanisms, including share buybacks or special dividends.

1 While PureTech maintains ownership of equity interests in its Founded Entities, the Company does not, in all cases, maintain control over these entities (by virtue of (i) majority voting control and (ii) the right to elect representation to the entities' boards of directors) or direct the management and development efforts for these entities. Consequently, not all such entities are consolidated in the Company's financial statements.

2 For more information in relation to the PureTech Level Cash and Cash Equivalents and Consolidated Cash and Cash Equivalents measures used in this Annual Report, please see pages 97 and 98 of the Financial Review.

3 The FDA and corresponding regulatory authorities will ultimately review our clinical results and determine whether our wholly-owned therapeutic candidates are safe and effective. No regulatory agency has made any such determination that our wholly-owned therapeutic candidates are safe or effective for use by the general public for any indication. On July 23, 2021, Imbrium Therapeutics exercised its option to license LYT-503/IMB-150 pursuant to which it is responsible for all future development activities and funding for LYT-503/IMB-150.

4 Long COVID is a term being used to describe the emerging and persistent complications following the resolution of COVID-19 infection, also known as post-acute COVID-19 syndrome (PACS).

5 Relevant ownership interests and references to equity ownership for Founded Entities contained in this strategic report (pages 2-72) were calculated on a partially diluted basis (as opposed to a voting basis) as of December 31, 2021, including outstanding shares, options and warrants, but excluding unallocated shares authorized to be issued pursuant to equity incentive plans. Vor, Karuna and Gelesis ownerships were calculated on a beneficial ownership basis in accordance with SEC rules as of March 4, 2022 and February 15, 2022 and March 31, 2022, respectively.

6 With the exception of Plenity® and EndeavorRx®, candidates are investigational and have not been cleared by the FDA for use in the U.S.

7 PureTech has a right to royalty payments, including sublicense payments, as a percentage of net sales.

8 Please see footnote 10 on page 6 for EndeavorRx® indication and overview.

9 These therapeutic candidates are regulated as devices and their development has been approximately equated to phases of clinical development.

10 Please see footnote 11 on page 7 for Important Safety Information about Plenity®.

1 Wholly Owned Programs

Our Programs[3]	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
LYT-100-ILD Deupirfenidone	IPF				
LYT-100-COV Deupirfenidone	Long COVID[4] respiratory complications and related sequelae				
LYT-100-LYMPH Deupirfenidone	Lymphatic flow disorders, including lymphedema				
LYT-200 Anti-Galectin-9 mAb	Solid tumors				
LYT-210 Anti-Delta-1 mAb	Solid tumors				
LYT-300 Oral Allopregnanolone	Neurological and neuropsychological conditions				
LYT-510 Oral Immunosuppressant	IBD/chronic pouchitis				
LYT-500 Oral IL-22 + Immunosuppressant	IBD				
LYT-503/IMB-150 (Partnered program) Non-opioid	IC/BPS				

Registration-enabling studies to begin in 1H2022 | Phase in progress | Phase completed

Lymphatic and Inflammation Platforms

- Glyph™ Technology Platform (Lymphatic Targeting)
- Orasome™ and Other Technology Platforms (Oral Biotherapeutics)
- Alivio™ Technology Platform (Inflammation Targeting)
- Meningeal Lymphatics Research Program

2 Founded Entities

Founded Entity	PureTech Ownership[5]	Therapeutic Candidate[6]		Indication	Stage of Development	Royalties[7]
KARUNA	5.6%	KarXT	P	Schizophrenia Alzheimer's disease psychosis	Phase 3 Phase 3 Ready	Royalties
AKILI	22.3%	Akili is pioneering the development of cognitive treatments through game-changing technologies. EndeavorRx[8][8] (formerly known as AKL-T01) is the first FDA cleared and CE marked video game treatment. In the U.S., EndeavorRx is indicated to improve attention function as measured by computer-based testing in children ages 8-12 years old with primarily inattentive or combined-type ADHD, who have a demonstrated attention issue.				
GELESIS	23.5%	Plenity[9,10] Plenity® for adolescents[9] GS200[9] GS300[9] GS500[9]	D D D D D	Weight management Adolescent weight management Weight management in T2D/prediabetes NASH/NAFLD Functional constipation	Commercial Pending Discussion with FDA Clinical Trial Complete Clinical Pivotal	Royalties
VOR	8.6%	VOR33 (CD33) VCAR33	B B	Acute myeloid leukemia Myelodysplastic syndromes, myeloproliferative neoplasms Bridge-to-transplant AML	Phase 1/2a Preclinical Phase 1/2	N/A
VEDANTA	41.4%	VE303 VE202 VE416 VE800 VE707	B B B B B	*C. difficile* IBD Food allergy Solid tumors Gram-negative infections	Phase 3 Ready Phase 2 Ready Phase 1/2 Phase 1 Preclinical	N/A
follica	76.0%	FOL-004	P/D	Androgenetic alopecia	Phase 3 Ready	Royalties
SONDE	44.6%	Sonde One for Respiratory[9] Sonde Mental Fitness[9]	D D	Respiratory risk detection and monitoring app Monitoring vocal features linked to depression, anxiety, and cognition	Commercial Release Commercial Release	N/A
entrega	74.3%	ENT-100	B	Oral delivery of biologics, vaccines and other drugs	Preclinical	N/A

The letters next to the therapeutic candidates denote whether the therapeutic candidate is a pharmaceutical product (P), biologic (B) or device (D).

3 PureTech Level Cash and Cash Equivalents as of December 31, 2021: $418.9m[2]

4 Our Return of Capital to Shareholders

Key Pipeline Components and Expected Milestones Through 2022

Through 2022, we anticipate many significant potential milestones across our Wholly Owned Programs and Founded Entities, including at least 10 clinical readouts, at least five clinical trial initiations and the full commercial rollout of two therapeutics. Of these, five clinical readouts and one clinical trial initiation are anticipated within our Wholly Owned Pipeline. Additionally, we expect the continued progress of discovery and preclinical programs, as well as the potential for additional strategic partnerships and transactions and the growth of value through our equity and royalty holdings in our Founded Entities. Our Wholly Owned Programs and certain of our Founded Entities' programs that contribute to our value are as follows:

Our Wholly Owned Programs Focused on Immunological, Fibrotic and Lymphatic System Disorders:

LYT-100, Our Lead Clinical-Stage Therapeutic Candidate Targeting a Range of Conditions Involving Inflammation and Fibrosis and Disorders of Lymphatic Flow: We are advancing our clinical-stage therapeutic candidate LYT-100 (deupirfenidone) for the potential treatment of conditions involving inflammation and fibrosis, including lung disease (IPF and Long COVID[11] respiratory complications and related sequelae) and disorders of lymphatic flow, such as lymphedema. We are also exploring the potential evaluation of LYT-100 in other inflammatory and fibrotic conditions such as radiation induced fibrosis, myocardial fibrosis and other organ system fibrosis based on the strength of existing clinical data around the use of pirfenidone in these indications. In the January 2022 post-period, we announced results from a randomized, double-blind crossover study in healthy older adults demonstrating that approximately 50% fewer subjects treated with LYT-100 experienced GI-related AEs compared to subjects treated with pirfenidone (17.4% vs. 34.0%). Based on these results, additional data generated from our robust LYT-100 clinical program and recent regulatory feedback, we intend to advance LYT-100 into late-stage clinical development for the treatment of IPF, streamlining the program by capitalizing on efficiencies of the 505(b)(2) regulatory pathway. The dose-ranging study, which is anticipated to begin in the first half of 2022, will enroll approximately 250 treatment-naïve patients to evaluate LYT-100 efficacy relative to placebo. The trial will also compare the relative tolerability and efficacy between LYT-100 and pirfenidone. Topline results from this study are expected by the end of 2023. We believe the results of this study, together with a Phase 3 study, could serve as the basis for registration in the U.S. Additionally, two Phase 2 clinical trials of LYT-100 progressed in 2021: 1) A Phase 2 trial of LYT-100-COV in adults with Long COVID respiratory complications and related sequelae. Topline results from this trial are expected in the first half of 2022. 2) A Phase 2a proof-of-concept study of LYT-100-LYMPH in patients with breast cancer-related, upper limb secondary lymphedema. Topline results from this trial are expected in 2022. In 2021, we initiated a three-month, open-label extension of the LYT-100-COV Phase 2 trial in adults with Long COVID respiratory complications and related sequelae who completed the first portion of the trial. The primary endpoint of the extension trial will measure change in distance walked on the 6MWT, with secondary endpoints to assess the longer-term safety and tolerability of LYT-100-COV through up to 182 days of treatment. We also initiated additional Phase 1 clinical trials in 2021 to further evaluate the PK, dosing and tolerability of LYT-100 in healthy volunteers and healthy older adults to inform the clinical development of LYT-100 across multiple indications. Results from these studies demonstrated that LYT-100 was well-tolerated at 824mg TID dosing with low rates of GI AEs that were comparable to placebo. These results will further inform our dose-ranging study design in treatment-naïve IPF patients. In April 2021, we announced the formation of a Clinical Advisory Board for IPF and other PF-ILDs. In August 2021, we presented the results of the Phase 1 multiple ascending dose and food effect study of LYT-100 at the virtual European Respiratory Society (ERS) International Congress. The results from the study were subsequently published in the journal *Clinical Pharmacology in Drug Development* in November 2021.

LYT-200 and LYT-210, Two Immuno-Oncology (IO) Therapeutic Candidates Harnessing Key Immune Cell Trafficking and Programming Mechanisms: The lymphatic system plays a crucial role in programming immune cells for precise functions and trafficking them to specific tissues. By modulating immune cell trafficking and programming, we are developing therapeutic candidates for the potential treatment of cancer and other immunological disorders. We are advancing LYT-200, targeting a foundational immunosuppressive protein, galectin-9, for the potential treatment of difficult-to-treat solid tumors including pancreatic ductal adenocarcinoma (PDAC), colorectal cancer (CRC) and cholangiocarcinoma (CCA), and LYT-210, targeting immunomodulatory gamma delta-1 T cells for a range of cancer indications. LYT-200 is being evaluated as a single agent in the first stage of an adaptive Phase 1/2 clinical trial. The primary objective of the Phase 1 portion of the trial is to assess the safety and tolerability of escalating doses of LYT-200 to identify a dose to carry forward into the Phase 2 portion of the trial. The Phase 1 portion will also assess the PK and pharmacodynamic (PD) profiles of LYT-200. Topline results from the Phase 1 portion of the study are anticipated in the first half of 2022. Pending these results, we intend to initiate the Phase 2 expansion cohort portion of the trial, which is designed to evaluate LYT-200 both as a single agent and in combination with chemotherapy or BeiGene's tislelizumab, an anti-PD-1 mAb for which we and an affiliate of BeiGene, Ltd. entered into a clinical trial and supply agreement in July 2021. Under the terms of the agreement, we will maintain control of the LYT-200 program, including global R&D and commercial rights, and BeiGene has agreed to supply tislelizumab for use in combination with LYT-200 for the planned Phase 2 study cohorts. In November 2021, the FDA granted orphan drug designation to LYT-200 for the treatment of pancreatic cancer. The FDA grants orphan drug designation to novel drug and biologic products for the treatment, diagnosis or prevention of conditions affecting fewer than 200,000 persons in the U.S. Orphan Drug designation qualifies PureTech for incentives under the Orphan Drug Act, including tax credits for some clinical trials and eligibility for seven years of market exclusivity in the U.S. if the drug is approved, in addition to our broad intellectual property coverage which can extend the exclusivity into 2038. In April 2021, we presented a scientific poster detailing additional promising preclinical results for LYT-210 at the 2021 American Association for Cancer Research (AACR) Annual Virtual Meeting. The research demonstrated that LYT-210 is both highly specific

11 Long COVID is a term being used to describe the emerging and persistent complications following the resolution of COVID-19 infection, also known as post-acute COVID-19 syndrome (PACS).

and highly potent, rapidly inducing cell death of immunomodulatory gamma delta-1 T cells, while sparing other T cells that play important roles in a healthy immune response. We expect to complete additional biomarker studies for LYT-210 in 2022.

LYT-300, Preclinical Therapeutic Candidate Developed Using our Glyph Technology Platform, Targeting Neurological and Neuropsychological Conditions: Using our Glyph platform, which harnesses the natural trafficking of dietary lipids via the lymphatics, we are advancing LYT-300, an oral form of allopregnanolone, for the potential treatment for a range of neurological and neuropsychological conditions. Allopregnanolone is a natural neurosteroid that is a positive allosteric modulator of γ-aminobutyric-acid type A ($GABA_A$) receptors, which are known to play a key biological role in depression, epilepsy and other neurological and neuropsychological conditions. In December 2021, we initiated a Phase 1 clinical study of LYT-300, which is designed to characterize the safety, tolerability and PK of orally administered LYT-300 in healthy volunteers. Results are expected in the second half of 2022 and will be used to inform the design of possible future studies evaluating LYT-300 in indications that could include depression, anxiety, sleep disorders, fragile X tremor-associated syndrome, essential tremor and epileptic disorders, among others. Also in December 2021, we presented preclinical proof-of-concept data at the 60th American College of Neuropsychopharmacology (ACNP) Annual Meeting supporting the clinical advancement of LYT-300. The data presented at ACNP showed that systemic exposure of natural allopregnanolone was achieved after oral administration of LYT-300 in multiple preclinical models of increasing complexity. In contrast, systemic levels of allopregnanolone were not observed following oral administration of natural unmodified allopregnanolone. These results demonstrate the potential of the Glyph technology platform to enhance the systemic absorption of natural bioactive molecules and other small molecules with poor oral bioavailability. We are also advancing our Glyph technology platform, which is designed to employ the lymphatic system's natural lipid absorption and transport process and has led to the nomination of a new therapeutic candidate, LYT-300, for continued expansion of our Wholly Owned Pipeline. We have successfully extended the platform to encompass more than 20 molecules as well as a range of novel linker chemistries that have demonstrated promising lymphatic targeting in preclinical studies. In 2021, preclinical proof-of-concept work was published in *Nature Metabolism* and the *Journal of Controlled Release* supporting the Glyph technology platform's ability to directly target the lymphatic system.

LYT-510, LYT-500 and LYT-503/IMB-150, our Therapeutic Candidates Developed Using our Alivio Technology Platform for Inflammatory Disorders: In June 2021, we announced the acquisition of the remaining 22% of shares outstanding in our Founded Entity, Alivio Therapeutics (Alivio). The underlying Alivio technology platform, which is designed to enable oral and locally targeted immunomodulation for the potential treatment of a range of chronic and acute inflammatory disorders, has been added to our lymphatic and inflammation programs. Alivio's therapeutic candidates, in development for inflammatory disorders including IBD, have also been integrated into our Wholly Owned Pipeline. The first of these candidates is LYT-510, an oral inflammation-targeting formulation of tacrolimus, a potent immunosuppressant drug, in development to treat IBD and chronic pouchitis. In multiple preclinical IBD models, LYT-510 showed significant improvements in several efficacy endpoints compared to untreated controls. Furthermore, the inflammation-targeting properties were shown to result in very low systemic blood levels compared to the current immunosuppressant formulations, which minimizes the potential for systemic side effects. We intend to file for regulatory approval to initiate first-in-human studies at year end 2022 and initiate a clinical study evaluating LYT-510 as a single agent for the potential treatment of IBD and chronic pouchitis in early 2023. In addition, LYT-500 is an orally-administered therapeutic candidate in development for the treatment of IBD that contains a unique combination of IL-22 and an approved potent anti-inflammatory drug and is designed to address the key underlying causes of IBD pathogenesis and progression, such as mucosal barrier disruption that are currently not adequately treated by the standard of care medicines. We expect preclinical proof-of-concept data for LYT-500 in the first half of 2022. LYT-503/IMB-150 is a therapeutic candidate being advanced as a partnered program for the potential treatment of IC/BPS, a chronic inflammatory condition of the bladder that lacks an effective treatment option. The LYT-503/IMB-150 therapeutic candidate is designed to selectively treat inflamed tissues along the bladder wall while minimizing the potential for drug-related side effects in healthy parts of the body. An IND application is expected to be filed for LYT-503/IMB-150 in 2022.

In addition to our Glyph and Alivio lymphatic and inflammation platforms, our Wholly Owned Programs include Orasome and other oral biotherapeutics platforms enabling the body to produce its own therapeutic protein in the gastrointestinal tract and enter the systemic circulation via the lymphatic system – and a meningeal lymphatics research program to develop potential treatments for neurodegenerative and neuroinflammatory diseases.

Orasome and Other Technology Platforms for Oral Administration of Therapeutics: We are developing versatile and programmable oral biotherapeutics approaches, such as our Orasome technology, to promote following oral administration of an expression system, intestinal tract cells, to produce virtually any type of therapeutic protein, including monoclonal antibodies, "on command" with transport to the circulatory system. We recently demonstrated in a preclinical model that administration of Orasomes carrying an expression system for a therapeutic protein to the GI tract of a rodent led to therapeutic protein detection in systemic circulation. In 2021, we established preclinical proof-of-concept supporting the potential of the Orasome technology platform to achieve production of therapeutic proteins in the gut of an animal following simulated oral administration of expression systems and transport of these proteins from the gut into systemic circulation. Proof-of-concept was observed with multiple formulations which are being further optimized to achieve a range of expression profiles for therapeutic proteins. We expect to generate additional data in 2022, with Orasomes and other technologies, across a range of preclinical models and therapeutic proteins. We expect to generate data to demonstrate that oral administration of Orasomes, carrying an expression system for a desired therapeutic protein, can achieve therapeutic levels of the protein in multiple species of preclinical models with achievement of safe repeat-dose administration. Using the Orasome technology platform, it may be possible for a patient to take an oral drug product that will permit their own GI tract cells to make virtually any type of protein. This approach also has the potential to provide a more convenient and significantly less expensive means to administer biological medicines. This work could lay the foundation for IND-enabling clinical studies for one or more additional therapeutic candidates to be included in our Wholly Owned Pipeline. In addition to Orasomes, we are also exploring the use of other approaches, such as certain exosomes isolated from milk as well as synthetic novel polymers and vesicles for delivering biotherapeutics.

Our Meningeal Lymphatics Research Program: We continued to advance our meningeal lymphatics research program, which harnesses the meningeal lymphatics to potentially treat a range of neurodegenerative and neuroinflammatory conditions. In April 2021, we announced the publication of preclinical research in *Nature*, suggesting that restoring lymphatic flow in the brain, either alone or in combination with passive immunotherapies such as antibodies directed at amyloid-beta, has the potential to address a range of neurodegenerative diseases, such as Alzheimer's and Parkinson's diseases, which potentially impairs the efficacy of passive immunotherapies such as amyloid-beta-targeting antibodies. The work also uncovered a link between dysfunctional meningeal lymphatics and damaging microglia activation in Alzheimer's disease, suggesting another route by which restoring healthy drainage patterns could improve clinical outcomes.

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Our Mission: Developing Breakthrough Medicines for Underserved and Serious Diseases

The programs within our Wholly Owned Programs and at our Founded Entities were initiated in close collaboration with leading academic and clinical experts. We discover, develop and aim to commercialize new therapies for underserved and often devastating diseases where limited or no treatment options currently exist for patients. We do this by building upon validated biology of known therapeutics while applying unique innovative steps that improve pharmacologic profiles.

Unlocking the Potential of Validated Biology

The common theme underlying all of our programs has been to start with a tremendous patient need. In many cases, these programs are identified based on signals of human efficacy and clinically validated biology, which has enabled us to advance therapeutic candidates with significantly de-risked profiles and robust development rationales, resulting in differentiated potential treatments for patients.

For example, the key innovation behind our Founded Entity, Karuna, was built around two validated drugs: xanomeline, a novel muscarinic agonist, and trospium, an approved muscarinic antagonist. We were able to ameliorate the GI tolerability issues of xanomeline by pairing it with a gut-restricted muscarinic antagonist to develop a novel formulation that enabled a new approach for the potential treatment of schizophrenia and other serious psychiatric and neurological conditions, an area of major unmet need. KarXT now represents a potential first-in-class and best-in-class therapy for schizophrenia.

We have continued to harness the power of this approach to develop new medicines by applying our innovation and technology that can unleash the full potential of a therapeutic that was previously held back from their full potential by key challenges, such as poor safety, tolerability, oral bioavailability or dosing.

LYT-100

Pirfenidone has been proven effective against fibrosis and inflammation, but significant tolerability issues negatively affect patient compliance and often result in suboptimal disease management. To tackle this problem, we are developing a proprietary clinical-stage therapeutic candidate, LYT-100 (selectively deuterated form of pirfenidone) that maintains the pharmacology of pirfenidone but has a highly differentiated PK profile that has translated into favorable tolerability, as demonstrated by data from multiple human clinical studies.

LYT-300/Glyph™ Technology Platform

Allopregnanolone is a natural neurosteroid with well-established biology that has demonstrated efficacy for the treatment of epilepsy, depression and other neurological indications. However, it is not orally bioavailable and is commercially formulated to be administered as a cumbersome 60-hour IV infusion. We have applied our innovative Glyph technology to generate LYT-300, which is an orally bioavailable prodrug of natural allopregnanolone. Our Glyph technology platform is based on the natural process of dietary lipid transport in the body. We use the Glyph technology to design prodrugs of natural bioactive molecules, such as allopregnanolone, for oral administration of drugs, that are transported via the lymphatic system and bypass first-pass liver metabolism. LYT-300 has been shown in preclinical models to enable allopregnanolone to be bioavailable.

LYT-510, LYT-500/Alivio™ Technology Platform

Our Alivio technology platform is designed to target biologics and other drugs to sites of inflammation in a localized manner while limiting their systemic exposure, which offers the potential to significantly improve both the safety and efficacy profile of the therapy. We are developing LYT-510 as an oral inflammation-targeting formulation of tacrolimus, a potent immunosuppressant drug, to treat IBD and chronic pouchitis. Tacrolimus is approved for certain indications, however its approval for IBD and chronic pouchitis has been hampered by systemic toxicities, narrow therapeutic window of activity and opportunistic infections that can arise from systemic immunosuppression. There is clinical data demonstrating that tacrolimus is effective in addressing IBD indications, but AEs have held it back. We believe that LYT-510 can overcome these clinical challenges with targeted drug delivery to the intestines, with the potential to be the first tacrolimus treatment approved for IBD in the U.S. In multiple preclinical IBD models, LYT-510 showed significant improvements in several efficacy endpoints compared to untreated controls. Furthermore, the inflammation-targeting properties were shown to result in very low systemic blood levels compared to the current immunosuppressant formulations, which minimizes the potential for systemic side effects. LYT-500 is an oral therapeutic candidate that we are developing for the potential treatment of mucosal barrier damage in people with IBD. We believe the targeted activation and oral formulation offered by Alivio offers a path to unlocking the full therapeutic potential of anti-inflammatory drugs in a way that matches the chronic, variable expression of autoimmune diseases.

Orasome™ and Other Technology Platforms for Oral Administration of Therapeutics

Validated biology has shown that intestinal cells can be engineered to produce clinically validated therapeutic proteins, such as EPO, GLP-1 and mAbs. Therapeutic proteins and nucleic acid therapeutics (e.g. mRNA) are primarily administered by injection. Using the Orasome technology platform, it may be possible for a patient to take an oral drug product that will permit their own gastrointestinal tract cells to make virtually any type of therapeutic protein. This approach also has the potential to provide a more convenient and significantly less expensive means to administer biological medicines. In addition to Orasomes, we are also exploring the use of other approaches, such as certain exosomes isolated from milk as well as synthetic novel polymers and vesicles for delivering biotherapeutics.

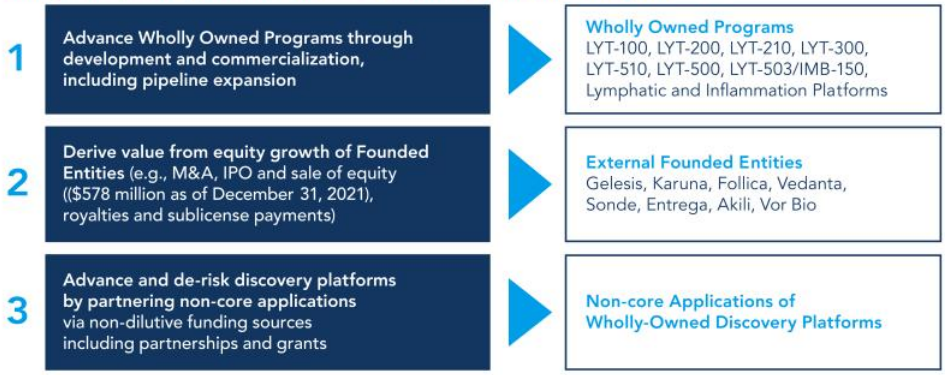
Our Model

We employ the following process to identify and develop therapeutic candidates:

- **Step 1: A Collaborative Discovery Process Leveraging Validated Biology and our Scientific Network:** We collaborate with the world's leading domain experts on a disease-specific discovery theme through our core areas of expertise around brain, immune and gastrointestinal systems, with a particular focus on immunological disorders. Our Wholly Owned Programs are built around this expertise and we prioritize programs that have the potential to reduce early development risk based on preliminary signals of activity in humans and promising tolerability profiles. We have proven our ability to efficiently leverage our cross-disciplinary research and discovery efforts across multiple indications and potential therapeutic areas. Our program collaborators and co-inventors across our Wholly Owned Programs and Founded Entities' programs include leading academic minds; recipients of major awards such as the Nobel Prize, the U.S. National Medal of Science, the Charles Stark Draper Prize and the Priestley Medal; members of prestigious institutions such as the Howard Hughes Medical Institute, all three of the National Academies and world-renowned academic institutions such as Harvard, MIT, Yale, Columbia, Johns Hopkins, Imperial College of London and Cornell, among others; and former senior executives and board members at some of the world's largest pharmaceutical companies.
- **Step 2: A Disciplined Approach to Program Advancement:** We employ a rigorous and disciplined approach to research and development. The breadth and depth of our Wholly Owned Programs and our Founded Entities' programs allow us to quickly pivot resources to the more promising therapeutic opportunities, strategically reallocate capital across programs and terminate Wholly Owned Programs we choose not to pursue without adversely impacting the development of other programs. Through our internal resources and with our extensive expert network and collaboration partners, we repeat key academic work and conduct focused experiments both internally and externally to rapidly advance those that we believe hold the greatest promise and deprioritize less attractive programs. Collectively, these activities decrease the risk of any individual program event negatively impacting our Wholly Owned Programs and enable us to preserve capital for the programs across our Wholly Owned Programs and Founded Entities that we believe have the greatest opportunity for value creation in alignment with our shareholders.
- **Step 3: A Capital Efficient Approach to Driving Clinical Development and Value Creation:** Our management team has successfully driven these therapeutic candidates from early-stage research and development, through POC and into clinical trials and has supported dedicated teams at our Non-Controlled Founded Entities through pivotal trials and FDA clearance. We have financed our development efforts through strategic collaborations, pharmaceutical partnerships, non-dilutive funding mechanisms, including through the sale of our Founded Entities' equity and through grants, and public and private equity financings. We leverage shared resources, institutional knowledge and infrastructure between our earlier stage Founded Entities and development efforts within our Wholly Owned Programs to advance our programs efficiently prior to POC. This approach has enabled the discovery and development of 27 therapeutics and therapeutic candidates to date, including two that have been cleared for marketing by the FDA and granted marketing authorization in the EEA, between our Wholly Owned Programs and our Founded Entities, in which we retain equity ownership ranging from 5.6% to 76.0%. We had PureTech Level Cash and Cash Equivalents of $418.9 million as of December 31, 2021[14]. From January 1, 2017 to December 31, 2021, our Founded Entities strengthened their collective balance sheets by attracting $1.9 billion in investments and non-dilutive funding, including $1.8 billion from third parties. As part of our disciplined capital management, we have been able to generate $578.0 million in non-dilutive funding, as of December 31, 2021, through the sales of portions of Founded Entity shares.

Our Strategy

Driving development of potential new medicines and accretion of value via three paths



14 For more information in relation to the PureTech Level Cash and Cash Equivalents and Consolidated Cash and Cash Equivalents measures used in this Annual Report, please see pages 97 and 98 of the Financial Review.

15 On July 23, 2021, Imbrium Therapeutics exercised its option to license LYT-503/IMB-150 pursuant to which it is responsible for all future development activities and funding for LYT-503/IMB-150.

Our goal is to identify, invent, develop and commercialize innovative new categories of therapeutics that are derived from our deep understanding of the brain, immune, and gastrointestinal systems, with a particular focus on immunological disorders, to address significant unmet medical needs. To achieve this goal, key components of our strategy include:

- Advancing Wholly Owned Programs through development and commercialization, including pipeline expansion:
  - Progressing LYT-100, LYT-200, LYT-210, LYT-300, LYT-510, LYT-500, and LYT-503/IMB-150[15] through clinical studies.
  - Harnessing our proprietary drug discovery and development capabilities to drive pipeline maturation and expansion: We are pioneering the development of therapeutic candidates by leveraging our unique insights into the lymphatic system and immunology and drug development. Our Wholly Owned Programs currently comprise seven proprietary therapeutic candidates and three innovative technology platforms. We intend to leverage our proprietary lymphatic and inflammation technology platforms, as well as our extensive network with world-leading scientists in immunology and lymphatics and major pharmaceutical companies, to generate and acquire additional novel therapeutic candidates. To do so, we will rely on the track record of our team, which has been instrumental in the generation of 27 therapeutics and therapeutic candidates to date between our Wholly Owned Programs and our Founded Entities, including two that have been cleared for marketing by the FDA and granted marketing authorization in the EEA, as well as our established internal identification and prioritization approach. In many cases, these programs are identified based on signals of human efficacy and clinically validated biology, which has enabled us to advance candidates with significantly de-risked profiles and robust development rationales. We will continue to take advantage of our differentiated model to manage the risk of any single program and quickly redeploy resources towards performing assets.
  - Maximizing the impact of our Wholly Owned Programs by expanding development across multiple indications: We aim to focus our development efforts on therapeutic candidates that have the potential to treat multiple diseases and plan to develop them in additional indications where warranted. For example, we believe that our lead therapeutic candidate LYT-100 has the potential to treat multiple inflammatory and fibrotic indications that affect the lung, heart and other organ systems. We are initially developing our other therapeutic candidates, LYT-200 and LYT-210, for the treatment of difficult-to-treat solid tumors, which will likely include PDAC, CRC and CCA. We are advancing LYT-300, an oral lipid prodrug version of allopregnanolone generated from our Glyph platform, for the potential treatment of a range of neurological and neuropsychological conditions. Lastly, we are developing LYT-510 for the potential treatment of IBD and chronic pouchitis, LYT-500, an oral combination therapy, for the potential treatment of IBD, and advancing LYT-503/IMB-150 as a partnered program for the potential treatment of IC/BPS. Each therapeutic candidate was generated from our Alivio technology platform.
- Deriving value from equity growth of our Founded Entities: Going forward, our Founded Entities may participate in private and public financings, enter into partnerships and collaborations, partner with equity investors, pharmaceutical and biotechnology companies and government and non-governmental organizations and generate revenues from sales of products. We hold equity ownership in our Founded Entities and benefit from their growth and catalysts such as M&A transactions, IPOs and royalties from sales. We also intend to strategically monetize our equity holdings in our Founded Entities over time after significant value inflection has occurred, generating non-dilutive financing. For example, PureTech generated cash proceeds of approximately $218 million in 2021 from the sales of equity in our Founded Entities.
- Advancing discovery platforms by partnering non-core applications via non-dilutive funding sources, including partnerships and grants, to enable retention of value: As we further develop our Wholly Owned Programs through key value inflection points, we may opportunistically enter into strategic partnerships when we believe that such partnerships could add value to the development or potential commercialization of our wholly-owned therapeutic candidates. We will also continue to pursue government grant funding and discovery partnerships that allow us to maintain most of the value of our platforms while offsetting operational costs.

We believe this combination of development of our Wholly Owned Programs, Founded Entity advancement and non-dilutive partnerships and funding provides us with a unique and multi-pronged engine fueling potential future growth and a diverse portfolio of differentiated treatment opportunities for patients.

By Order of the Board

Daphne Zohar
Founder, Chief Executive Officer and Director
April 25, 2022

PureTech's Wholly Owned Programs

Our programs

Therapeutic Candidate[1]	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
LYT-100-ILD Deupirfenidone	IPF					
LYT-100-COV Deupirfenidone	Long COVID[2] respiratory complications and related sequelae					
LYT-100-LYMPH Deupirfenidone	Lymphatic flow disorders, including lymphedema					
LYT-200 Anti-Galectin-9 mAb	Solid tumors					
LYT-210 Anti-Delta-1 mAb	Solid tumors					
LYT-300 Oral Allopregnanolone	Neurological and neuropsychological conditions					
LYT-510 Oral Immunosuppressant	IBD/chronic pouchitis					
LYT-500 Oral IL-22 + Immunosuppressant	IBD					
LYT-503/IMB-150 (Partnered program) Non-opioid	IC/BPS					

Phase completed Phase in progress Registration-enabling studies to begin in 1H2022

Our Head of Research, Anne Burkhardt, and her team works to advance our Wholly Owned Programs in our headquarters.

1 The FDA and corresponding regulatory authorities will ultimately review our clinical results and determine whether our wholly-owned therapeutic candidates are safe and effective. No regulatory agency has made any such determination that our wholly-owned therapeutic candidates are safe or effective for use by the general public for any indication.

2 Long COVID is a term being used to describe the emerging and persistent complications following the resolution of COVID-19 infection, also known as post-acute COVID-19 syndrome (PACS).

LYT-100

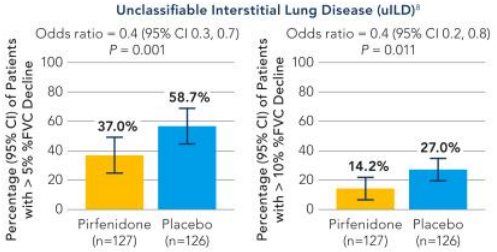
Therapeutic Candidate[1]	PureTech Ownership	Indication	Stage of Development
LYT-100	Wholly-owned	Idiopathic pulmonary fibrosis (IPF)	Registration-enabling studies planned
		Long COVID[2] respiratory complications and related sequelae	Phase 2
		Lymphatic flow disorders, including lymphedema	Phase 2
		Exploring potential opportunities in other inflammatory and fibrotic conditions, such as radiation induced fibrosis, myocardial fibrosis, and other organ system fibrosis	Clinical studies being planned

- Our lead wholly-owned therapeutic candidate, LYT-100 (deupirfenidone), is being advanced for the potential treatment of conditions involving inflammation and fibrosis, including lung disease (IPF and Long COVID respiratory complications and related sequelae) and disorders of lymphatic flow, such as lymphedema. We are also exploring the potential evaluation of LYT-100 in other inflammatory and fibrotic conditions, such as radiation induced fibrosis, myocardial fibrosis and other organ system fibrosis based on the strength of existing clinical data around the use of pirfenidone in these indications. LYT-100 is a selectively deuterated form of pirfenidone that is designed to retain the potent and clinically validated anti-fibrotic and anti-inflammatory activity of pirfenidone, but with a highly differentiated PK profile that has translated into favorable tolerability, as supported by data from multiple human clinical studies. To date, LYT-100 has been studied in more than 400 subjects and demonstrated a favorable safety profile as part of our ongoing development work and indication prioritization.

Key Points of Innovation & Differentiation

- Pirfenidone (Esbriet®[3]) slows the progression of IPF and has been approved for the treatment of IPF in the U.S. and other countries. IPF is a chronic orphan condition that causes progressive scarring of the lungs. Median overall survival of IPF patients is 3-5 years. Pirfenidone is one of the two standard of care treatments for IPF, with nintedanib (OFEV®[3]) being the other drug. Despite its proven efficacy, there are serious limitations to pirfenidone's clinical use primarily due to severe GI-related tolerability issues, which have significantly curtailed its effectiveness in patients with IPF[4]. The other standard of care treatment for IPF, nintedanib, has similar GI-related tolerability issues and limitations that have limited its broad usage. Although the combined sales of these two standard of care IPF drugs are over $3B, only about 25% of IPF patients are currently being treated with either of these drugs[5]. The vast majority of IPF patients are not currently on any approved therapies, primarily due to tolerability issues associated with these drugs. In a large post-marketing analysis of 10,996 patients diagnosed with IPF, only 13.2% received treatment with pirfenidone during a five-year follow-up period[6]. Additionally, real-world experience with pirfenidone in the IPF treatment setting highlights significant problems with treatment compliance, resulting in approximately half of the patients that start therapy either discontinuing therapy, dose-reducing or switching to other therapies, all of which lead to suboptimal disease management. We are developing LYT-100-ILD to offer an improved tolerability profile compared to current standard of care drugs, which may enable better patient compliance and potentially lead to improved disease outcomes. Pirfenidone has also shown activity in investigational clinical studies in patients with unclassifiable interstitial lung disease (uILD), radiation induced fibrosis, myocardial fibrosis and other organ system fibrosis and has demonstrated activity in a preclinical model of lymphedema and radiation-induced fibrosis.

Pirfenidone: Clinically Validated Anti-Fibrotic and Anti-Inflammatory



- Pirfenidone FDA-approved for IPF with breakthrough designation for uILD
- Over a dozen late-stage & real-world efficacy studies demonstrate efficacy in IPF[9]
- Clinical proof-of-concept studies in FSGS, uILD, radiation-induced fibrosis & other inflammatory & fibrotic diseases
- BUT GI-related tolerability issues significantly limit its usage, resulting in ~50% who discontinue, dose adjust, or switch[10]
- ~75% of IPF patients are not on standard of care therapy[6]
- Despite drawbacks, pirfenidone sales >$1B / year

1 We have an active IND on file with the FDA for LYT-100. The FDA and corresponding regulatory authorities will ultimately review our clinical results and determine whether our wholly-owned therapeutic candidates are safe and effective. No regulatory agency has made any such determination that LYT-100 is safe or effective for use by the general public for any indication.

2 Long COVID is a term being used to describe the emerging and persistent complications following the resolution of COVID-19 infection, also known as post-acute COVID-19 syndrome (PACS).

3 Esbriet®, OFEV® and AUSTEDO® are trademarks of Genentech, Boehringer Ingelheim Pharmaceuticals and Auspex Pharmaceuticals, Inc., respectively, and are not owned by or affiliated with PureTech Health. LYT-100 is an investigational drug not approved by any regulatory authority.

4 Rubino C. M., Bhavnani S. M., Ambrose P. G., Forrest A., Loutit J. S. Effect of food and antacids on the pharmacokinetics of pirfenidone in older healthy adults. Pulmonary Pharmacology & Therapeutics. 2009 Aug;22(4):279-285. DOI: 10.1016/j.pupt.2009.03.003.

5 Based on 2021 ESBRIET® and OFEV® total WW sales of $3.7B; Ofev sales are inclusive of SSc-ILD, PF-ILD and IPF indications.

6 Dempsey TM, Payne S, Sangaralingham L, Yao X, Shah ND, Limper AH. Adoption of the Anti-Fibrotic Medications Pirfenidone and Nintedanib for Patients with Idiopathic Pulmonary Fibrosis. Ann Am Thorac Soc. 2021 Jan 19. doi: 10.1513/AnnalsATS.202007-901OC. Epub ahead of print. PMID: 33465323.

7 Noble, P. W., Albera, C., Bradford, W. Z., Costabel, U., du Bois, R. M., Fagan, E. A., Fishman, R. S., Glaspole, I., Glassberg, M. K., Lancaster, L., Lederer, D. J., Leff, J. A., Nathan, S. D., Pereira, C. A., Swigris, J. J., Valeyre, D., & King, T. E., Jr (2016). Pirfenidone for idiopathic pulmonary fibrosis: analysis of pooled data from three multinational phase 3 trials. The European Respiratory Journal, 47(1), 243–253. https://doi.org/10.1183/13993003.00026-2015.

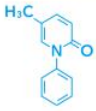
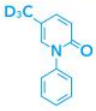
8 ERS 2019: http://bit.ly/2LJ9WCC

9 Saad, M. I., Mcleod, L., Hodges, C., Vlahos, R., Rose-John, S., Ruwanpura, S., & Jenkins, B. J. (2021). ADAM17 Deficiency Protects against Pulmonary Emphysema. American Journal of Respiratory Cell and Molecular Biology, 64(2), 183-195. doi:10.1165/rcmb.2020-0214oc.

10 Cottin, V., Koschel, D., Günther, A., Albera, C., Azuma, A., Sköld, C. M., Tomassetti, S., Hormel, P., Stauffer, J. L., Strombom, I., Kirchgaessler, K. U., Maher, T. M. (2018). Long-term safety of pirfenidone: Results of the prospective, observational PASSPORT study. ERJ Open Research, 4(4), 00084-2018. doi:10.1183/23120541.00084-2018.

Key Points of Innovation & Differentiation (continued)

- LYT-100 is a selectively deuterated form of pirfenidone that is designed to retain the potent and clinically-validated anti-fibrotic and anti-inflammatory activity of pirfenidone with a highly differentiated PK profile that has translated into favorable tolerability, as demonstrated by data from multiple human clinical studies.
- As recently demonstrated in a crossover study comparing LYT-100 to pirfenidone in healthy older adults, lower maximal LYT-100 drug concentration (Cmax) with exposure that is bioequivalent to pirfenidone was achieved. This is supportive of the observed improved tolerability.
- A PK profile of LYT-100 that is substantially better tolerated than pirfenidone while maintaining comparable efficacy has the potential to allow the patients to stay on the drug longer. As a result, we believe LYT-100-ILD has the potential to replace pirfenidone as standard of care and to become a backbone therapy in the treatment for IPF.

Pirfenidone	LYT-100
	
✔ Clinically validated efficacy ✗ Associated with GI AEs ✗ Higher exposure limited by tolerability	✔ Differentiated PK profile while retaining pharmacology ✔ Substantially improved AE profile ✔ Potential to enhance exposure that could improve efficacy, MTD not determined

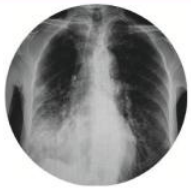
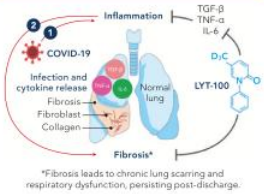
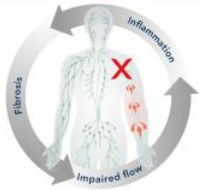
Program Discovery Process by the PureTech Team

- LYT-100 (deupirfenidone) was originally developed by Auspex Pharmaceuticals, Inc. (Auspex, now a wholly owned subsidiary of Teva Pharmaceuticals), a company that pioneered the deuteration technology and successfully developed deutetrabenazine (Austedo®), becoming the first and only deuterated drug that has received FDA approval[3]. We selected and acquired LYT-100 (from Teva Pharmaceuticals) in July 2019 based on insights into the lymphatic system gained internally and via unpublished findings through our network of collaborators, coupled with the relationships of our team members and their insights into the program while in development at Auspex. We believe that the commercial success of the first and only deuterated drug, Austedo, based on a comparable efficacy to tetrabenazine but a highly differentiated, favorable safety and tolerability profile, could potentially serve as a good precedence for LYT-100.

Patient Need & Market Potential

Fibrosis and Inflammation-Related Lung Diseases

LYT-100: Tackling Inflammatory & Fibrotic Diseases

LYT-100-ILD	LYT-100-COV	LYT-100-LYMPH
~130K in the US with **IPF**[11]	Over **500M** people have been infected by **COVID-19**[12]	**~1M** in the US with **lymphedema**[15]
		
• Progressive fibrotic diseases leading to fatal lung dysfunction. Current standards of care for IPF associated with significant tolerability issues • **Initiating registration-enabling studies in 1H 2022**	• Up to 1/3 of severe COVID-19 patients develop lung fibrosis[13] • Up to 54% of hospitalized COVID-19 patients develop lasting dyspnea[14] • **Topline results from Phase 2 expected in 1H 2022**	• Lymphatic damage initiates vicious cycle of inflammation & fibrosis which further impairs fluid flow & tissue regeneration[16,17] • **Topline results from Phase 2a POC expected in 2022**

- Fibrosis and inflammation are a common mechanism across several lung diseases. These are acute diseases with high mortality or that lead to long-term fibrosis; chronic diseases linked to a specific cause, like a virus or autoimmune disease; and diseases like IPF, where the causes are unclear but have been postulated to include viruses, genetic factors and a variety of environmental exposures. For the majority of these lung conditions, there are few approved treatments that address the underlying inflammation and fibrosis affecting the lungs. Many of these diseases are progressive, and there is a clear unmet need to halt the inflammation and progressive fibrosis in order to preserve lung function.

11 Martinez, F. J., Collard, H. R., Pardo, A., Raghu, G., Richeldi, L., Selman, M., Swigris, J. J., Taniguchi, H., Wells, A. U. (2017). Idiopathic pulmonary fibrosis. Nature Reviews Disease Primers, 3(17074). doi:https://doi.org/10.1038/nrdp.2017.74.

12 COVID-19 map. Johns Hopkins Coronavirus Resource Center. (2021). https://coronavirus.jhu.edu/map.html.

13 Han, X., Fan, Y., Alwalid, O., Li, N., Jia, X., Yuan, M., Li, Y., Cao, Y., Gu, J., Wu, H., & Shi, H. (2021). Six-month Follow-up Chest CT Findings after Severe COVID-19 Pneumonia. Radiology, 299(1), E177–E186. https://doi.org/10.1148/radiol.2021203153.

14 Lerum, T. V., Aaløkken, T. M., Brønstad, E., Aarli, B., Ikdahl, E., Lund, K., Durheim, M. T., Rodriguez, J. R., Meltzer, C., Tonby, K., Stavem, K., Skjønsberg, O. H., Ashraf, H., & Einvik, G. (2021). Dyspnoea, lung function and CT findings 3 months after hospital admission for COVID-19. The European respiratory journal, 57(4), 2003448. https://doi.org/10.1183/13993003.03448-2020.

15 Lymphedema. Vascular Cures. (2017). https://vascularcures.org/lymphedema/.

16 Gousopoulos, E., Proulx, S. T., Bachmann, S. B., Scholl, J., Dionyssiou, D., Demiri, E., Halin, C., Dieterich, L.C., Detmar, M. (2016). Regulatory T cell transfer ameliorates lymphedema and promotes lymphatic vessel function. JCI Insight, 1(16). doi:10.1172/jci.insight.89081.

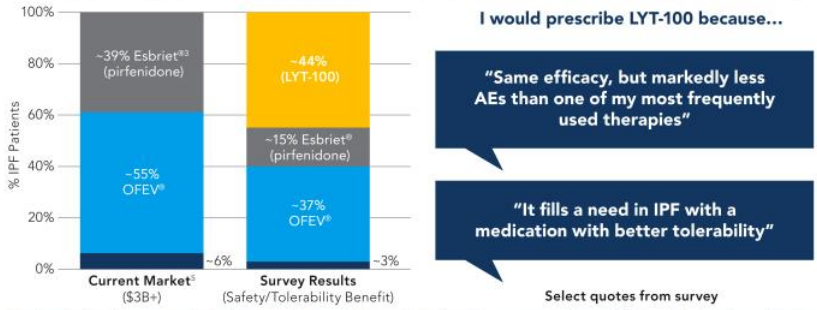
17 Avraham, T., Daluvoy, S., Zampell, J., Yan, A., Haviv, Y. S., Rockson, S. G., & Mehrara, B. J. (2010). Blockade of transforming growth factor-beta1 accelerates lymphatic regeneration during wound repair. The American journal of pathology, 177(6), 3202–3214. https://doi.org/10.2353/ajpath.2010.100594.

Patient Need & Market Potential (continued)

- IPF
  - There are approximately 130,000 people living with IPF in the U.S. IPF is a progressive condition characterized by irreversible scarring of the lungs that worsens over time, making it difficult to breathe. The prognosis of IPF is poor, with the median survival after diagnosis generally estimated at two to five years.
  - Even in IPF, for which pirfenidone is approved, there remains a need for more tolerable treatment options. Despite the limitations of this therapy, pirfenidone sales peaked above $1 billion each year from 2018 to 2021.

LYT-100-ILD: Independent Research Shows Profile Attractive to Surveyed Pulmonologists[18]

Pulmonologists would prescribe LYT-100 to ~44% of their new IPF patients (even without enhanced efficacy compared to SOC)



Certain results from this survey are depicted in the graphic above (right panel). Data from this survey are consistent with findings of independent publications that point to significant tolerability issues, particularly GI-based AEs, as the greatest limitations of the current standard of care in IPF.

- In the 2022 post-period, we engaged an independent third-party market research firm to conduct a survey of 100 pulmonologists who actively treat patients with IPF, to assess the potential commercial opportunity for LYT-100-ILD in IPF. In this survey, pulmonologists highlighted an unmet need for treatments with improved tolerability profiles. When physicians were asked the primary reasons patients discontinue or dose reduce current standard of care for IPF, 80-90% highlighted GI AEs as a main cause. Pulmonologists in this survey were also presented with a hypothetical profile[18] of LYT-100-ILD, labeled "Product X", that indicated an improved tolerability profile with comparable efficacy relative to standard of care in IPF. Based on this profile, physicians indicated they would prescribe Product X to nearly 44% of their new IPF patients. Furthermore, nearly 80% of physicians indicated they would prescribe Product X more than pirfenidone. Based on this survey, LYT-100 is expected to have a significant impact on the IPF market based on its improved tolerability profile and similar efficacy compared to standard of care, which is consistent with findings from the prior market research.
- Long COVID (PACS) Respiratory Complications and Related Sequelae
  - The COVID-19 pandemic has affected over 500 million people around the world. There is increasing data around the longer-term complications of COVID-19, referred to as Long COVID (PACS) including data regarding respiratory issues that persist following recovery. Survivors of the virus can have persistent shortness of breath and develop progressive lung fibrosis that could potentially last for years.
  - Post-acute injuries are hypothesized to be due to a cascade of inflammation and fibrosis that begins during the acute phase of COVID-19 and continues after the infection resolves. Up to one-third of severe COVID-19 patients develop lung fibrosis post symptom onset. Over 40% of hospitalized COVID-19 patients have lasting dyspnea and up to 33% of severe COVID-19 patients develop lung fibrosis.
  - COVID-19 post-acute injuries appear to mimic respiratory complications of other viral pneumonias like Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS). Up to one-third of SARS and MERS survivors had abnormal pulmonary testing and lung imaging findings that persisted for years.
- Lymphedema
  - Lymphedema is a chronic, disfiguring and painful condition that afflicts millions of people globally and is characterized by severe swelling in parts of the body, typically the arms or legs, due to the build-up of lymph fluid and inflammation, fibrosis and adipose deposition. By conservative estimates, lymphedema afflicts approximately one million people in the U.S., including approximately 500,000 breast cancer survivors. Secondary lymphedema is the most prevalent form of lymphedema. Secondary lymphedema can develop after surgery, infection, or trauma, and is frequently caused by cancer or cancer treatments such as radiation and chemotherapy, that cause damage to or mandate the removal of lymph nodes.
  - The current standard of care for lymphedema is symptom management, primarily with compression and physical therapy to control swelling. These approaches are cumbersome, uncomfortable and do not address the progression of the underlying disease. Even with management, many patients will progress from mild-to-moderate lymphedema to more severe forms. No approved drugs exist to treat the underlying causes of lymphedema. We believe the lack of treatments for lymphedema represents a major unmet medical need.

18 100 pulmonologists were surveyed, no pricing information/assumptions was shared. Research completed in the April 2022 post-period based on the latest target product profile and findings were consistent with our prior market research.

Milestones Achieved & Development Status

- In the January 2022 post-period, we announced results from a randomized, double-blind crossover study in healthy older adults demonstrating that approximately 50% fewer subjects treated with LYT-100 (deupirfenidone) experienced GI-related AEs compared to subjects treated with pirfenidone (17.4% vs. 34.0%).
  - The double-blind, randomized, crossover study evaluated the tolerability of LYT-100 550 mg TID versus pirfenidone 801 mg TID in 49 older healthy adults aged 60-79, an age group that is representative of the IPF patient population. The dose of LYT-100 used in this study was selected based on PK and modeling data from prior studies, which together suggest that 550 mg TID results in similar drug exposure levels achieved with 801 mg TID of pirfenidone. The study results demonstrated that 38% fewer subjects treated with LYT-100 experienced any AE compared with those treated with pirfenidone (30.4% vs. 48.9%). Additionally, approximately 50% fewer subjects experienced GI-related AEs with LYT-100 compared with pirfenidone (17.4% vs. 34.0%), most notably nausea (15.2% with LYT-100 vs. 29.8% with pirfenidone), which is the most common AE associated with pirfenidone. No serious AEs were reported in the study, and there was one AE-related discontinuation in each arm. Though not powered to show statistical significance, this study provides evidence that LYT-100 has the potential to offer an important tolerability advantage over pirfenidone and will help to inform our development plans with this therapeutic candidate in IPF.

LYT-100: Data to Date Demonstrate Tolerability Advantage Over Pirfenidone

LYT-100 demonstrates lower Cmax with same AUC compared to pirfenidone

Healthy Older Adult Crossover Study (N=49[19])		
TEAE	**LYT-100 550mg TID n (%)**	**Pirfenidone 801mg TID n (%)**
Gastrointestinal	**8 (17.4%)**	**16 (34.0%)**
– Nausea	7 (15.2%)	14 (29.8%)
– Vomiting	2 (4.3%)	3 (6.4%)
– Abdominal Pain/ Distension	1 (2.2%)	3 (6.4%)
Nervous System	**8 (17.4%)**	**15 (31.9%)**
– Headache	6 (13.0%)	9 (19.1%)
– Dizziness	1 (2.2%)	7 (14.9%)
– Somnolence	1 (2.2%)	2 (4.3%)

Clinical data demonstrate favorable tolerability

Multiple Ascending Dose Study[20]
Well-tolerated at all doses studied[21] without dose titration
All treatment-related **AEs** were **mild & transient**

Healthy Older Adult Crossover Study
Achieved **~50% reduction** in healthy older adults experiencing **GI-related AEs compared to pirfenidone**

TEAE = treatment emergent adverse event
Discontinuations for AEs: 1 during pirfenidone administration, 1 during LYT-100 administration

- In the January 2022 post-period, we announced Paul Ford, M.D., Ph.D., joined PureTech as SVP of Clinical Development to oversee the LYT-100 development program in IPF. Dr. Ford is an experienced clinical pulmonologist with more than 20 years of research and development expertise dedicated to IPF and other respiratory conditions. He has built and advanced programs from early-to late-stage development at companies including Novartis, Galapagos and Galecto, and he has been instrumental in the enrollment of nearly 1,500 patients with IPF across several clinical studies.
- In November 2020, we announced the completion of a Phase 1 randomized, double-blind multiple ascending dose (MAD) and food effect study, which was designed to evaluate the safety, tolerability and PK profile of LYT-100 in healthy volunteers. The study demonstrated favorable proof-of-concept for the tolerability and PK profile of LYT-100. In August 2021, we presented the results of the study at the virtual European Respiratory Society (ERS) International Congress. In November 2021, the full study was published in *Clinical Pharmacology in Drug Development*.
  - All AEs that were possibly or probably related to LYT-100 were mild and transient and there were no discontinuations. No serious AEs or dose-limiting toxicities were observed in the study. The maximum tolerated dose was not determined after dosing up to 1,000 mg twice per day.
  - The food effect portion of the study evaluated two common PK measures that are used to determine the optimal dose of a therapeutic candidate – area under the curve (AUC) and Cmax. Under fed conditions, the AUC of LYT-100 was reduced by about 19%, which is comparable to the AUC reduction of 16% seen with pirfenidone as stated in the Esbriet® U.S. Prescribing Information. The Cmax reduction observed with LYT-100 was 23%, while the Cmax reduction seen with pirfenidone was 49% as stated in the Esbriet® (pirfenidone) U.S. Prescribing Information.
- In 2021, we initiated additional Phase 1 clinical trials to further evaluate the PK, dosing and tolerability of LYT-100 in healthy volunteers and healthy older adults to inform the clinical development of LYT-100 across multiple indications. Results from these studies demonstrated that LYT-100 was well-tolerated at 824mg TID dosing with low rates of GI AEs that were comparable to placebo. These results will further inform our dose-ranging study design in treatment-naïve IPF patients.
- In April 2021, we announced the formation of a Clinical Advisory Board for IPF and other PF-ILDs. These physicians and researchers with deep expertise in the clinical development of novel therapies in PF-ILDs include Bill Bradford, M.D., Ph.D., biopharma advisor with broad expertise in drug development; Vincent Cottin, M.D., Professor of Respiratory Medicine at Université Claude Bernard Lyon and Coordinator of the National Coordinating Reference Center for Rare Pulmonary Diseases at Louis Pradel Hospital, Hospices Civils de Lyon, Lyon, France; Kevin Flaherty, M.D., Professor at the University of Michigan specializing in IPF and other ILDs; Toby Maher, M.D., Ph.D., Professor of Clinical Medicine and Director of Interstitial Lung Disease at Keck School of Medicine of the University of Southern California; Paul Noble, M.D., Chair of the Department of Medicine at Cedars-Sinai Medical Center and a noted researcher in lung inflammation and fibrosis; and Marlies Wijsenbeek, M.D., Ph.D., pulmonary physician at the Erasmus Medical Center.
- Long COVID (PACS) respiratory complications and related sequelae
  - In December 2020, we announced the initiation of a global, randomized, double-blind, placebo-controlled Phase 2 trial to evaluate the efficacy, safety and tolerability of LYT-100-COV in adults with Long COVID respiratory complications and related sequelae.
  - In 2021, we initiated the open-label extension of the LYT-100-COV Phase 2 trial in patients who completed the first portion of the trial. The primary endpoint of the extension trial will measure change in distance walked on the 6MWT, with secondary endpoints to assess the longer-term safety and tolerability of LYT-100 up to 182 days of treatment.
  - In preclinical rodent studies, LYT-100 was observed to suppress levels of IL-6 and TNF-alpha induced by lipopolysaccharide administration, which we believe reinforces the potential of LYT-100 to reduce the acute inflammation and cytokine release that has been associated with SARS-CoV-2 infection. Anti-fibrotic activity was also observed with LYT-100 in preclinical studies. Lung fibrosis has also been observed in some patients following the acute phase of COVID-19. For more information on our clinical trial, visit ClinicalTrials.gov.

19 44 completed study (5 early terminated: 2 for AEs, 3 for non-medical reasons).

20 Chen, M.C., Korth, C.C., Harnett, M.D., Elenko, E. and Lickliter, J.D. (2022), A Randomized Phase 1 Evaluation of Deupirfenidone, a Novel Deuterium-Containing Drug Candidate for Interstitial Lung Disease and Other Inflammatory and Fibrotic Diseases. Clinical Pharmacology in Drug Development. https://doi.org/10.1002/cpdd.1040.

21 LYT-100 was administered in doses of 100 mg, 250 mg, 500 mg, 750 mg and 1000 mg BID over five days.

Milestones Achieved & Development Status (continued)	• Lymphedema – In December 2020, we announced the initiation of a Phase 2a proof-of-concept study of LYT-100-LYMPH in patients with breast cancer-related, upper limb secondary lymphedema. The primary endpoint of the study is safety and tolerability of LYT-100-LYMPH. Secondary endpoints include outcome measures relevant to lymphedema, including relative limb volume, bioimpedance spectroscopy (a measure of extracellular fluid change), tonometry (a measure of fibrosis) and serum levels of inflammatory and fibrotic biomarkers. The study will also examine patient reported outcomes using validated self-report instruments specific to upper-arm lymphedema. The study is not adequately powered to evaluate drug effect versus placebo with statistical significance, but we believe the totality of the data will be suitable to inform the design of future clinical protocols. For more information on our clinical trial, visit ClinicalTrials.gov. – In preclinical studies, LYT-100 showed greater anti-fibrotic and anti-inflammatory activity compared to pirfenidone. Additionally, LYT-100 was tested by one of our academic collaborators in a preclinical model of lymphedema which showed that LYT-100 halted progression of lymphedema and reduced the overall volume of the affected area. These results still need to be confirmed in clinical trials.
Expected Milestones	• We plan to initiate a Phase 2 dose-ranging trial of LYT-100 in patients with IPF in the first half of 2022 with topline results expected by the end of 2023. We also plan to pursue a streamlined development program for LYT-100 in IPF, capitalizing on efficiencies of the 505(b)(2) pathway. Pending positive clinical and regulatory feedback, the program will advance into a Phase 3 study. We believe the results of the Phase 2 study, together with a Phase 3 study, could serve as the basis for registration in the U.S. • Topline results from the Phase 2 trial of LYT-100-COV in adults with Long COVID respiratory complications and related sequelae are anticipated in the first half of 2022. • We expect topline results from the Phase 2a proof-of-concept study of LYT-100-LYMPH in patients with breast cancer-related, upper limb secondary lymphedema in 2022.
Intellectual Property	• As of December 31, 2021, the LYT-100 patent portfolio includes 31 active patents acquired, and one issued patent and one patent application licensed from Auspex. These patents and application provide broad coverage of compositions of matter, formulations and methods of use for deuterated pirfenidone, including the LYT-100 deupirfenidone compound, comprising six issued U.S. patents which are expected to expire in 2028 (without patent term extensions, which could extend the exclusivity to 2033), one U.S. patent which is expected to expire in 2035 and 25 patents issued in 23 foreign jurisdictions, without taking into account any possible patent term extension or regulatory exclusivities. We have also filed additional patent applications on deupirfenidone, including 13 pending U.S. patent applications, three international PCT applications and 13 foreign applications directed to the use of deuterated pirfenidone, including LYT-100, for the treatment of a range of conditions involving inflammation and fibrosis, including lung disease (IPF and Long COVID respiratory complications and related sequelae) and disorders of lymphatic flow, such as lymphedema. We expect that any issued patents claiming priority to these applications will expire in 2039 through 2042, exclusive of possible patent term adjustments or extensions or other exclusivities.

LYT-100 Program

Therapeutic Candidate[1]	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
LYT-100-ILD Deupirfenidone	IPF					
LYT-100-COV Deupirfenidone	Long COVID[2] respiratory complications and related sequelae					
LYT-100-LYMPH Deupirfenidone	Lymphatic flow disorders, including lymphedema					

Phase completed | Phase in progress | Registration-enabling studies to begin in 1H2022

LYT-200

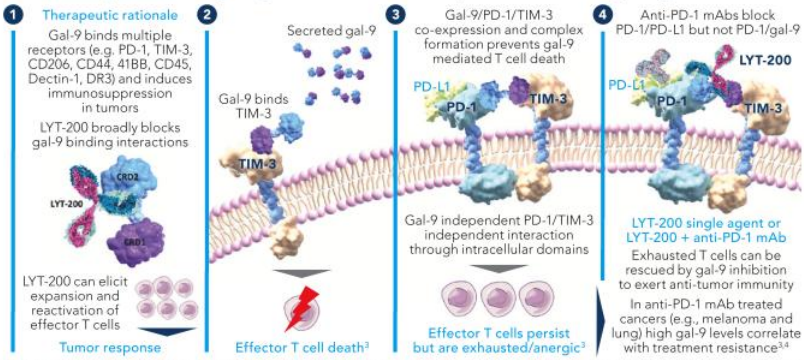
Therapeutic Candidate[1]	PureTech Ownership	Indication	Stage of Development
LYT-200	Wholly-owned	Solid tumors	Phase 1

- LYT-200 is a fully human IgG4 monoclonal antibody, or mAb, designed to inhibit the activity of galectin-9, a key molecule expressed by tumors and immune cells and shown to suppress the immune system from recognizing and destroying cancer cells. We are developing LYT-200 for difficult-to-treat cancer indications, including pancreatic ductal adenocarcinoma (PDAC), colorectal cancer (CRC) and cholangiocarcinoma (CCA).

Key Points of Innovation & Differentiation

- Immune checkpoint inhibitors, including therapies that target programmed cell death protein 1, or PD-1, programmed death ligand 1, or PDL-1, and cytotoxic T-lymphocyte-associated antigen 4, or CTLA-4, have been developed to counteract multiple mechanisms of immune evasion by a number of different tumor types. Recent reports suggest that marketed drugs against these targets had sales exceeding $28 billion in 2020[2]. Unfortunately, a large proportion of patients, especially those with immunologically silent tumors such as PDAC, CCA and some types of CRC respond sub-optimally to such agents.
- Galectin-9 promotes and facilitates multiple immunosuppressive pathways by, for example, expanding regulatory T cells, shifting macrophages from the M1 to M2 phenotype, and inducing apoptosis of activated CD4+ and CD8+ T cells. High expression of galectin-9 is evident in tumors and in cancer patients' blood and correlates with poor survival outcomes and aggressive disease in multiple solid tumor types. We are advancing LYT-200 to inhibit the multiple effects of galectin-9 and thereby potentially removing a key immunosuppressive barrier that would enable the immune system to attack and destroy the tumor.

Galectin-9 is a ligand for PD-1 regulating T cell death and immune responses in PD-1/PDL-1 expressing tumors



- A 2021 study published in *Nature Communications* proposed that the molecular mechanism by which PD-1 and galectin-9 interact to shield tumors from the immune system demonstrates for the first time that galectin-9 is a ligand for PD-1 and emphasizes its importance as a promising target for immunotherapy[3]. The work revealed that PD-1 physically interacts with galectin-9 and TIM-3 to attenuate galectin-9/TIM-3-induced T cell apoptosis and maintain effector T cells in the tumor microenvironment in an exhausted functional state. It also showed that interferons significantly upregulate galectin-9 expression and secretion in both immune and cancer cells. Overall, the work provided further evidence that galectin-9 acts as a key regulator of the immune response to tumors and supports its importance as a potential target for cancer treatment.
- Under normal physiological conditions, galectin-9 is expressed at low levels, which supports the potential safety of LYT-200 in clinical settings. Lack of toxicity/tolerability issues to date in our good laboratory practice (GLP) studies with LYT-200 – even at extremely high doses, such as 300 mg/kg in non-human primates (~100 mg/kg human equivalent dose) – further supports this view.
- We are not aware of any other clinical development program targeting galectin-9 as a therapeutic target, and thus, we believe that LYT-200 may represent the most advanced clinical program against this target. None of the other human galectins have been documented to play such a global role as galectin-9 in immunosuppression in the context of cancer. We also believe that LYT-200 has the potential to be used as a single agent and safely in combination with checkpoint inhibitors and other chemotherapeutics, depending on the cancer.

Program Discovery Process by the PureTech Team

- In order to identify approaches with the potential to provide significant therapeutic benefit to cancer patients, we undertook a global, proactive search to identify therapeutic targets that mediate multiple mechanisms of immunosuppression. Through our extensive network of advisors and collaborators, we identified a foundational immunosuppressive mechanism involving galectin-9, the therapeutic target of LYT-200, which was the basis of certain intellectual property that we licensed from New York University prior to publication in *Nature Medicine*[5].

Patient Need & Market Potential

- In the U.S., there are approximately 62,210 new pancreatic cancer patients, of which 52% present with metastatic disease, approximately 151,030 new CRC patients, of which 22% present with metastatic disease, and approximately 8,000 new CCA patients, of which 50% present with metastatic disease, in each case, per year. Unfortunately, a large proportion of patients, especially those with immunologically silent tumors such as PDAC, CCA and some types of CRC respond sub-optimally to immune checkpoint inhibitors, representing a significant patient population that has yet to receive benefit from any immuno-therapy agents.

Milestones Achieved & Development Status

- In November 2021, the FDA granted orphan drug designation to LYT-200 for the treatment of pancreatic cancer. The FDA grants orphan drug designation to novel drug and biologic products for the treatment, diagnosis or prevention of conditions affecting fewer than 200,000 persons in the U.S. Orphan drug designation qualifies PureTech for incentives under the Orphan Drug Act, including tax credits for some clinical trials and eligibility for seven years of market exclusivity in the U.S. if the drug is approved, in addition to our broad intellectual property coverage which can extend the exclusivity into 2038.

1 We have an active IND on file with the FDA for LYT-200. The FDA and corresponding regulatory authorities will ultimately review our clinical results and determine whether our wholly-owned therapeutic candidates are safe and effective. No regulatory agency has made any such determination that LYT-200 is safe or effective for use by the general public for any indication.

2 GlobalData Sales and Forecast Database (2021).

3 Yang, Riyao, et al. "Galectin-9 Interacts with PD-1 and TIM-3 to Regulate T Cell Death and Is a Target for Cancer Immunotherapy." Nature Communications, 5 Feb. 2021, www.nature.com/articles/s41467-021-21099-2 (preclinical data).

4 Limagne, E., Richard, C., Thibaudin, M., Fumet, J. D., Truntzer, C., Lagrange, A., Favier, L., Coudert, B., & Ghiringhelli, F. (2019). Tim-3/galectin-9 pathway and mMDSC control primary and secondary resistances to PD-1 blockade in lung cancer patients. Oncoimmunology, 8(4), e1564505. https://doi.org/10.1080/2162402X.2018.1564505. (preclinical data).

5 Daley, D., Mani, V., Mohan, N. et al. Dectin 1 activation on macrophages by galectin 9 promotes pancreatic carcinoma and peritumoral immune tolerance. Nat Med 23, 556 – 567 (2017). https://doi.org/10.1038/nm.4314.

Milestones Achieved & Development Status (continued)

– In November 2021, we announced that a poster presentation describing the adaptive Phase 1/2 trial of LYT-200 for the potential treatment of difficult-to-treat solid tumors was given at the Society for Immunotherapy of Cancer (SITC) 36th Annual Meeting.

– In July 2021, we announced a clinical trial and supply agreement with an affiliate of BeiGene, Ltd. to evaluate BeiGene's tislelizumab, an anti-PD-1 monoclonal antibody, in combination with LYT-200. Under the terms of the agreement, we will maintain control of the LYT-200 program, including global R&D and commercial rights. BeiGene has agreed to supply tislelizumab for use in combination with LYT-200 for the planned Phase 2 study cohorts.

– In 2021, we progressed our adaptive Phase 1/2 clinical trial to evaluate LYT-200 as a potential treatment for metastatic solid tumors. The primary objective of the Phase 1 portion of the trial is to assess the safety and tolerability of escalating doses of LYT-200 in order to identify a dose to carry forward into the Phase 2 portion of the trial. The Phase 1 trial will also assess LYT-200's PK and PD profiles. Pending these results, we intend to initiate the Phase 2 expansion cohort portion of the trial, which is designed to evaluate LYT-200 either alone and/or in combination with BeiGene's tislelizumab or chemotherapy and anti-PD-1 therapy for the treatment of multiple solid tumor types, including pancreatic cancer and CCA. For more information on our clinical trial, visit ClinicalTrials.gov.

• Preclinical results

– LYT-200 has been observed to have high specificity for its primary target galectin-9: This was established using a protein array that assessed binding of LYT-200 to more than 5,000 cell bound and secreted human proteins.

– LYT-200 blocks the galectin-9-CD206 interaction: LYT-200 is able to block functional activity of galectin-9, including its interactions with a specific binding partner/receptor, e.g., CD206. This was established using an ELISA assay demonstrating a galectin-9/CD206 interaction, which could be inhibited by the addition of LYT-200.

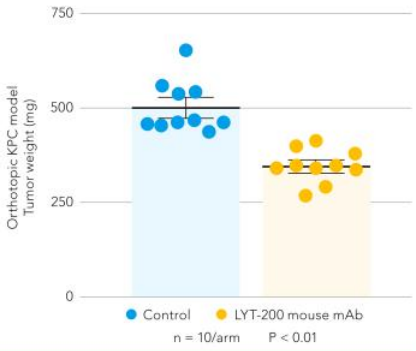
– LYT-200 protects MOLM-13 T cells from galectin-9-mediated apoptosis: LYT-200 has also been observed to protect T cells from apoptosis mediated by galectin-9. For example, galectin-9 was shown to significantly increase apoptotic death of MOLM-13 cells. Treatment with LYT-200 in the presence of galectin-9 significantly reduced the percentage of T cells undergoing apoptosis in a dose dependent manner.

– LYT-200 exceeded anti-PD-1 activity in the B16F10 melanoma model, a gold standard for measuring checkpoint inhibitor efficacy: To further characterize the potential of LYT-200 as a single agent, we created a mouse isotype of LYT-200 (mIgG1-200). mIgG1 200 (LYT-200 designed for mouse in vivo models) reduced mean tumor weights by approximately 50% while an anti-PD-1 antibody reduced mean tumor weights by approximately 22%, which is what is typically seen in the model. We also observed that when an anti-PD-1 antibody was used in combination with mIgG1-200, the number of tumor-infiltrating cytotoxic T cells detected in tumors approximately doubled. These data demonstrate efficacy of mIgG1-200, both as a single agent and in combination with a checkpoint inhibitor.

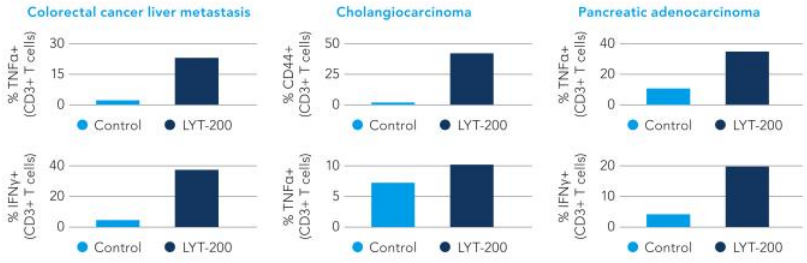
– LYT-200 inhibited tumor growth, induced T cell activation and increased survival in the orthotopic pancreatic cancer KPC model where anti-PD1 agents are ineffective: The orthotopic KPC mouse model is commonly used as a preclinical model for evaluating PDAC biology and therapeutic agent efficacy. Anti-PD-1 checkpoint inhibitors have previously proven ineffective in this syngeneic model. Single agent activity of mIgG1-200 was observed in the KPC mouse pancreatic cancer model as illustrated in the figure below. We have evaluated the combination of mIgG1 200 with the standard of care for pancreatic cancer, (e.g., chemotherapy: gemcitabine/nab-paclitaxel). We observed a clear survival improvement with mIgG1 200, both as a single agent and in combination with clinical standard of care chemotherapy.

– LYT-200 activates T cells in cultured patient-derived organoid tumors, or PDOTs: One of the major challenges in oncology research is the translation from mouse models to humans, particularly in the case of immuno-oncology. To address this concern, we explored LYT-200 activity in cultured PDOTs that mimic human tumor composition within the context of a tumor microenvironment. The aim of treating PDOTs was to assess the ability of LYT-200 to induce T cell activation, which may predict how LYT-200 would behave in humans. LYT-200 potently and reproducibly activated T cells in 56% of the samples tested (n=23).

LYT-200 mouse mAb activity in orthotopic pancreatic cancer KPC model



Examples of in vitro T cell activation with LYT-200[6]



– GLP toxicology studies were carried out in Sprague Dawley rats and cynomolgus monkeys. No safety pharmacology findings that were attributed to LYT-200 at doses as high as 300 mg/kg/week were observed with repeat dose exposure.

6 Analyzed n = 23 tumor samples; Success defined as: >20% upregulation of at last two out of three T cell activation markers; Success achieved in 56% of tumors with majority showing >2 fold activation; Representative data from individual tumors per annotated tumor type are shown.

Expected milestones	• LYT-200 is currently being evaluated as a single agent in the first stage of an adaptive Phase 1/2 clinical trial. Pending these results, we intend to initiate the Phase 2 expansion cohort portion of the trial, which is designed to evaluate LYT-200 both as a single agent and in combination with chemotherapy or BeiGene's tislelizumab, an anti-PD-1 mAb. We expect to report topline results from the Phase 1 portion in the first half of 2022.
Intellectual property	• We have broad intellectual property coverage for these antibody-based immunotherapy technologies, including exclusive rights to six families of patent filings that are exclusively licensed from or co-owned with New York University which cover antibodies that target galectin-9, including LYT-200, methods of using these antibodies and related immuno-oncology technologies. In addition, the intellectual property portfolio includes three families of PureTech-owned patent applications covering the use of anti-galectin-9 antibodies in the diagnosis and treatment of solid tumors. • As of December 31, 2021, there are nine families of intellectual property within this patent portfolio covering compositions of matter for antibodies targeting galectin-9, including LYT-200, and methods of use for the treatment of solid tumors, such as pancreatic cancer, CRC, melanoma, gastric cancer, breast cancer and various other cancers. This intellectual property comprises two issued U.S. patents which are expected to expire in 2038, 10 pending U.S. patent applications, which if issued, are expected to expire 2037-2042 (exclusive of possible patent term adjustments or extensions or other exclusivities), four international PCT applications, twenty-four pending foreign applications and five issued patents in foreign jurisdictions.

LYT-200 Program

Therapeutic Candidate[1]	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
LYT-200 Anti-Galectin-9 mAb	Solid tumors					

Phase completed Phase in progress

LYT-210

Therapeutic Candidate[1]	PureTech Ownership	Indication	Stage of Development
LYT-210	Wholly-owned	Solid tumors	Preclinical

- LYT-210 is a preclinical therapeutic candidate designed to target immunomodulatory gamma delta-1 T cells, and is being developed for a range of cancer indications.

Key Points of Innovation & Differentiation

- Immune checkpoint inhibitors, including therapies that target PD-1, PDL-1 and cytotoxic T-lymphocyte-associated antigen 4, or CTLA-4, have been developed to counteract multiple mechanisms of immune evasion by a number of different tumor types. Recent reports suggest that marketed drugs against these targets had sales exceeding $28 billion in 2020[2]. Unfortunately, a large proportion of patients, especially those with immunologically silent tumors such as PDAC, CCA and some types of CRC, respond sub-optimally to such agents.

Monoclonal antibody aimed at immunosuppressive gamma delta-1 T cells

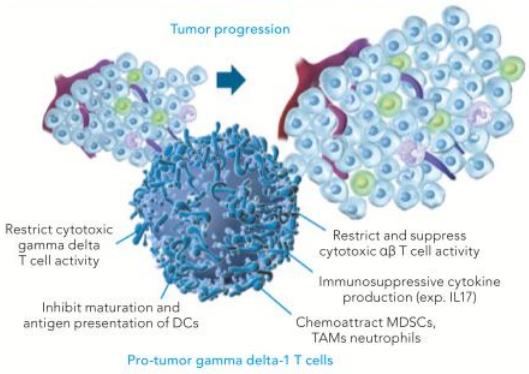
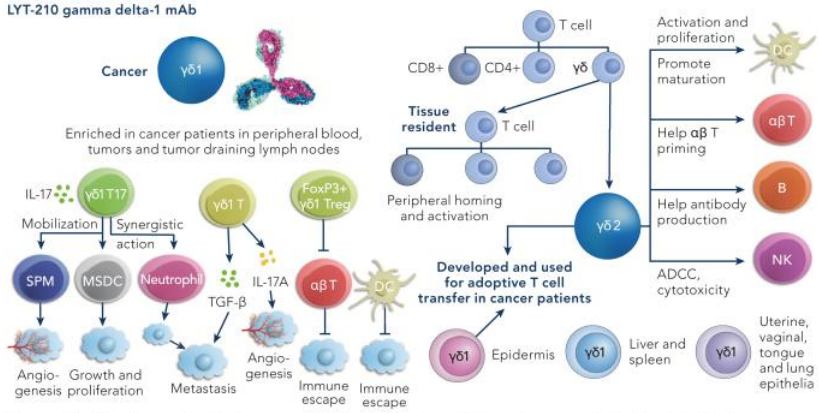


Image adapted from CellPress: REVIEW: gamma delta T cells: Unexpected Regulators of Cancer Development and Progression.

Key
DC = dendritic cell
TAM = tumor associated macrophage
MDSC = myeloid derived suppressor cell
IL17 = interleukin 17
αβ = alpha beta
γδ = gamma delta
γδ1 = gamma delta-1
γδ1 T17 = gamma delta interleukin 17 producing cells
γδ1 Treg = gamma delta-1 T regulatory cell
γδ2 = gamma delta-2
FoxP3 = forkhead box P3
SPM = small peritoneal macrophages
MSDC = myeloid derived suppressor cells
TGF-β = transforming growth factor beta
B = B cells
NK = natural killer cells
CD8+ = cluster of differentiation 8
CD4+ = cluster of differentiation 4

LYT-210 gamma delta-1 mAb



- Gamma delta-1 T cells execute potent immunosuppressive function via multiple mechanisms, as illustrated on the left side of the figure above (LYT-210 gamma delta-1 mAb), which facilitates cancer progression. We have designed LYT-210 to eliminate gamma delta-1 T cells, and thereby potentially relieve immunosuppression, which we believe could enable immune mediated cancer attack.
- We believe that gamma delta-1 T cells represent an important new IO target because they:
  - Activate multiple immunosuppressive pathways in the tumor microenvironment, or TME;
  - Have expression correlated with poor outcomes for multiple solid tumor types; and
  - Target immunosuppressive gamma delta T cells in vivo, which improved survival and reactivated cytotoxic T cells in the TME in the KPC orthotopic pancreatic cancer mouse model where approved checkpoint inhibitors are ineffective.
- We are targeting immunosuppressive, tumorigenic gamma delta-1 T cells for depletion, rather than administering cytotoxic gamma delta-2 T cells as a cell therapy, which is a complementary gamma delta T cell modality.

Program Discovery Process by the PureTech Team

- In order to identify approaches with the potential to provide significant therapeutic benefit to cancer patients, we undertook a global, proactive search to discover important new scientific insights and technologies that could address the challenge of multiple mechanisms of immunosuppression in current therapeutics. As a result of this search, and through our extensive network of advisors and collaborators, we identified a foundational immunosuppressive mechanism involving immunosuppressive gamma delta-1 T cells, which was the basis of LYT-210.

1 The FDA and corresponding regulatory authorities will ultimately review our clinical results and determine whether our wholly-owned therapeutic candidates are safe and effective. No regulatory agency has made any such determination that LYT-210 is safe or effective for use by the general public for any indication.
2 GlobalData Sales and Forecast Database, 2020 sales data pulled 1/24/2022.

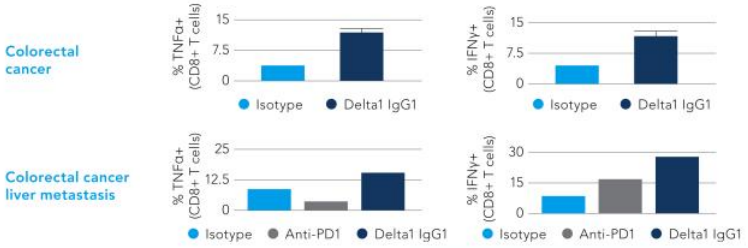
Patient Need & Market Potential

- In the U.S., there are approximately 62,210 new pancreatic cancer patients, of which 52% present with metastatic disease, approximately 151,030 new CRC patients, of which 22% present with metastatic disease, and approximately 8,000 new CCA patients, of which 50% present with metastatic disease, in each case, per year. Unfortunately, a large proportion of patients, especially those with immunologically silent tumors such as PDAC, CCA and some types of CRC respond sub-optimally to immune checkpoint inhibitors, representing a significant patient population that has yet to receive benefit from any immuno-therapy agents.

Milestones Achieved & Development Status

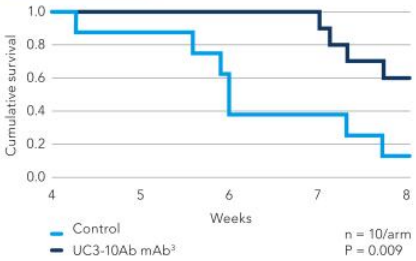
- In April 2021, we presented new research at the American Association for Cancer Research (AACR) Annual Meeting demonstrating that LYT-210 is both highly specific and highly potent, rapidly inducing cell death of immunomodulatory gamma delta-1 T cells, while sparing other T cells, such as cytotoxic gamma delta T cells, that play important roles in a healthy immune response. The research was conducted using both patient blood and cancer tissue.
- Antibodies against gamma delta-1 T cells reactivated immunosuppressed T cells in the TME in PDOTs: To better assess the potential activity of the anti-delta-1 antibody, we employed PDOTs from primary and metastatic tumors spanning various solid tumor types such as pancreatic, CRC, CCA, hepatocellular cancer and neuroendocrine tumors of the gastrointestinal (GI) tract in order to assess the prevalence of tumor-infiltrating gamma delta-1 T cells and the capacity of the antibodies to restore tumor-infiltrating immune cell effector activity. We observed positive responses in approximately 60% of the PDOTs we analyzed, representing 19 patients, which showed that direct treatment of PDOTs with LYT-210 resulted in robust reactivation of effector T cells.
- The figure below illustrates representative data from CRC patients, from a collection of 19 human tumor organoid samples where we ran this experiment.

Examples of *in vitro* T cell activation with antibodies against gamma delta-1 T cells



- Absence of gamma delta T cells greatly increased survival in a pancreatic cancer mouse model: In order to assess the relevance of gamma delta T cells in the development and progression of pancreatic cancer, we assessed the survival of immunocompetent mice which have gamma delta T cells (wild type) in a KPC mouse pancreatic model. Mice were treated with an antibody, UC3-10A6, which functionally blocks immunosuppressive mouse gamma delta T cells. As shown in the figure below, when mice harboring pancreatic tumors are treated with an antibody against immunosuppressive gamma delta T cells, survival was greatly increased, as represented by the navy curve.
- Mucosa-infiltrating pathogenic gamma delta-1 T cells may contribute to autoimmune diseases: Intraepithelial lymphocytes expressing gamma delta-1 T cells are tissue-resident T cells that play a key role in homeostasis of the intestinal epithelium. It has been recently observed that chronic inflammation can permanently reconfigure the tissue-resident T cell compartment resulting in the repopulation of the GI mucosa with pathogenic and cytotoxic gamma delta-1 T cells. Establishment of pathogenic gamma delta-1 T cells along the GI tract tilts the gut environment towards a chronic inflammatory state, contributing to the pathophysiology of GI tract and inflammatory diseases, such as refractory celiac disease.

Pancreatic cancer mouse survival with gamma delta T cell depletion and blockage



Expected Milestones

- We expect to complete additional biomarker studies for LYT-210 in 2022.

Intellectual property

- We have broad intellectual property coverage for these antibody-based immunotherapy technologies, including exclusive rights to two patent families that are exclusively licensed from or co-owned with New York University which cover antibodies that target immunosuppressive agents and mechanisms and methods of use for use related immuno-oncology technologies and antibodies directed to pro-inflammatory gamma delta T cells for use in the treatment of inflammatory conditions, such as autoimmune disorders.
- As of December 31, 2021, there are two families covering compositions of matter and methods of use for antibodies targeting gamma delta-1 T cells, including LYT-210, which are directed to the use of these antibodies for the treatment of cancer. This intellectual property in total comprises one granted U.S. patent, two pending U.S. patent applications and eight foreign patent applications. Any patents issuing from pending applications with respect to LYT-210 are expected to expire in between 2037 and 2041, of which expiration dates are exclusive of possible patent term adjustments or extensions or other periods of exclusivity.

LYT-210 Program

Therapeutic Candidate[1]	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
LYT-210 Anti-Delta-1 mAb	Solid tumors					

Phase completed Phase in progress

3 Tool antibody that blocks mouse immunosuppressive gamma delta T cells.

LYT-300

Therapeutic Candidate[1]	PureTech Ownership	Indication	Stage of Development
LYT-300	Wholly-owned	Neurological and neuropsychological conditions	Phase 1

- Using our Glyph platform, which harnesses the natural trafficking of dietary lipids via the lymphatics, we have developed LYT-300, an oral lipid prodrug version of allopregnanolone. By trafficking LYT-300 via the lymphatics, we are able to overcome first-pass metabolism by the liver and achieve significant oral bioavailability of natural allopregnanolone in preclinical models. In 2021, we initiated a Phase 1 clinical study of LYT-300 in healthy volunteers as part of our ongoing strategy for developing this agent as a potential treatment for neurological and neuropsychological conditions with significant unmet need, such as depression, anxiety, sleep disorders, fragile X tremor-associated syndrome, essential tremor and epileptic disorders, among others.

Key Points of Innovation & Differentiation

- Allopregnanolone, a positive allosteric modulator of $GABA_A$ receptors, has therapeutic potential across a wide range of neurological conditions like depression, epilepsy and other neurological and neuropsychological conditions, but has poor oral bioavailability as a result of first-pass liver metabolism.
- An intravenous formulation of allopregnanolone is approved by the FDA as a 60-hour infusion for the treatment of post-partum depression, though the method of administration has limitations.
- To overcome the poor oral bioavailability of allopregnanolone, medicinal chemistry approaches have been applied to synthesize orally bioavailable analogs. Several of these modified allopregnanolone analogs have demonstrated varying degrees of clinical activity across different indications. The variable clinical activity of these compounds may be due to the possibility that chemical modifications are interfering with optimal $GABA_A$ receptor engagement and consequently their on-target mode of action. Hence, these chemically distinct analogs of allopregnanolone may not have the same pharmacologic effects as the natural unmodified allopregnanolone.
- Using our proprietary Glyph technology, which is designed for lymphatic targeting and to avoid first-pass metabolism, we have developed LYT-300, an oral prodrug of the endogenous, natural neurosteroid, allopregnanolone.
- Results from preclinical studies conducted thus far have demonstrated that LYT-300 is orally bioavailable and that relevant concentrations may be achievable in human plasma. One example of the data we have generated in non-human primates is shown below.

Program Discovery Process by the PureTech Team

- LYT-300 is the most advanced therapeutic candidate developed from our synthetic lymphatic-targeting chemistry platform called Glyph, which employs the body's natural lipid absorption and transport process to orally administer drugs via the lymphatic system.

Patient Need & Market Potential

- Allopregnanolone and related endogenous neurosteroids have been recognized for their potential to treat a range of neurological and neuropsychological conditions including depression, anxiety, sleep disorders, fragile X tremor-associated syndrome, essential tremor and epileptic disorders, among others. The major hurdles associated with the translation of these compounds have been:
  - The inability to create oral formulations of these neurosteroids; and
  - The inability to chronically administer compounds to patients
- An injectable formulation of allopregnanolone, which was approved by the FDA as a 60-hour infusion to treat postpartum depression, speaks to the challenges that limit the scope of clinical translation with this class of compounds.
- Oral formulations of allopregnanolone and other neurosteroids could potentially have significant advantages for the potential treatment of a range of neurological and neuropsychological conditions.

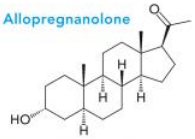
LYT-300: Oral Allopregnanolone for Neurological and Neuropsychological Conditions

The graph below depicts the dose-normalized plasma levels of free allopregnanolone after a single oral drug administration (equivalent to 2.8 mg/kg allopregnanolone) to non-human primates that were fed a standardized diet prior to dosing:

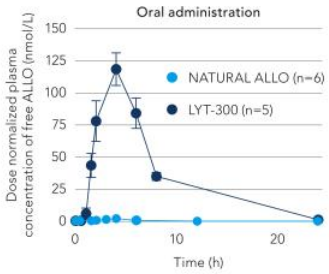
Brexanalone for IV injection
marketed as Zulresso®[2]

Required 60-hr IV infusion limits usage

Allopregnanolone



LYT-300 Systemic Exposure
Non-Human Primate



LYT-300 Development Rationale

- Designed to avoid first-pass metabolism by trafficking via the lymphatic system
- Oral bioavailability observed in canine and non-human primate PK studies
- Results from Phase 1 clinical study expected in 2H 2022

Oral administration

1 The FDA and corresponding regulatory authorities will ultimately review our clinical results and determine whether our wholly-owned therapeutic candidates are safe and effective. No regulatory agency has made any such determination that LYT-300 is safe or effective for use by the general public for any indication.

2 Zulresso® is a trademark of Sage Therapeutics and is not owned by or affiliated with PureTech Health. LYT-300 is an investigational drug not approved by any regulatory authority.

Milestones Achieved & Development Status	• In December 2021, we initiated a Phase 1 clinical study of LYT-300 in healthy volunteers as part of our ongoing strategy to develop this agent as potential treatment for neurological and neuropsychological conditions, including depression, anxiety, sleep disorders, fragile X tremor-associated syndrome, essential tremor and epileptic disorders, among others. The Phase 1 study of LYT-300 involves multiple parts, including the evaluation of a single ascending dose, multiple ascending doses and the effect of food on oral absorption of the prodrug. Safety, tolerability and PK will be assessed. Given the $GABA_A$ receptor modulating activity of allopregnanolone, the study will also explore the impact of LYT-300 on beta-EEG, a marker of $GABA_A$ target engagement, thus potentially providing early insights into the mechanistic effects of LYT-300. • In December 2021, we presented preclinical proof-of-concept data at the 60th American College of Neuropsychopharmacology (ACNP) Annual Meeting that support the clinical advancement of LYT-300 for the potential treatment of neurological and neuropsychological conditions. The data presented at ACNP showed that systemic exposure of natural allopregnanolone was achieved after oral administration of LYT-300 in multiple preclinical models of increasing complexity. In contrast, systemic levels of allopregnanolone were not observed following oral administration of natural unmodified allopregnanolone. These results demonstrate the potential of the Glyph technology platform to enhance the systemic absorption of natural bioactive molecules and other small molecules with poor oral bioavailability. • Oral bioavailability of LYT-300 has been confirmed in small and large animal PK studies. Results support the potential utility of this prodrug approach for oral administration of natural allopregnanolone and other small molecule therapeutics with intrinsic liabilities related to hepatic first-pass metabolism.
Expected Milestones	• Results from the Phase 1 clinical study of LYT-300 are expected in the second half of 2022 and will be used to inform the design of possible future studies evaluating LYT-300 in indications that could include depression, anxiety, sleep disorders, fragile X tremor-associated syndrome, essential tremor and epileptic disorders, among others.
Intellectual Property	• Within the extensive Glyph intellectual property portfolio, which covers a wide range of novel linker chemistries, LYT-300 is specifically covered by four patent families comprising one international PCT application, seven foreign patent applications, and six U.S. patent applications as of December 31, 2021, two of which families are co-owned with Monash University and two of which are PureTech owned. Any patents to issue from these patent applications are expected to expire in 2039 or 2042, exclusive of possible patent term adjustments or extensions or other forms of exclusivity.

LYT-300 Program

Therapeutic Candidate[1]	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
LYT-300 Oral Allopregnanolone	Neurological and neuropsychological conditions					

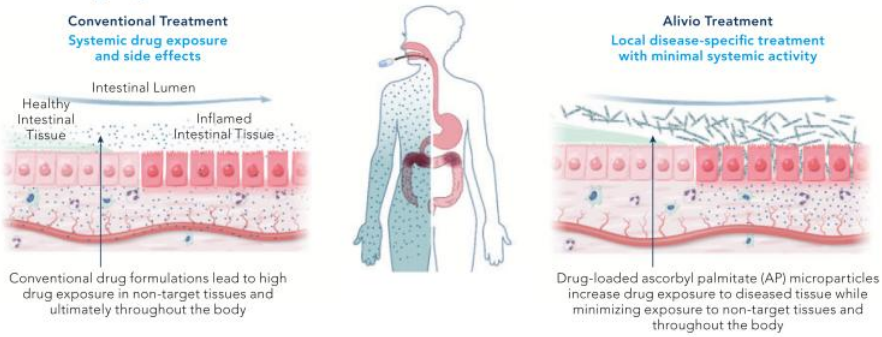
Phase completed Phase in progress

LYT-510, LYT-500

Therapeutic Candidate[1]	PureTech Ownership	Indication	Stage of Development
LYT-510	Wholly-owned	Inflammatory bowel disease and chronic pouchitis	Preclinical
LYT-500	Wholly-owned	Inflammatory bowel disease	Preclinical

- LYT-510 is our lead candidate generated from our Alivio™ technology platform and is an oral inflammation-targeting formulation of tacrolimus, a potent immunosuppressant drug, in development to treat inflammatory bowel disease (IBD) and chronic pouchitis. While tacrolimus is FDA-approved for certain indications, it has been evaluated in several clinical studies as a potential treatment for IBD, where it has demonstrated strong efficacy with high response and remission rates. However, despite the compelling efficacy, IBD patients are at risk for significant side effects due to systemic exposure, which has prevented tacrolimus' advancement for these indications. We believe that our oral formulation that targets tacrolimus to inflamed tissue, with minimal systemic exposure to healthy tissues, can overcome these limitations to potentially provide a safe and effective oral treatment for IBD patients. More broadly, this approach offers a path to unlocking the full therapeutic potential of multiple immunosuppressant and anti-inflammatory drugs that have well established clinical efficacy in a way that matches the chronic, variable expression of autoimmune diseases.
- LYT-500 is an oral combination therapy in development for IBD. Using our Alivio technology platform, we have combined two active agents into a single therapeutic candidate designed to enhance the local treatment and healing of inflamed tissues, while minimizing systemic exposure of these agents.

Inflammation-Targeting Immunomodulation Platform



Key Points of Innovation & Differentiation

- Using our Alivio technology platform, a biologic agent and/or small molecule drug can be administered in an oral dosage form that offers the potential to selectively act at the inflamed tissues locally to maximize efficacy, while minimizing toxicity by reducing systemic exposure of the drugs.
- LYT-510 is an oral inflammation-targeting formulation of tacrolimus in development to treat IBD and chronic pouchitis. Tacrolimus is a potent immunosuppressant drug that is FDA approved for prophylaxis of organ rejection in patients receiving allogeneic kidney, liver or heart transplants and topically for the treatment of atopic dermatitis. Clinical studies have demonstrated that tacrolimus can be an effective agent to induce remission in IBD patients following a short-term treatment regimen. However, the current tacrolimus products have found limited use because of a narrow therapeutic window, which has the potential to cause various systemic side effects including hypertension, paresthesia, neuropathy, renal impairment, and opportunistic infections. We believe that LYT-510 can overcome these clinical challenges by targeting tacrolimus to inflamed intestinal tissue and minimizing systemic exposure. With this enhanced PK profile, we believe that LYT-510 has the potential to be the first tacrolimus treatment approved for IBD in the U.S.
- LYT-500 is an oral therapeutic candidate in development for the potential treatment of mucosal barrier damage in people with IBD. It contains a unique combination of IL-22 and an immunosuppressant drug, which is designed to address the two key underlying causes of IBD pathogenesis and progression, namely mucosal barrier disruption and inflammation. Unlike many therapies in development for IBD, LYT-500 is designed with a dual mechanism of action to provide both mucosal repair and targeted resolution of tissue inflammation, which are critical for optimal disease management.

Program Discovery Process by the PureTech Team

- A key challenge faced in developing new drugs for the treatment of autoimmune and inflammatory disease is that attractive drug targets are frequently expressed in both diseased and normal tissue. Consequently, we are interested in identifying ways to address autoimmune disease in a more targeted manner. We have been inspired by the key observation that pathologic inflammation driven by dysfunctional immune signaling frequently manifests at specific sites in tissues and organs. However, the current treatments and therapeutic approaches act broadly to suppress the immune system throughout the body. This mismatch substantially limits the potential targets that can be pursued due to narrow therapeutic windows. Moreover, combining therapies to address multiple aspects of the autoimmune diseases is quite challenging due to both distinct and overlapping drug toxicity profiles. Working with leading scientists, we identified and in-licensed a technology platform in May 2016 that was created by Jeffrey Karp, Ph.D., Professor of Medicine at Harvard Medical School and Brigham and Women's Hospital, and Robert Langer, Sc.D., David H Koch Institute Professor at MIT. As demonstrated in multiple publications, our Alivio technology platform can be used to develop therapeutic candidates that selectively target inflamed tissues and release drugs in proportion to the severity of inflammation.

Patient Need & Market Potential

- IBD is estimated to affect approximately 3.9 million people in the U.S.[2], with monoclonal antibody therapies being the preferred treatment option for patients with moderate-to-severe disease. However, these therapies must be provided through multiple injections over time and are associated with several limitations including a lack of efficacy for some patients, dose-limiting AEs, loss of efficacy over time via anti-drug antibody development and the potential for opportunistic infections or malignancies.
- We believe that an ideal solution for treating IBD and chronic pouchitis would be an oral drug therapy that targets multiple mechanisms of disease pathogenesis while minimizing the potential for systemic side effects. We believe LYT-510 and LYT-500, developed from our Alivio technology platform, can potentially fulfill this goal.

1 The FDA and corresponding regulatory authorities will ultimately review our clinical results and determine whether our wholly-owned therapeutic candidates are safe and effective. No regulatory agency has made any such determination that LYT-510 or LYT-500 are safe or effective for use by the general public for any indication.

2 Inflammatory Bowel Disease (IBD) in the United States. (2021, November 09). https://www.cdc.gov/ibd/data-statistics.htm

Milestones Achieved & Development Status	• In multiple preclinical IBD models, LYT-510 showed significant improvements in several efficacy endpoints compared to untreated controls. Furthermore, the inflammation-targeting properties were shown to result in very low systemic blood levels compared to the current immunosuppressant formulations, which minimizes the potential for systemic side effects. • In 2020, the U.S. Department of Defense (DOD) Technology/Therapeutic Development awarded $3.3 million to support the advancement of LYT-510 into the clinic. • Progress in the preclinical development of LYT-500 is demonstrated by the following achievements: – We have developed an inflammation-targeting IL-22 composition with analytical data to support high IL-22 loading, high encapsulation efficiency, preservation of biologic activity, enzyme-mediated drug release and stability in simulated intestinal fluids. In addition, we have a comparable data set for an inflammation-targeting composition that combines IL-22 with an immunosuppressant drug. – We have completed initial preclinical evaluation of an inflammation-targeting IL-22 composition in a preclinical IBD model, where we demonstrated improvement in multiple endpoints related to mucosal healing. – We have demonstrated efficacy of the inflammation-targeting drug combination in a rodent IBD model, with improvements observed across several endpoints related to mucosal healing and inflammation. – We have developed oral dosage forms to enable preclinical testing of the inflammation-targeting IL-22 alone and in combination with an immunosuppressant drug and have initiated animal studies to evaluate their efficacy.
Expected Milestones	• We intend to file for regulatory approval to initiate first-in-human studies at year end 2022 and initiate a clinical study evaluating LYT-510 as a single agent for the potential treatment of IBD and chronic pouchitis in early 2023. • We expect preclinical proof-of-concept data for LYT-500 in the first half of 2022.
Intellectual Property	• The intellectual property portfolio supporting LYT-510 and LYT-500 consists of coverage around both the broader inflammation-targeting platform and the specific drug combination candidate. Platform intellectual property is supported by one patent family that has been exclusively licensed from the Brigham and Women's Hospital, which includes seven issued patents to date and five pending applications within and outside the U.S. In addition, intellectual property specific to the LYT-510 and LYT-500 candidates includes two patent families which are owned by Alivio that consist of 13 patent applications within and outside the U.S.

LYT-510 and LYT-500 Programs

Therapeutic Candidate[1]	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
LYT-510 Oral Immunosuppressant	IBD/Chronic pouchitis					
LYT-500 Oral IL-22 + Immunosuppressant	IBD					

Phase completed Phase in progress

LYT-503/IMB-150

Therapeutic Candidate[1]	PureTech Ownership	Indication	Stage of Development
LYT-503/IMB-150 (Partnered program)	Wholly-owned (licensed)	Interstitial cystitis/bladder pain syndrome	Preclinical

- LYT-503/IMB-150 is being advanced through a collaboration with Imbrium Therapeutics for the potential treatment of IC/BPS. LYT-503/IMB-150 was developed using our Alivio technology platform, which involves selectively restoring immune homeostasis at inflamed sites in the body while reducing their impact on the rest of the body's immune system. This long sought-after approach has the potential to broadly enable new medicines to treat a range of chronic and acute inflammatory disorders, including drugs whose use has been limited due to issues of systemic toxicity or problematic PK profiles.

Key Points of Innovation & Differentiation	• To achieve our vision of selective immunomodulation, we are advancing our proprietary Alivio technology platform centered on a class of self-assembling therapies that selectively bind to inflamed tissue. The platform allows for the development of inflammation-targeting therapeutic candidates using a wide array of active pharmaceutical ingredients, or APIs, including small molecules, biologics and nucleic acids. Using this technology, LYT-503/IMB-150 is designed to provide local therapy at the inflamed lesions along the bladder surface of IC/BPS patients while minimizing the potential for related systemic toxicities.
Program Discovery Process by the PureTech Team	• A key challenge in new drug development for autoimmune and inflammatory disease is that attractive drug targets are frequently expressed in both diseased and normal tissue. Consequently, we were interested in identifying ways to address autoimmune disease in a targeted manner such that healthy cells and tissues are not impacted by the drug. We were inspired by the key observation that pathologic inflammation frequently manifests at specific sites in tissues and organs and is driven by dysfunctional immune signaling. However, traditional approaches act broadly to suppress the immune system throughout the body affecting both the disease and healthy tissues. The current approaches therefore substantially limit the potential targets that can be pursued due to narrow therapeutic windows. Working with leading scientists, we identified and in-licensed a technology platform in May 2016 that was created by Jeffrey Karp, Ph.D., Professor of Medicine at Harvard Medical School and Brigham and Women's Hospital, and Robert Langer, Sc.D., David H Koch Institute Professor at MIT. As demonstrated in multiple publications, our Alivio technology platform can be used to develop therapeutic candidates that selectively target inflamed tissues and release drugs in proportion to the severity of inflammation.
Patient Need & Market Potential	• IC/BPS is a chronic bladder condition that consists of discomfort or pain in the bladder or surrounding pelvic region and is often associated with frequent urination. It is estimated to affect four million to 12 million people in the U.S. Current treatments fail to control pain in many patients.
Milestones Achieved & Development Status	• In December 2018, we entered into an option and license agreement with Imbrium Therapeutics to advance LYT-503/IMB-150 through clinical development and potential commercialization as a treatment for IC/BPS. • In August 2021, we announced that Imbrium Therapeutics had exercised its license option to develop LYT-503/IMB-150. PureTech received an option exercise payment of $6.5 million and is eligible to receive up to $53 million in additional development milestone payments for this program and royalties on potential product sales.
Expected Milestones	• Imbrium is planning to file an IND application for LYT-503/IMB-150 in 2022.
Intellectual Property	• The intellectual property portfolio supporting LYT-503/IMB-150 consists of coverage around both the Alivio technology platform and the drug candidate. Platform intellectual property is supported by one patent family, which has been exclusively licensed from the Brigham and Women's Hospital and includes seven issued patents and two pending applications within and outside the U.S. Intellectual property specific to the LYT-503/IMB-150 candidate. In addition, the LYT-503/IMB-150 IP includes one patent family which is owned by Alivio that consists of two issued patents and five applications within and outside the U.S.

LYT-503/IMB-150 Program

Therapeutic Candidate[1]	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
LYT-503/IMB-150 (Partnered program) Non-opioid	Interstitial cystitis/bladder pain syndrome (IC/BPS)					

Phase completed Phase in progress

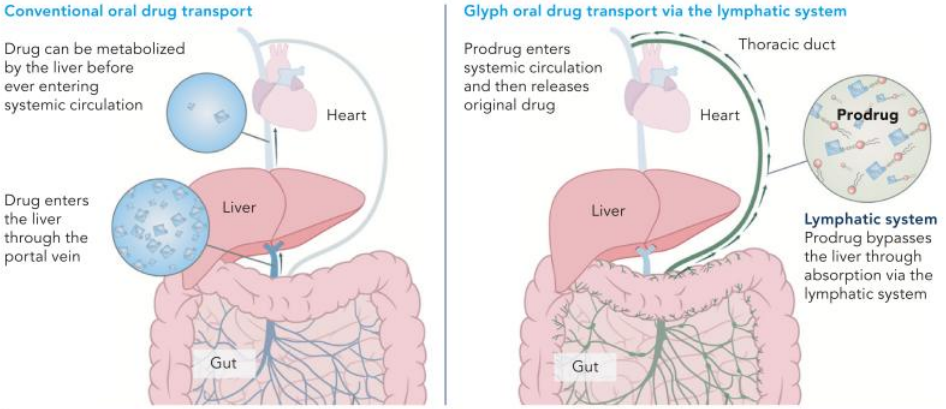
1 The FDA and corresponding regulatory authorities will ultimately review our clinical results and determine whether our wholly-owned therapeutic candidates are safe and effective. No regulatory agency has made any such determination that LYT-503/IMB-150 is safe or effective for use by the general public for any indication. On July 23, 2021, Imbrium Therapeutics exercised its option to license LYT-503/IMB-150 pursuant to which it is responsible for all future development activities and funding for LYT-503/IMB-150.

Glyph™: Lymphatic Targeting Chemistry Platform

Therapeutic Candidate	PureTech Ownership	Description
Glyph Technology Platform	Wholly-owned	Lymphatic-targeting chemistry platform leveraging the body's natural lipid absorption and transport process to orally administer drugs via the lymphatic system

- We are advancing a synthetic lymphatic-targeting chemistry platform called Glyph, which is designed to employ the lymphatic system's natural lipid absorption and transport process and has led to the nomination of LYT-300 for continued expansion of our Wholly Owned Pipeline. Consumed nutrients and most orally administered pharmaceuticals are initially absorbed by the small intestine mucosa, distributed to the liver by the portal vein before entering systemic circulation. Importantly, many consumed dietary lipids, particularly triglycerides, enter systemic circulation by an alternate route. Triglycerides, which are composed of three fatty acid chains tethered to a 3-carbon glycerol molecule, are absorbed by small intestine mucosal enterocytes where they are incorporated into large lipid-protein complexes (chylomicrons) and released into the submucosa. Chylomicrons are too large to enter blood vessels and are instead taken up by submucosal lymphatic vessels. Once in the lymphatic vessels, they are transported to mesenteric lymph nodes associated with the GI tract where they pass into larger lymphatic vessels connected to the thoracic duct, then merge with systemic circulation as illustrated in the figure below on the right. This is in contrast to conventional systemic circulation via the gut and liver as shown in the figure below on the left.

Glyph: A synthetic lymphatic-targeting chemistry platform



- Our proprietary Glyph technology platform takes advantage of the fact that one of the triglyceride-associated fatty acids remains bound to dietary lipids during intestinal absorption, chylomicron conversion, lymphatic vessel uptake and eventual transport into the circulatory system. Using a modular set of proprietary chemical entities, small molecule pharmaceutical compounds can be attached to triglycerides where, following oral administration, the small molecule is directed into the mesenteric lymphatic system and on to systemic circulation. The process of drug release from the triglyceride is governed by self-cleaving chemical structures, with different release-timing features, that tether the small molecule to the module connected to the triglyceride. The figure below is a representation of the proprietary chemistry for the design of our lymphatic targeting technology. The active pharmaceutical ingredient (API) is meant to indicate an example of a pharmaceutical small molecule that is attached to the triglyceride group (Glyceride in the figure on the next page) using proprietary linker chemistry (linker in the figure on the next page) to create a prodrug of the API. The prodrug also includes a proprietary self-immolative or cleaving chemistry (SI in the figure on the next page) that can be tuned to release the API in its intact original form.

Key Points of Innovation & Differentiation

- We believe this platform provides the following capabilities:
  - Targeting the mesenteric lymphatics: This lymphatic targeting technology has important features that offer potential advantages in the creation of orally-administered medicines, especially those that need to reach immune system drug targets present in the GI tract mucosa and submucosa, such as intestine-associated immune cells, or in the mesenteric lymphatic vasculature, such as circulating immune cells, and mesenteric lymph nodes, such as lymph node stromal cells, antigen-presenting cells and lymph node-associated immune cells.
  - Enabling and enhancing oral bioavailability by bypassing first-pass metabolism: We believe this technology could provide a broadly applicable modular means to potentially enable oral administration of a range of bio-active natural molecules, such as neurosteroids, cannabinoids, and a large number of parenterally administered drugs, that are otherwise not orally bioavailable. This technology also has the potential to significantly enhance the bioavailability of orally-administered drugs that suffer from substantial first-pass hepatic metabolism, especially those utilized in combination therapies, that act as modulators (inducers and/or inhibitors) of drug-metabolizing systems in the liver.

Program Discovery Process by the PureTech Team

- We sought out different approaches that could selectively traffic therapeutic molecules through the lymphatic system to target immune cells in the lymph nodes. Based on insights gained internally and via unpublished findings through our network of collaborators, we became aware of certain technology being developed at Monash University that had the potential to selectively target the lymphatic system. We obtained an exclusive license to this technology and the related intellectual property from Monash University. We have since further developed the platform and have generated our own intellectual property associated with the Glyph technology platform.
- We have developed an oral lipid prodrug of natural allopregnanolone, LYT-300, which is our first therapeutic candidate derived from our Glyph platform designed to treat a range of neurological and neuropsychological conditions such as depression, anxiety, sleep disorders, fragile X tremor-associated syndrome, essential tremor and epileptic disorders, among others.

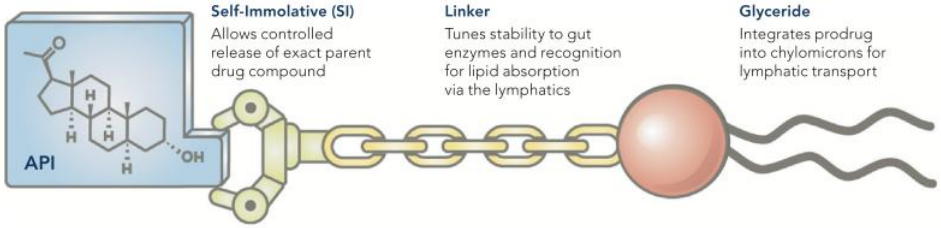
Milestones Achieved & Development Status

- In September 2021, preclinical proof-of-concept research was published in *Nature Metabolism*, which provides further support for the therapeutic potential of our Glyph technology platform[1]. The study showed for the first time that restoring normal function of the mesenteric lymphatics may reverse insulin resistance and modify obesity-associated metabolic disease. The study also found that inhibition of COX-2 and VEGF-C signaling within the mesenteric lymphatics resulted in a repatterning of the lymphatic vasculature, which in turn led to reduced branching and significantly less leakage of lymphatic fluids rich in lipids and pro-inflammatory mediators. Targeted inhibition of COX-2 function with a celecoxib prodrug developed using our lymphatic targeting Glyph technology platform led to a normalization of multiple biomarkers, including VEGF-C concentrations specifically within mesenteric lymph and surrounding adipose tissue, and to levels observed in control animals that were not fed a high-fat diet. This correlated with reduced lymphatic vessel branching and leakage as well as restoration of glycemic control, and weight gain was blocked in the animals fed a high-fat diet. In fact, targeted administration of the celecoxib Glyph prodrug led to a 10-fold greater uptake of celecoxib in mesenteric lymph and more effective restoration of lymphatic function and glycemic control compared to the administration of unmodified celecoxib, which is commercially available.
- In February 2021, preclinical proof-of-concept for our Glyph technology platform was published in the *Journal of Controlled Release*[2]. The additional results highlighted in the publication support the ability of the platform to target administration of drugs such as mycophenolic acid (MPA), an immunosuppressant, into lymph and directly into gut-draining mesenteric lymph nodes (MLNs). As a key nexus of immune cell trafficking, MLNs play major roles in the pathophysiology of a range of conditions including inflammatory and autoimmune diseases, cancer and metabolic diseases. As published, oral administration of a Glyph-based prodrug of MPA (Glyph-MPA) resulted in a >80-fold increase in uptake of total MPA into the lymphatic system and a >20-fold increase in MPA concentrations in MLNs relative to what was achieved with oral dosing of free MPA. Furthermore, MPA administered orally as Glyph-MPA was significantly more potent than free MPA in inhibiting T cell proliferation in mice challenged with antigen. Plasma levels were similar with Glyph-MPA and MPA, indicating low potential for the emergence of new systemic side effects. Additionally, a prodrug of a fluorescent tracer was shown to rapidly accumulate in MLNs following administration. Together, these findings provide further support of the potential of our Glyph technology for oral administration of small molecule drugs directly to the lymphatic system, including drugs with immunomodulatory properties.
- In the April 2022 post-period, preclinical proof-of-concept research was published in *Frontiers in Pharmacology*, which demonstrated our Glyph platform can enhance the oral bioavailability of buprenorphine, a clinically-validated opioid replacement therapy, further expanding the range of clinically-validated drug classes shown to be amendable to the Glyph technology.
- We have successfully extended our lymphatic targeting platform to encompass more than 20 molecules as well as a range of novel linker chemistries that have demonstrated promising lymphatic targeting in preclinical studies. We expect to select therapeutic candidates from this and ongoing discovery work.
- We believe the Glyph technology platform could provide a broadly applicable modular means to potentially enable oral administration of a range of bio-active natural molecules, such as neurosteroids, cannabinoids and a large number of parenterally administered drugs that are otherwise not orally bioavailable, or such as orally-administered drugs that suffer from substantial first-pass hepatic metabolism or those drugs, especially those utilized in drug combination therapies, that act as modulators (inducers and/or inhibitors) of drug-metabolizing systems in the liver. To demonstrate the utility of our Glyph lipid prodrug platform, we chose a natural bio-active neurosteroid allopregnanolone as the subject of our inquiry, which has resulted in the LYT-300 program. However, we believe that this benefit has the potential to be widely applied to nearly any natural molecules or therapeutic compatible with the synthetic approach which suffers from hepatic first-pass metabolism as has been evaluated by us and our collaborators.

Intellectual property

- We have broad intellectual property coverage for our proprietary Glyph technology platform, which includes exclusively licensed and co-owned patent applications, as well as company-owned patent applications. These patent applications cover compositions of matter, methods of use and methods of treatment encompassing specific chemical modifications, including a wide range of novel linker chemistries, as well as various classes of lymphatic targeting therapeutics, which include prodrugs for a large number of APIs, for use in the treatment of a wide range of diseases and disorders. The most advanced of these is LYT-300, which is an oral form of FDA-approved allopregnanolone, a natural neurosteroid, that we believe may be applicable to a range of neurological conditions.
- As of December 31, 2021, our Glyph technology platform intellectual property portfolio consists of 17 patent families comprising 19 U.S. patent applications, 20 foreign patent applications and three foreign patents. Of these, company-owned intellectual property consists of nine U.S. patent applications in nine patent families. We exclusively licensed and co-own a patent portfolio of eight patent families comprising 33 U.S. and foreign patent applications and three foreign patents from Monash University. Any patents to issue from the in-licensed patent applications are expected to expire in 2035-2036 and any issued patents from the co-owned and company-owned patent applications are expected to expire in 2038-2042, exclusive of possible patent term adjustments or extensions or other forms of exclusivity.

Schematic representation of our lymphatic targeting prodrug technology



1 Cao, E., Watt, M.J., Nowell, C.J. et al. Mesenteric lymphatic dysfunction promotes insulin resistance and represents a potential treatment target in obesity. Nat Metab 3, 1175–1188 (2021). https://doi.org/10.1038/s42255-021-00457-w

2 Kochappan, R., Cao, E., Han, S., Hu, L., Quach, T., Senyschyn, D., Ferreira, V. I., Lee, G., Leong, N., Sharma, G., Lim, S. F., Nowell, C. J., Chen, Z., von Andrian, U. H., Bonner, D., Mintern, J. D., Simpson, J. S., Trevaskis, N. L., Porter, C. J. H. (2021). Targeted delivery of mycophenolic acid to the mesenteric lymph node using a triglyceride mimetic prodrug approach enhances gut-specific immunomodulation in mice. Journal of Controlled Release, 332, 636–651. https://doi.org/10.1016/j.jconrel.2021.02.008

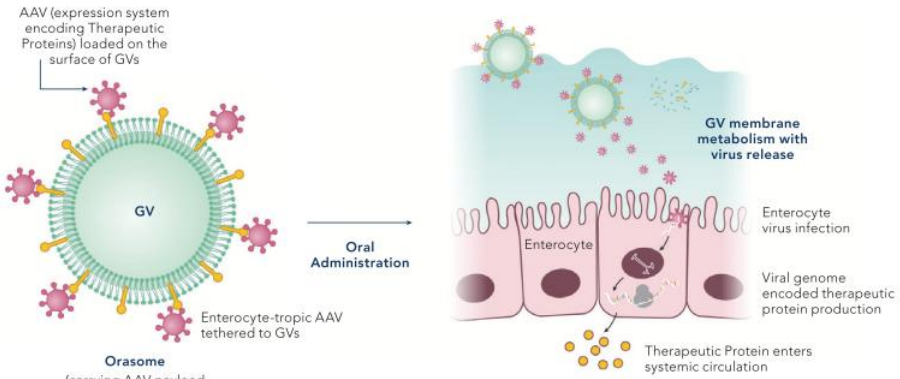
Orasome™ and Other Technology Platforms for Oral Administration of Therapeutics

Therapeutic Candidate	PureTech Ownership	Description
Orasome Technology Platform	Wholly-owned	Programmable and scalable approach for oral administration of nucleic acids and other biologics

- We are developing versatile and programmable oral biotherapeutics approaches, such as Orasome technology, to potentially enable the oral administration of macromolecule therapeutic payloads, including antisense oligonucleotides, short interfering RNA, mRNA, modular expression vector systems, peptides and nanoparticles that are otherwise administered exclusively by injection.
- Our Orasome technology platform was inspired by the in vivo trafficking of ubiquitous, naturally occurring extracellular vesicles, which are often referred to as exosomes or ectosomes, and we have engineered them for transport through the GI tract. We believe human cell-isolated exosomes/ectosomes have promise as vehicles for systemic drug administration due to their observed tolerability over synthetic polymer-based administration technologies. However, the fragile nature of exosomes/ectosomes from human cells limits their usage for oral administration and the type of post-isolation manipulations that can be applied in order to optimize such vesicles for exogenous drug cargo loading and storage.
- Our Orasome technology platform, for example, utilizes both synthetic and naturally occurring components isolated from multiple sources to yield glycocalyx-stabilized vesicles (GVs). We have engineered and formulated these vesicles to remain stable following oral consumption and transit through the upper GI tract. Orasome GVs are readily amenable to manufacturing at scale and at relatively low cost based on the accessibility of the various components and simplicity of assembly.

Orasome Technology

The figure below depicts one of the approaches we are exploring for the administration of oral biotherapeutics:



AAV = Adeno Associated Virus; GV = Glycocalyx Vesicles

- Our Orasome GVs are being engineered to transport macromolecular medicines to selected mucosal cell types of the intestinal tract where the therapeutics act either directly in the GI tract, transit through the mucosa to the underlying lymphatic vascular network or, in the case of cargos that yield mRNAs, enable the body to produce its own therapeutic proteins and peptides, such as antibodies within mucosal cells that are secreted into the mucosal lymphatic vascular network for subsequent systemic distribution. Using our Orasome technology platform, we believe it may be possible for a patient to take an oral drug product that will permit their own GI tract cells to make virtually any type of therapeutic protein. We believe this approach also has the potential to provide a more convenient and significantly less expensive means to administer biological medicines.
- In addition to Orasomes, we are also exploring the use of other approaches, such as certain exosomes isolated from milk as well as synthetic novel polymers and vesicles for delivering biotherapeutics.

Key Points of Innovation & Differentiation

- Our proprietary oral administration technology, such as our Orasome technology platform, has the potential to transform the treatment paradigm for diseases such as rheumatoid arthritis, diabetes, other autoimmune diseases and cancer for which the standard of care often requires intravenous infusion or subcutaneous injection of monoclonal antibodies (e.g., anti-PD-1, anti-tumor necrosis factor) or therapeutic proteins/peptides (e.g., glucagon-like peptide-1, insulin, granulocyte colony-stimulating factor GCSF, Factor VIII and IX, cytokines and erythropoietin), among others.

PureTech is well-positioned to unleash the potential of oral biotherapeutics

Limitations of protein-based therapeutics

- **Intravenous or subcutaneous administration** (infusion reactions, barrier for repeat dosing)
- **Lengthy scale-up timeline**

Limitations of mRNA-based therapeutics and vaccines

- **Intravenous, intramuscular or subcutaneous administration** (infusion reactions, co-medications needed for dosing, very limited repeat dose options)
- **Formulation-based immune and cellular toxicities** (protein synthesis by liver hepatocytes)
- **High dose requirement for protein production**

Potential advantages of the Orasome™ technology platform:

- **Orally administered** (flexible repeat dosing)
- **Body manufactures the therapeutic proteins**
- **Very low immune and cell toxicity** (protein synthesis in GI tract)
- **Low dose requirement for protein production**

Program Discovery Process by the PureTech Team

- We sought out different approaches to enable the oral administration of macromolecule therapeutic payloads that are otherwise administered exclusively by injection. We have independently developed our Orasome technology platform and have generated data and intellectual property supporting oral administration of macromolecule therapeutic payloads. We are also developing other oral administration technologies and intellectual property.

Milestones Achieved and Development Status

- In 2021, we established preclinical proof-of-concept supporting the potential of the Orasome technology platform to achieve production of therapeutic proteins in the gut of an animal following simulated oral administration of expression systems and transport of these proteins from the gut into systemic circulation. Proof-of-concept was observed with multiple formulations involving Orasome technology which are being further optimized to achieve a range of expression profiles for therapeutic proteins.

Expected Milestones

- We expect to generate additional data in 2022, with Orasomes and other technologies, across a range of preclinical models and therapeutic proteins. We expect to generate data to demonstrate that oral administration of Orasomes, carrying an expression system for a desired therapeutic protein, can achieve therapeutic levels of the protein in multiple species of preclinical models with achievement of safe repeat-dose administration.
- This work could lay the foundation for IND-enabling clinical studies for one or more additional therapeutic candidates to be included in our Wholly Owned Pipeline. We intend to leverage our proprietary technology platforms, such as orasomes, as well as our extensive network with major pharmaceutical companies and world-leading scientists, to generate additional novel therapeutic candidates.

Intellectual Property

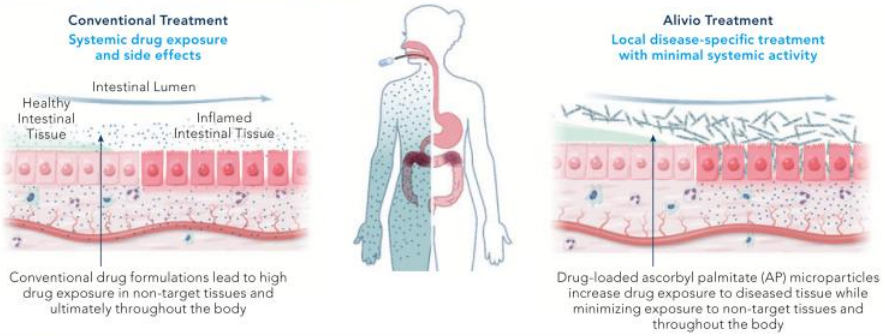
- We have broad intellectual property coverage for our Orasome technology platform. Our Orasome technology platform intellectual property portfolio covers compositions of matter, methods of use and methods of treatment spanning various platform-based technologies, as well as various broad classes of Orasome-formulated therapeutics, which include nucleic acid-based therapeutics (such as messenger RNA, short interfering RNA and antisense oligonucleotide-based approaches), small molecules, biologics (such as peptides, proteins and antibodies), expression systems for biologics and other therapeutics for use in the treatment of a wide range of diseases and disorders, including various immunological disorders, such as cancers and inflammatory diseases.
- As of December 31, 2021, PureTech's Orasome technology platform patent portfolio consists of four U.S. and nine foreign patent applications and one pending international PCT application in five patent families. Any patents to issue from these patent applications are expected to expire in 2037 through 2041, exclusive of possible patent term adjustments or extensions or other forms of exclusivity.
- With regards to milk exosomes, we exclusively licensed a patent portfolio consisting of two patent families from 3P Biotechnologies, Inc., based on certain milk exosome technology originating from the University of Louisville. We also exclusively licensed a patent portfolio consisting of two patent families from NuTech Ventures, based on certain milk extracellular vesicle technology originating from the University of Nebraska.

Alivio™ Technology Platform

Therapeutic Candidate	PureTech Ownership	Description
Alivio Technology Platform	Wholly-owned	Pioneering inflammation-targeted disease immunomodulation

- Using our Alivio technology platform, we are pioneering inflammation-targeted disease immunomodulation, which involves selectively restoring immune homeostasis at inflamed sites in the body, while having the potential for minimal impact on the rest of the body's healthy tissues, as a novel strategy to more effectively treat a range of chronic and acute inflammatory disorders. This long sought-after approach has the potential to broadly enable new medicines to treat a range of chronic and acute inflammatory disorders, including drugs that were previously limited by issues of systemic toxicity or undesirable PK.

Inflammation-Targeting Immunomodulation Platform

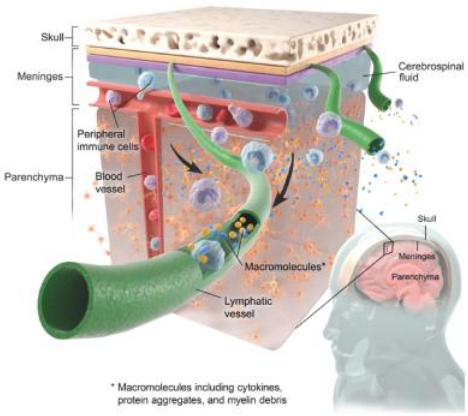


Key Points of Innovation & Differentiation	• To achieve our vision of selective immunomodulation, we are advancing our Alivio technology platform centered on a class of self-assembling therapies that selectively bind to inflamed tissue. The platform allows for the development of inflammation-targeting therapeutic candidates using a wide array of active pharmaceutical ingredients (APIs) including small molecules, biologics and nucleic acids. Using this technology, we can design therapeutic candidates that have the potential to treat autoimmune diseases locally at the site of inflammation while avoiding systemic toxicities.
Program Discovery Process by the PureTech Team	• A key challenge in new drug development for autoimmune and inflammatory disease is that attractive drug targets are frequently expressed in both diseased and normal tissue. Consequently, we were interested in identifying ways to address autoimmune disease in a targeted manner such that healthy cells and tissues are not impacted by the drug. We were inspired by the key observation that pathologic inflammation frequently manifests at specific sites in tissues and organs and is driven by dysfunctional immune signaling. Traditional approaches act broadly to suppress the immune system throughout the body affecting both the disease and healthy tissues. The current approaches therefore substantially limit the potential targets that can be pursued and frequently result in narrow therapeutic windows. Working with leading scientists, we identified and in-licensed a technology platform in May 2016 that was created by Jeffrey Karp, Ph.D., Professor of Medicine at Harvard Medical School and Brigham and Women's Hospital, and Robert Langer, Sc.D., David H Koch Institute Professor at MIT. As demonstrated in multiple publications, our Alivio technology platform can be used to develop therapeutic candidates that selectively release drugs at inflamed sites of targeted tissues and spares healthy tissues.
Patient Need & Market Potential	• Preclinical results suggest our Alivio technology platform could be applied to diseases such as IBD, inflammatory arthritis, organ transplantation and IC/BPS. These diseases collectively impact tens of millions of patients in the U.S. alone and have limited treatment options. IC/BPS is a chronic bladder condition that consists of discomfort or pain in the bladder or surrounding pelvic region and is often associated with frequent urination. It is estimated to affect four million to 12 million people in the U.S. Current treatments fail to control pain in many patients. IBD is estimated to affect approximately 3.9 million people in the U.S.
Milestones Achieved & Development Status	• In August 2021, we announced that Imbrium exercised a license option under the companies' research and development collaboration agreement to develop LYT-503/IMB-150. In connection with the option exercise, we received an upfront payment of $6.5 million and are eligible to receive up to $53 million in additional development milestone payments for this program as well as royalties on product sales. • Using our Alivio technology platform, we are developing LYT-510, an oral inflammation-targeting formulation of tacrolimus, a potent immunosuppressant drug, to treat IBD and chronic pouchitis, LYT-500, an oral combination therapy for the treatment of IBD, and LYT-503/IMB-150, our therapeutic candidate being advanced in collaboration with Imbrium Therapeutics for the potential treatment of IC/BPS.
Expected Milestones	• We intend to file for regulatory approval to initiate first-in-human studies at year end 2022 and initiate a clinical study evaluating LYT-510 as a single agent for the potential treatment of IBD and chronic pouchitis in early 2023. • We expect preclinical proof-of-concept data for LYT-500 in the first half of 2022. • Imbrium is planning to file an IND application for LYT-503/IMB-150 in 2022. • We are evaluating other potential therapeutic candidates leveraging Alivio technology platform for Wholly Owned Pipeline expansion.
Intellectual Property	• Intellectual property portfolio covering the Alivio inflammation-targeting technology platform consists of six patent families. Collectively, across these patent families, there are 18 issued patents within and outside the U.S. with claims covering inflammation-targeting compositions, methods of making and methods of using as drug products. Within these families, there are a total of eight patent applications pending in the U.S. and foreign countries. All patents and patent applications covering the platform technologies have been obtained from the Brigham and Women's Hospital under an exclusive licensing agreement in all territories.

Meningeal Lymphatics Research Program

Therapeutic Candidate	PureTech Ownership	Description
Meningeal Lymphatics Research Program	Wholly-owned	Harnessing meningeal lymphatics to potentially treat a range of neurodegenerative and neuroinflammatory conditions

- The lymphatic system is an important part of the immune system, GI system and central nervous system, or CNS. Loss of lymphatic flow can play a critical role in diseases of these systems. The recent discovery of meningeal lymphatics in the brain, an area once thought to have immune privilege, has shed new light on neurodegenerative diseases and lymphatic vessel aging.



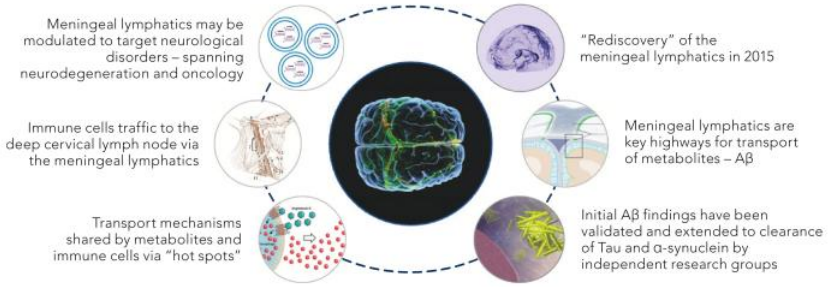
Key Points of Innovation & Differentiation

- Among the macromolecules that are drained via the lymphatics are pathogenic macromolecules such as amyloid-beta (Aβ) and tau, which are both associated with Alzheimer's disease, or AD, pathology, as well as alpha-synuclein, which is associated with Parkinson's disease. Blocking the lymphatic flow increases levels of these molecules in the brain. In animal models of AD, AD-associated tauopathies and Parkinson's disease, blockage of meningeal lymphatic flow significantly exacerbated disease progression and severity whereas improving flow through aged meningeal lymphatics improved cognitive function in these animal models. With aging, the lymphatic vessels that drain the brain become dysfunctional and no longer drain as efficiently. The "lymphedematous characteristics" of meningeal lymphatic vessels in aged animals might be leading to inefficient clearance of pathologic macromolecules and potentially increased risk for neurodegenerative diseases. Therefore, restoration of lymphatic flow may be a novel class of therapies for neurodegeneration associated with poor lymphatic drainage.

Program Discovery Process by the PureTech Team

- One of our academic collaborators discovered a functional lymphatic system in the meninges of the brain that forms the basis of our meningeal lymphatics research program. These meningeal lymphatics have been described as the "brain drain," a route through which macromolecules are flushed from the brain in cerebrospinal fluid. We believe that augmenting meningeal lymphatic vasculature function may potentially improve outcomes for a range of neurodegenerative and neuroinflammatory conditions that are not currently effectively treated.

CNS lymphatics: Harnessing an overlooked immune and metabolite transport network



Milestones Achieved & Development Status

- In April 2021, we announced the publication of preclinical research in *Nature*, suggesting that restoring lymphatic flow in the brain, either alone or in combination with passive immunotherapies such as antibodies directed at amyloid-beta, has the potential to address a range of neurodegenerative diseases, such as Alzheimer's and Parkinson's diseases, which potentially impairs the efficacy of passive immunotherapies such as amyloid-beta-targeting antibodies. The work also uncovered a link between dysfunctional meningeal lymphatics and damaging microglia activation in Alzheimer's disease, suggesting another route by which restoring healthy drainage patterns could improve clinical outcomes.

Intellectual Property

- We have broad intellectual property coverage around our meningeal lymphatics discovery research program, which includes exclusively licensed patent applications covering compositions of matter, methods of use and methods of treatment encompassing its platform-based brain lymphatic technologies, including the identification of macromolecular targets, as well as various classes of brain lymphatic targeting therapeutics for use in the treatment of a wide range of neurodegenerative and neuroinflammatory conditions, as well as various neuropathies and cancers.
- As of December 31, 2021, our meningeal lymphatics discovery research program patent portfolio consists of four patent families comprising six patent applications in U.S. and foreign countries, and two international PCT applications exclusively licensed from the University of Virginia Licensing & Ventures Group. Any patents to issue from the in-licensed patent applications are expected to expire in 2037 through 2041, exclusive of possible patent term adjustments or extensions or other forms of exclusivity.

PureTech's Founded Entities

Founded Entities

Founded Entity	PureTech Ownership[1]	Therapeutic Candidate[2]		Indication	Stage of Development	Royalties[3]
	5.6%	KarXT	P	Schizophrenia Alzheimer's disease psychosis	Phase 3 Phase 3 Ready	Royalties
	22.3%	Akili is pioneering the development of game-changing technologies to usher in a new era of cognitive medicine. EndeavorRx®[4] (formerly known as AKL-T01) is the first FDA cleared and CE marked video game treatment. In the U.S., EndeavorRx is indicated to improve attention function as measured by computer-based testing in children ages 8-12 years old with primarily inattentive or combined-type ADHD, who have a demonstrated attention issue.				
	23.5%	Plenity®[5,6] Plenity® for adolescents[5] GS200[5] GS300[5] GS500[5]	D D D D D	Weight management Adolescent weight management Weight management in T2D/prediabetes NASH/NAFLD Functional constipation	Commercial Pending Discussion with FDA[7] Clinical Trial Complete Clinical Pivotal	Royalties
	8.6%	VOR33 (CD33) VCAR33	B B	Acute myeloid leukemia Myelodysplastic syndromes, myeloproliferative neoplasms Bridge-to-transplant AML	Phase 1/2a Preclinical Phase 1/2	N/A
	41.4%	VE303 VE202 VE416 VE800 VE707	B B B B B	*C. difficile* IBD Food allergy Solid tumors Gram-negative infections	Phase 3 Ready Phase 2 Ready Phase 1/2 Phase 1 Preclinical	N/A
	76.0%	FOL-004	P/D	Androgenetic alopecia	Phase 3 Ready	Royalties
	44.6%	Sonde One for Respiratory[5] Sonde Mental Fitness[5]	D D	Respiratory risk detection and monitoring app Monitoring vocal features linked to depression, anxiety, and cognition	Commercial Release Commercial Release	N/A
entrega	74.3%	ENT-100	B	Oral delivery of biologics, vaccines and other drugs	Preclinical	N/A

The letters next to the therapeutic candidates denote whether the therapeutic candidate is a pharmaceutical product (P), biologic (B) or device (D).

1 Relevant ownership interests and references to equity ownership for Founded Entities contained in this strategic report (pages 2-72) were calculated on a diluted basis (as opposed to a voting basis) as of December 31, 2021, including outstanding shares, options and warrants, but excluding unallocated shares authorized to be issued pursuant to equity incentive plans. Vor Bio, Karuna and Gelesis ownerships were calculated on a beneficial ownership basis in accordance with SEC rules as of March 4, 2022 and February 15, 2022 and March 31, 2022, respectively.

2 With the exception of Plenity and EndeavorRx, candidates are investigational and have not been cleared by the FDA for use in the U.S.

3 PureTech Health has a right to royalty payments as a percentage of net sales.

4 Please see footnote 10 on page 6 for EndeavorRx® indication and overview.

5 These therapeutic candidates are regulated as devices and their development has been approximately equated to phases of clinical development.

6 Please see footnote 11 on page 7 for Important Safety Information about Plenity®.

7 Contingent on FDA review of the research plan.

[Pages 58-74 have been removed]

PureTech's Founded Entities — continued
Founded Entities in Order of Approximate Value of PureTech's Holdings

PureTech's Founded Entities — continued
Founded Entities in Order of Approximate Value of PureTech's Holdings

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PureTech's Founded Entities — continued
Founded Entities in Order of Approximate Value of PureTech's Holdings

ESG Report

Patients

Our commitment to making the world a better place by creating and advancing innovative new medicines

PureTech is a clinical-stage biotherapeutics company dedicated to discovering, developing and commercializing highly differentiated medicines for devastating diseases where limited or no treatment options currently exist for patients. These include inflammatory, fibrotic and immunological conditions, intractable cancers, lymphatic and gastrointestinal diseases and neurological and neuropsychological disorders, among others. It is our unyielding commitment to this mission that we continue to advance our therapeutic candidates in order to deliver innovative and differentiated medicines for patients in need (see pages 35-56 for our Wholly Owned Program overview).

Our research process begins by identifying new medicines where the underlying mechanism is de-risked by validated biology. We then apply our deep development expertise, proprietary platform technologies, and strategic collaborations to solve key challenges in efforts to unlock the value of each asset. Finally, we advance highly innovative and validated programs that have the potential to change the treatment paradigm for a number of serious diseases into therapeutic candidates.

This product innovation framework has generated 27 therapeutics and therapeutic candidates, of which 16 are clinical stage and 2 have gone from inception at PureTech through successful FDA and EU regulatory clearances for marketing.

Safety of clinical trial participants

The safety of participants who enroll in our clinical trials is an extremely high priority. When sponsoring an IND application, we recognize our responsibility both to clinical trial participants and to regulatory agencies. We have detailed protocols in place including Standard Operating Procedure for Adverse Event Reporting, and our employees who are engaged with clinical trials – either as clinical staff or their designee – are responsible for conducting such trials in compliance with good clinical practice.

PureTech is committed to ensuring that all of its clinical trials follow the standards of the International Conference on Harmonisation (ICH) Good Clinical Practice guidelines and the World Medical Association Declaration of Helsinki on the Ethical Principles for Medical Research Involving Human Subjects. The Company applies these standards to all trials conducted by or on its behalf. So that the trials meet these standards, PureTech seeks approval for clinical trials of investigative medicines from independent ethics committees and local regulatory authorities.

To confirm that a patient is aware of risks involved in a clinical trial, we ensure that every patient has voluntarily committed to the trial and has provided informed consent of their willingness to participate. Informed consent requirements are set out in the PureTech Clinical Research Policy.

PureTech relies on the use of human biological specimens in the development of its innovative therapies, and its Human Biological Specimens Policy specifies that collecting, obtaining, storing and using human biological samples requires informed consent, and that PureTech treat both donors and specimens with respect. PureTech's Chief Medical Officer and Chief Scientific Officer are jointly responsible for ensuring that PureTech follows, 1) applicable bioethical principles, and 2) U.S. and applicable international regulatory requirements and standards. In 2021, there were no FDA sponsored inspections related to clinical trial management and pharmacovigilance that resulted in PureTech receiving Voluntary Action Indicated (VAI) and Official Action Indicated (OAI) from FDA.

Drug safety

None of the therapeutic candidates from within PureTech's Wholly Owned Pipeline are currently on the market. In 2021, PureTech received no FDA warning letters, no products were delayed due to a lack of regulatory approval and no product recalls took place.

Equitable pricing, affordability and access

As we progress the therapeutic candidates from within PureTech's Wholly Owned Pipeline toward the market, we are committed to pursuing equitable pricing, affordability and access when those therapeutic candidates get to market, if we are successful in achieving the regulatory approvals or clearances required to launch them. We will routinely conduct comprehensive market research as we advance our therapeutic candidates. We recognize that equitable access to medicines is key to solving many public health issues and will continue to consider factors around equitable access to medicines as we advance our therapeutic candidates.

Animal testing

Animal research plays an essential and currently irreplaceable role in the advancement of healthcare. PureTech conducts animal testing only when necessary to advance the development of therapeutics and is required by regulatory authorities such as the FDA, before human testing of new medicines can take place. Most of our studies involving animals are conducted at external qualified and certified vendors.

We follow the guidelines set out under the USDA Animal Welfare Act and are committed to the humane and ethical treatment of animals: thoughtful use of animals will minimize the number used while producing quality data and providing the greatest benefit to humans. Before using laboratory animals in research, alternatives must be considered.

We apply the 3 Rs standard:

REPLACE	REDUCE	REFINE
Use alternative methods where this is possible	Use the minimum number of animals	Minimize pain, suffering and distress, and improve the welfare of the animals used

People

Our employees are an indispensable asset in driving our mission forward, to deliver medical innovations to patients and create a long-term value for shareholders. We recognize that employee satisfaction is a pillar to our success and hence we have zero-tolerance for behavior and actions that may disrupt the collaborative culture. We instead aim to foster engaging and respectful community.

PureTech is proud of its record of attracting and retaining high-quality talent. We aim to create a workplace that enables high achieving people to be successful while also fostering a collegiate atmosphere. Our employees are predominately located near our headquarters in Boston, MA with three individuals based in London.

As of December 31, 2021, we have total of 95 employees of which 54 employees work in R&D roles while 41 are engaged in general and administrative functions. None of our employees are subject to a collective bargaining agreement or represented by a trade or labor union. We consider our relationship with our employees to be excellent.

In 2021, PureTech conducted its first employee engagement survey to assess current levels of satisfaction and identify how the company can better support employees going forward. The results of the employee survey showed that PureTech performs highly when it comes to encouraging teamwork. The company culture builds agile teams that collaborate cross functionally and remain resilient and committed to the company vision. A high level of trust in management was reported, and PureTech's employees see themselves as purposeful, goal driven and passionate about working to contribute to the company's success.

Employee survey yielded high participation and high satisfaction rates[6]:

- 3.9 — My manager and I have a trusting and respectful relationship
- 3.8 — I work hard with dedication and tenacity and do whatever it takes to overcome obstacles
- 3.5 — I work in an environment where my mistakes are considered an opportunity for me to learn
- 3.9 — Teamwork is encouraged on my team

As a response to findings that indicated employees would appreciate higher levels of information sharing internally, we implemented increased communication from senior leadership, utilizing a range of internal communications approaches. These include:

- Lunch and learn initiatives
- Regular town halls lead by the CEO with open Q&A session
- Email updates
- Intranet updates
- Group conference calls

Employee recruitment

Our Wholly Owned Programs are advancing quickly and the PureTech team is growing rapidly to deliver on our mission to discover, develop and aim to commercialize new therapies for devastating disease where limited or no treatment options currently exist for patients. Our Wholly Owned Programs have enabled us to create new positions and attract new talent, as is evident from the new hires in 2021. Aligned with this, we have also moved away from positions that have historically supported the creation of new Founded Entities.

PureTech employees as at December 31, 2021

Total number of employees	**95**
Employee growth	48%
Employee turnover[7]	25%
Internal promotions	17%

Partnerships and sustainable recruiting

As part of our development of a sustainable and diverse talent pipeline, we source our talent through our outstanding network of world leading scientists and local top tier universities at the heart of the world's biotech hub in Boston, as well as through partnerships with local university cooperative education programs. Co-op programs provide students with opportunities to alternate periods of academic study with several months of full-time employment related to their academic majors and interests. Undergraduate co-op students can join PureTech for six month paid internships in our Research department, adding to our talent acquisition pipeline.

6 Based on 1-5 rating scale
7 As compared to ~45% in the healthcare industry at large, with PureTech's turnover rate further impacted by the continuing shift of business focus to our Wholly Owned Programs

We also seek to attract new talent through participating in annual life science career fairs targeted at graduate MS/PhD students and is committed to developing the next generation of life science professionals that will carry on our mission.

Additionally, we partner with Project Onramp, which facilitates internships for Massachusetts undergraduate students from under-resourced, under-represented group and/or who are first-generation college students, by bringing on paid summer interns in business operations.

PROJECT ONRAMP

Diversity and inclusion

We are committed to a policy of non-discrimination and equal opportunity for all employees and qualified applicants without regard to race, color, religion, gender and gender identity, pregnancy, sexual orientation, national origin, ancestry, age, physical or mental disability, genetic information, veteran status, military service, application for military service or any other status protected by law.

Women employees and women managers as at December 31, 2021

Women employees	45%
Women managers	33%

We strongly believe that diverse board and senior management team generates better performance, retains exceptional talent, and enhances shareholder value. This unwavering commitment has resulted in a top-down approach to secure diversity and inclusion at PureTech (as seen on page 74).

MassBio

In 2021, PureTech became a Mass Bio Open Letter 2.0 signatory, advocating for equity and inclusivity in the healthcare industry. This aims to increase representation of Black, Brown, and Indigenous People of Color (BIPOC) within Massachusetts' life sciences sector.

Pay equity

We are committed to equitable pay. While we do not currently report on the gender pay gap as we are out of scope of the UK's Equality and Human Rights Commission regulation due to the size of our company, we are committed to workplace transparency and equality as seen in our various human capital programs supporting career development, workplace equity, and diversity and inclusion. This mission is reflected strongly on our board and at management level as seen on page 74.

Employee development and retention

We uphold the value of human capital development at PureTech, encouraging managers and employees to discuss job performance and goals on an informal, day-to-day basis alongside formal performance evaluations conducted annually. Regular one-on-ones between employees and supervisors are highly encouraged and facilitate alignment between management and employee expectations and goals.

Employees are able to enter and track their personal development goals on an online portal, which gives visibility to managers to see their team's efforts and progress. This portal is utilized across all departments and is part of PureTech's commitment to supporting employees in their growth and development.

We support the continued development of our employees by providing funding for in person and online programs on a case-by-case basis in areas relevant to their work. Some of the other development trainings include:

HR training

- A mandatory training at onboarding to understand PureTech practices and policies
- Special training based on job function; e.g. employees who perform GxP work are assigned matrices by the Quality Assurance department
- Employee bias training to understand bias at workplace provided by Yamartino Group
- A mandatory annual anti-harassment training provided to all employees by an outside law firm

Health and safety and first aid training

- A mandatory annual safety training provided to all employees in accordance with the Occupational Safety and Health Administration (OSHA)
- An optional first aid training, provided to all employees by Safety Trainers

IT training

- A mandatory annual training, provided to all employees by Risk Management Solutions (RMS)
- A mandatory cybersecurity training provided to all employees, followed by assigned training

PureTech supports the continued development of our employees by providing in person and online trainings in areas relevant to their work. Support for educational programs is available to all employees and considered on a case-by-case basis.

8 Board composition at March 24, 2022.
9 Board composition at December 31, 2021.

Employee benefits

The physical, financial, social and emotional health of our employees is a priority at PureTech. As a result, we provide a range of benefits for employees. Following a US model since this is where the majority of our employees are based, we offer the following perks and benefits:


Premium health plan with an option to choose from PPO or HMO plan


Dental plan


Vision plan


Short-term disability plan


Long-term disability plan


Life insurance


Medical FSA


Dependent Care FSA


Health Reimbursement Account (HRA)


Benefits continuation (COBRA)


Paid parental leave (Up to 12 weeks)


Nursing room


401(k) retirement plan with 3% non-elective contribution by the company


Performance share plan


1-on-1 financial coaching


Technology reimbursement program


Pre-tax parking and transit benefits


Gym membership in addition to an onsite gym facility


Entertainment discounts


Employee led Social Committee


Employee led Cultural Committee


Onsite free snacks & drinks


Flexibility to work from home

In 2021, some benefits were adjusted in response to the changing nature of work due to COVID-19, for example, gym membership reimbursement eligibility was extended to virtual fitness programs.

PureTech has a performance share plan in place under which the majority of employees are granted stock options upon joining the organization and periodically, to ensure appropriate market-based compensation and incentive alignment with the goals of the organization and its shareholders.

Employee health and safety

The COVID-19 global pandemic that changed the world in 2020 has shifted the way we operate. It is our unyielding commitment to keeping each other and the community safe that has allowed us to implement a COVID-19 action plan and policy. The COVID-19 policy was swiftly drafted and implemented in response to the pandemic, outlining general and special safety procedures based on employee roles, compliance requirements, travel restrictions, exposure responses, and other operational protocols. Additionally, onsite COVID-19 testing requirements were implemented to keep employees, their families, and our community safe.

During 2021, PureTech took steps to evolve its hybrid working model in response to the COVID-19 pandemic, to allow scientists to work onsite safely with minimized risk. To ease the transition to a hybrid model, an online desk booking system was introduced, enabling employees to plan their return to the office flexibly. Other remote operation initiatives included continued utilization of SaaS products to enable employee collaboration, communications and workflow management with minimum disruption.

Employee engagement

We are committed to maintaining and expanding a positive and interconnected company culture. To foster employee engagement and collaboration, the following initiatives were launched in 2021:

Employee intranet

- To provide access to internal and external resources
- To provide online staff directory, spotlighting employee birthdays and work anniversaries
- To serve as a centralized portal for human resources documents

Formation of employee-led Cultural Committee

- To create programs that celebrate diversity, promote equity, and encourage respect for one another

Formation of employee-led Social Committee

- To organize social events to foster a sense of community amongst one another

Community engagement

As a member of the world's top biotech hub in Boston, we are committed to giving back to our community. In 2021 and in January 2021 post-period, we contributed to the following charitable initiatives:

Life Sciences Cares	Life Science Cares is a non-profit organization with a mission to leverage the intellectual, financial, and human capital of the life sciences industry in efforts to reduce the effects of poverty in Boston, Philadelphia, San Diego and the Bay Area.
The Greater Boston Food Bank (GBFB)	GBFB is the largest hunger-relief organization in New England committed to increasing our food distribution by providing three meals a day to every person in need in Eastern Massachusetts while supporting healthy lives and healthy communities. GBFB is a member of Feeding America, the nation's largest hunger-relief organization.
Lymphatic Education & Research Network (LE&RN)	LE&RN is committed to educating the public about lymphatic disease and the need for treatment and research. LE&RN hosts symposiums several times a year in which patients, family members, and the medical community are provided with the opportunity to hear from experts in the field.
Langer Prize for Innovation & Entrepreneurial Excellence Fellowship	Sponsored by the Langer Prize Endowment, the fellowship will award unrestricted grants of up to $100,000 to assist researchers particularly those working in chemical and biological engineering in pursuing "blue-sky" ideas that may lead to important technical and commercial innovations.
Fred Hutchinson Cancer Research Center	Fred Hutchinson Cancer Research Center is dedicated to the elimination of cancer and related diseases as causes of human suffering and death.

[Pages 80-89 have been removed]

Risk management

The execution of the Group's strategy is subject to a number of risks and uncertainties. As a clinical-stage biotherapeutics company, the Group operates in an inherently high-risk environment. The overall aim of the Group's risk management effort is to achieve an effective balancing of risk and reward, although ultimately no strategy can provide an assurance against loss.

Risks are formally identified by the Board and appropriate processes are put in place to monitor and mitigate them on an ongoing basis. If more than one event occurs, it is possible that the overall effect of such events would compound the possible effect on the Group. The principal risks that the Board has identified as the key business risks facing the Group are set out in the table below along with the consequences and mitigation of each risk. These risks are only a high-level summary of the principal risks affecting our business; any number of these or other risks could have a material adverse effect on the Group or its financial condition, development, results of operations, subsidiary companies and/or future prospects. Further information on the risks facing the Group can be found on pages 217 to 251, which also includes a description of circumstances under which principal and other risks and uncertainties might arise in the course of our business and their potential impact.

Risk	Impact*	Management Plans/Actions
1 Risks related to science and technology failure The science and technology being developed or commercialized by some of our businesses may fail and/or our businesses may not be able to develop their intellectual property into commercially viable therapeutics or technologies. There is also a risk that certain of the businesses may fail or not succeed as anticipated, resulting in significant decline of our value.	The failure of any of our businesses could decrease our value. A failure of one of the major businesses could also impact the perception of PureTech as a developer of high value technologies and possibly make additional fundraising at PureTech or any Founded Entity more difficult.	Before making any decision to develop any technology, extensive due diligence is carried out that covers all the major business risks, including technological feasibility, market size, strategy, adoption and intellectual property protection. A capital efficient approach is pursued such that some level of proof of concept has to be achieved before substantial capital is committed and thereafter allocated. Capital deployment is generally tranched so as to fund programs only to their next value milestone. Members of our Board serve on the board of directors of several of the businesses so as to continue to guide each business's strategy and to oversee proper execution thereof. We use our extensive network of advisors to ensure that each business has appropriate domain expertise as it develops and executes on its strategy and the R&D Committee of our Board reviews each program at each stage of development and advises our Board on further actions. Additionally, we have a diversified model with numerous assets such that the failure of any one of our businesses would not result in a failure of all of our businesses.
2 Risks related to clinical trial failure Clinical trials and other tests to assess the commercial viability of a therapeutic candidate are typically expensive, complex and time-consuming, and have uncertain outcomes. Conditions in which clinical trials are conducted differ, and results achieved in one set of conditions could be different from the results achieved in different conditions or with different subject populations. If our therapeutic candidates fail to achieve successful outcomes in their respective clinical trials, the therapeutics will not receive regulatory approval and in such event cannot be commercialized. In addition, if we fail to complete or experience delays in completing clinical tests for any of our therapeutic candidates, we may not be able to obtain regulatory approval or commercialize our therapeutic candidates on a timely basis, or at all.	A critical failure of a clinical trial may result in termination of the program and a significant decrease in our value. Significant delays in a clinical trial to support the appropriate regulatory approvals could impact the amount of capital required for the business to become fully sustainable on a cash flow basis.	We have a diversified model such that any one clinical trial outcome would not significantly impact our ability to operate as a going concern. We have dedicated internal resources to establish and monitor each of the clinical programs in order to try to maximise successful outcomes. We also engage outside experts to help design clinical programs to help provide valuable information and mitigate the risk of failure. Significant scientific due diligence and preclinical experiments are done prior to a clinical trial to attempt to assess the odds of the success of the trial. In the event of the outsourcing of these trials, care and attention are given to assure the quality of the vendors used to perform the work.

* When assessing potential impact of a given risk, we looked at the potential effects on our research and development activities, financial health and overall business operations.

Risk	Impact*	Management Plans/Actions
3 Risks related to regulatory approval The pharmaceutical industry is highly regulated. Regulatory authorities across the world enforce a range of laws and regulations which govern the testing, approval, manufacturing, labelling and marketing of pharmaceutical therapeutics. Stringent standards are imposed which relate to the quality, safety and efficacy of these therapeutics. These requirements are a major determinant of whether it is commercially feasible to develop a drug substance or medical device given the time, expertise, and expense which must be invested. We may not obtain regulatory approval for our therapeutics. Moreover, approval in one territory offers no guarantee that regulatory approval will be obtained in any other territory. Even if therapeutics are approved, subsequent regulatory difficulties may arise, or the conditions relating to the approval may be more onerous or restrictive than we expect.	The failure of one of our therapeutics to obtain any required regulatory approval, or conditions imposed in connection with any such approval, may result in a significant decrease in our value.	We manage our regulatory risk by employing highly experienced clinical managers and regulatory affairs professionals who, where appropriate, will commission advice from external advisors and consult with the regulatory authorities on the design of our preclinical and clinical programs. These experts ensure that high-quality protocols and other documentation are submitted during the regulatory process, and that well-reputed contract research organizations with global capabilities are retained to manage the trials. We also engage with experts, including on our R&D Committee, to help design clinical trials to help provide valuable information and maximize the likelihood of regulatory approval. Additionally, we have a diversified model with numerous assets such that the failure to receive regulatory approval or subsequent regulatory difficulties with respect to any one therapeutic would not adversely impact all of our therapeutics and businesses.
4 Risks related to therapeutic safety There is a risk of adverse reactions with all drugs and medical devices. If any of our therapeutics are found to cause adverse reactions or unacceptable side effects, then therapeutic development may be delayed, additional expenses may be incurred if further studies are required, and, in extreme circumstances, it may prove necessary to suspend or terminate development. This may occur even after regulatory approval has been obtained, in which case additional trials may be required, the approval may be suspended or withdrawn or additional safety warnings may have to be included on the label. Adverse events or unforeseen side effects may also potentially lead to product liability claims being raised against us as the developer of the therapeutics and sponsor of the relevant clinical trials. These risks are also applicable to our Founded Entities and any trials they conduct or therapeutic candidates they develop.	Adverse reactions or unacceptable side effects may result in a smaller market for our therapeutics, or even cause the therapeutics to fail to meet regulatory requirements necessary for sale of the therapeutic. This, as well as any claims for injury or harm resulting from our therapeutics, may result in a significant decrease in our value.	We design our therapeutics with safety as a top priority and conduct extensive preclinical and clinical trials which test for and identify any adverse side effects. Despite these steps and precautions, we cannot fully avoid the possibility of unforeseen side effects. To mitigate the risk further we have insurance in place to cover product liability claims which may arise during the conduct of clinical trials.
5 Risks related to therapeutic profitability We may not be able to sell our therapeutics profitably if reimbursement from third-party payers such as private health insurers and government health authorities is restricted or not available because, for example, it proves difficult to build a sufficiently strong economic case based on the burden of illness and population impact. Third-party payers are increasingly attempting to curtail healthcare costs by challenging the prices that are charged for pharmaceutical therapeutics and denying or limiting coverage and the level of reimbursement. Moreover, even if the therapeutics can be sold profitably, they may not be accepted by patients and the medical community. Alternatively, our competitors – many of whom have considerably greater financial and human resources – may develop safer or more effective therapeutics or be able to compete more effectively in the markets targeted by us. New companies may enter these markets and novel therapeutics and technologies may become available which are more commercially successful than those being developed by us. These risks are also applicable to our Founded Entities and could result in a decrease in their value.	The failure to obtain reimbursement from third party payers, as well as competition from other therapeutics, could significantly decrease the amount of revenue we may receive from therapeutic sales for certain therapeutics. This may result in a significant decrease in our value.	We engage reimbursement experts to conduct pricing and reimbursement studies for our therapeutics to ensure that a viable path to reimbursement, or direct user payment, is available. We also closely monitor the competitive landscape for all of our therapeutics and adapt our business plans accordingly. Not all therapeutics that we are developing will rely on reimbursement. Also, while we cannot control outcomes, we try to design studies to generate data that will help support potential reimbursement.

Risk	Impact*	Management Plans/Actions
6 Risks related to intellectual property protection We may not be able to obtain patent protection for some of our therapeutics or maintain the secrecy of its trade secrets and know-how. If we are unsuccessful in doing so, others may market competitive therapeutics at significantly lower prices. Alternatively, we may be sued for infringement of third-party patent rights. If these actions are successful, then we would have to pay substantial damages and potentially remove our therapeutics from the market. We license certain intellectual property rights from third parties. If we fail to comply with our obligations under these agreements, it may enable the other party to terminate the agreement. This could impair our freedom to operate and potentially lead to third parties preventing us from selling certain of our therapeutics.	The failure to obtain patent protection and maintain the secrecy of key information may significantly decrease the amount of revenue we may receive from therapeutic sales. Any infringement litigation against us may result in the payment of substantial damages by us and result in a significant decrease in our value.	We spend significant resources in the prosecution of our patent applications and maintenance of our patents, and we have an in-house patent counsel and patent group to help with these activities. We also work with experienced external attorneys and law firms to help with the protection, maintenance and enforcement of our patents. Third party patent filings are monitored to ensure the Group continues to have freedom to operate. Confidential information (both our own and information belonging to third parties) is protected through use of confidential disclosure agreements with third parties, and suitable provisions relating to confidentiality and intellectual property exist in our employment and advisory contracts. Licenses are monitored for compliance with their terms.
7 Risks related to enterprise profitability We expect to continue to incur substantial expenditure in further research and development activities. There is no guarantee that we will become operationally profitable, and, even if we do so, we may be unable to sustain operational profitability.	The strategic aim of the business is to generate profits for our shareholders through the commercialization of technologies through therapeutic sales, strategic partnerships and sales of businesses. The timing and size of these potential inflows are uncertain. Should revenues from our activities not be achieved, or in the event that they are achieved but at values significantly less than the amount of capital invested, then it would be difficult to sustain our business.	We retain significant cash in order to support funding of our Founded Entities and our Wholly Owned Pipeline. We have close relationships with a wide group of investors and strategic partners to ensure we can continue to access the capital markets and additional monetization and funding for our businesses. Additionally, our Founded Entities are able to raise money directly from third party investors and strategic partners.
8 Risks related to hiring and retaining qualified employees We operate in complex and specialized business domains and require highly qualified and experienced management to implement our strategy successfully. We and many of our businesses are located in the United States which is a highly competitive employment market. Moreover, the rapid development which is envisaged by us may place unsupportable demands on our current managers and employees, particularly if we cannot attract sufficient new employees. There is also the risk that we may lose key personnel.	The failure to attract highly effective personnel or the loss of key personnel would have an adverse impact on our ability to continue to grow and may negatively affect our competitive advantage.	The Board annually seeks external expertise to assess the competitiveness of the compensation packages of its senior management. Senior management continually monitors and assesses compensation levels to ensure we remain competitive in the employment market. We maintain an extensive recruiting network through our Board members, advisors and scientific community involvement. We also employ an executive as a full-time in-house recruiter. Additionally, we are proactive in our retention efforts and include incentive-based compensation in the form of equity awards and annual bonuses, as well as a competitive benefits package. We have a number of employee engagement efforts to strengthen our PureTech community.

Risk	Impact*	Management Plans/Actions
9 Risks related to business, economic or public health disruptions Business, economic or geopolitical disruptions or global health concerns could seriously harm our development efforts and increase our costs and expenses.	Broad-based business, economic or geopolitical disruptions could adversely affect our ongoing or planned research and development activities. For example, the COVID-19 global pandemic resulted in extended shutdowns of certain businesses around the world. More recently, the Russian invasion of Ukraine has created significant economic disruption as a result of sanctions by the International community and the almost complete shutdown of the Ukrainian economy and business, including healthcare, in Ukraine. Global health concerns, such as COVID-19, or geopolitical events, like the invasion of Ukraine, could also result in social, economic, and labor instability in the countries in which we or the third parties with whom we engage operate. We cannot presently predict the scope and severity of any potential business shutdowns or disruptions, but if we or any of the third parties with whom we engage, including the suppliers, clinical trial sites, regulators and other third parties with whom we conduct business, were to experience shutdowns or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively impacted. It is also possible that global health concerns or geopolitical events such as these one could disproportionately impact the hospitals and clinical sites in which we conduct any of our current and/or future clinical trials, which could have a material adverse effect on our business and our results of operation and financial impact.	To date, we have seen limited impact on our research and development activities and the operation of our company more generally, but we will continuously monitor the COVID-19 pandemic and the invasion of Ukraine and their impact on our business going forward. It is possible that we may see further impact as the situation continues to develop. With respect to the COVID-19 pandemic, we have continued to be proactive in limiting the number of staff on site, requiring that all on-site employees test twice a week and providing personal protective equipment to our staff.

Brexit

The United Kingdom withdrew from the European Union on January 31, 2020 (Brexit) and the transition period for such withdrawal ended on December 31, 2020. Although the Board has considered the potential impact of Brexit as part of its risk management, given that we principally operate in the United States and hold substantially all assets in U.S. dollars, we do not believe there have been or will be any material financial effect on our business, or any significant operational issues which have arisen or could arise, as a result of Brexit.

Viability

PureTech Health plc
Viability Statement

In accordance with the UK Corporate Governance Code (Governance Code) published in July 2018, the Directors have assessed the prospects of the Company, and with respect to the December 31, 2021, financial position, we have sufficient available funding to extend operations into the first quarter of 2025. This period is deemed appropriate having assessed the financial health as of December 31, 2021. Further, we expect our Wholly Owned Programs (or "Internal segment") to significantly progress during this period and for key Controlled Founded Entities and Non-Controlled Founded Entities to reach significant development milestones over the period of the assessment.

We anticipate our funding to be used to advance our Wholly Owned Programs, to continue research and development efforts, to discover and progress new therapeutic candidates and to fund the Company's head office costs into the first quarter of 2025. We have also reserved capital to support our Founded Entities, should they require it, to reach significant development milestones over the period of the assessment in conjunction with our external partners. It should be noted that the majority of funding has been allocated to the advancement of the Wholly Owned Programs.

The Directors confirm that they have a reasonable expectation that we will continue to operate and meet our obligations as they fall due over the period of the assessment. In making this statement the Directors carried out a robust assessment of the principal risks, including those that would threaten our business model, future performance, solvency or liquidity.

This assessment was made in consideration of our strong financial position, current strategy and management of principal risks. The following facts support the Directors' view of the viability:

- We have significant influence over the spending and strategic direction of our Wholly Owned Programs and Controlled Founded Entities.
- Our business model is structured so that we are not reliant on the successful outcomes of any one therapeutic or technology within the Wholly Owned Programs, or any Controlled Founded Entity or Non-Controlled Founded Entity.

In addition, the fact that the Wholly Owned Programs, Controlled Founded Entities and Non-Controlled Founded Entities (with the exception of Gelesis and Akili) are currently in the research and development stage means that these therapeutics, technologies and entities are not reliant on cash inflows from product sales or services during the period of this assessment. This also means that we are not highly susceptible to conditions in one or more market sectors in this time frame. Although engaging with collaboration partners is highly valuable from a validation and, in some cases, funding perspective, we are not solely reliant on cash flows from such sources over the period of assessment.

Our consolidated cash and cash equivalents as of December 31, 2021, was $465.7 million. Our PureTech Level cash and cash equivalents as of December 31, 2021, was $418.9 million. Our PureTech Level cash and cash equivalents position is highly liquid and is forecasted to support infrastructure costs, Wholly Owned Program research and development activities and the appropriate funding of key Controlled Founded Entities and Non-Controlled Founded Entities, in order to reach significant developmental milestones over the period of the assessment.

The Board reviews the near-term liquidity and regularly considers funding plans of our Wholly Owned Programs, Controlled Founded Entities and Non-Controlled Founded Entities in our assessment of long-term cash flow projections.

While the review has considered all of the principal risks identified, the Board is focused on the pathway to regulatory approval of each therapeutic candidate being developed within our Wholly Owned Pipeline as well as those of our Founded Entities. Further, the Board has considered milestone and royalty funding based on existing collaboration and partnership arrangements, and the ability of the Wholly Owned Program, and each Controlled Founded Entity and Non-Controlled Founded Entity to enter into new collaboration agreements, all of which could be expected to generate cash in-flows but were not included in the assessment. Additionally, given that spending and investment decisions are largely discretionary, there is management control on reducing discretionary spending if unforeseen liquidity risks arise.

The Directors note that our ownership stakes in the Controlled Founded Entities and Non-Controlled Founded Entities are expected to be illiquid in nature, with the exception of our ownership stakes in Karuna and Vor, which are both publicly traded on Nasdaq as well as Gelesis which recently listed on the New York Stock Exchange on January 14, 2022. See Recent Developments below regarding our Founded Entity Akili potential merger. While we anticipate holding these ownership stakes through the achievement of significant milestones or other events, we will continue to be diligent in exploring monetization opportunities after key value accretion has occurred similar to the execution of the sale of 1,000,000 common shares of Karuna for aggregate proceeds of $118.0 million on February 9, 2021, and the sale of 750,000 common shares of Karuna for an aggregate proceeds of $100.1 million on November 9, 2021. We also expect that certain of these Founded Entities may not be successful and this could result in a loss of the amounts previously invested. However, even in this scenario, our liquidity is expected to remain sufficient to achieve the remaining milestone events and fund infrastructure costs.

The Directors have concluded, based on our strong financial position and readily available cash reserves, that we are highly likely to be able to fund our infrastructure requirements, advance multiple clinical trials within our Wholly Owned Pipeline, including trials in more advanced stages, and contribute the amounts considered necessary for the Controlled Founded Entities and Non-Controlled Founded Entities to reach significant development milestones over the period of the assessment. Therefore, there is a reasonable expectation that we have adequate resources and will continue to operate and meet our obligations over the period of the assessment.

Key Performance Indicators – 2021

The key performance indicators (KPIs) below measure our performance against our strategy. As PureTech's strategy has evolved, new KPIs have replaced older metrics that are no longer representative of our progress.

Amount of funding secured for Founded Entities[1,2]

$731.9m

$709.3m (96.9%) came from third parties

2020: $247.8m
2019: $666.8m
2018: $274.0m
2017: $102.9m

Progress
Karuna, Akili, Gelesis, Vor, Vedanta and Sonde all raised funds in the form of financings and non dilutive grants in 2021, including $709.3 million by third party financial and strategic investors.

Number of programs created for pipeline expansion[2]

2

2020: 3
2019: 1
2018: 1
2017: 1

Progress
In 2021, we expanded our Wholly Owned Pipeline with the acquisition of our Founded Entity, Alivio, and the integration of Alivio's therapeutic candidates, LYT-500 and LYT-503/IMB-150, into the Wholly Owned Pipeline. LYT-503/IMB-150 is being advanced in collaboration with Imbrium Therapeutics, which is responsible for all future development activities and funding for LYT-503/IMB-150.

Proceeds generated from sales of Founded Entity equity[2]

$218.1m

2020: $350.6 million
2019: $9.3 million

Progress
A key component of our strategy is to derive value from the equity growth of our Founded Entities. In 2021, we generated cash proceeds of approximately $218 million from the sales of equity in our Founded Entities, which we intend to use to fund our operations and growth and to further expand and advance our clinical-stage Wholly Owned Pipeline, while still maintaining significant equity ownership.

Number of Wholly Owned Programs advanced through clinical phases[2]

1

2020: 3
2019: 0

Progress
We advanced one of our Wholly Owned Programs, LYT-300, into the clinic in 2021. We initiated a Phase 1 clinical study of LYT-300 in healthy volunteers to evaluate the drug as a potential treatment of neurological and neuropsychological conditions with significant unmet need, such as depression, anxiety, sleep disorders, fragile X tremor-associated syndrome, essential tremor and epileptic disorders, among others.

Number of clinical trial initiations[2]

11

2020: 6
2019: 6

Progress
PureTech initiated five clinical trials, Karuna initiated four clinical trials, Vor initiated one clinical trial and Akili initiated one clinical trial in 2021.

Number of clinical readouts[2]

6

2020: 5
2019: 5

Progress
PureTech (two), Karuna (one), Gelesis (one), and Vedanta (two) reported clinical results from across their pipelines in 2021.

1 Funding figure includes private equity financings, loans and promissory notes, public offerings or grant awards. Funding figure excludes future milestone considerations received in conjunction with partnerships and collaborations. Funding figure does not include Gelesis' gross proceeds of $105.0 million from its January 2022 post-period SPAC merger.
2 Number represents figure for the relevant fiscal year only and is not cumulative.

Financial Review

Reporting Framework

You should read the following discussion and analysis together with our Consolidated Financial Statements, including the notes thereto, set forth elsewhere in this report. Some of the information contained in this discussion and analysis or set forth elsewhere in this report, including information with respect to our plans and strategy for our business and financing our business, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including the risks set forth on pages 90 to 93 and in the Additional Information section from pages 217 to 251, our actual results could differ materially from the results described in or implied by these forward-looking statements.

Our audited Consolidated Financial Statements as of December 31, 2021 and 2020, and for the years ended December 31, 2021, 2020 and 2019, have been prepared in accordance with UK-adopted International Financial Reporting Standards (IFRS). The Consolidated Financial Statements also comply fully with IFRSs as issued by the International Accounting Standards Board (IASB).

The following discussion contains references to the Consolidated Financial Statements of PureTech Health plc, or the Company, and its consolidated subsidiaries, together the Group. These financial statements consolidate the Company's subsidiaries and include the Company's interest in associates and investments held at fair value. Subsidiaries are those entities over which the Company maintains control. Associates are those entities in which the Company does not have control for financial accounting purposes but maintains significant influence over financial and operating policies. Where the Company has neither control nor significant influence for financial accounting purposes, we recognize our holding in such entity as an investment at fair value. For purposes of our Consolidated Financial Statements, each of our Founded Entities are considered to be either a "subsidiary", an "associate" or an "investment held at fair value" depending on whether PureTech Health plc controls or maintains significant influence over the financial and operating policies of the respective entity at the respective period end date. For additional information regarding the accounting treatment of these entities, see Note 1 to our Consolidated Financial Statements included in this report. For additional information regarding our operating structure, see "—Basis of Presentation and Consolidation" below. Fair value of Investments held at fair value, does not take into consideration contribution from milestones that occurred after December 31, 2021, the value of our interests in our consolidated Founded Entities (Vedanta, Follica, Sonde, and Entrega), our Wholly Owned Programs, or our cash.

Business Background and Results Overview

The business background is discussed from pages 1 to 72, which describe in detail the business development of our Wholly Owned Programs and Founded Entities.

Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our wholly-owned or Controlled Founded Entities' therapeutics candidates, which may or may not occur. Our Founded Entities, Gelesis, Inc. ("Gelesis"), and Akili Interactive Labs, Inc. ("Akili"), which we have not controlled since 2019 and 2018, respectively, have products cleared for sale, but our Wholly Owned Programs and our Controlled Founded Entities have not yet generated any meaningful revenue from product sales.

We deconsolidated a number of our Founded Entities, specifically Karuna Therapeutics, Inc. ("Karuna"), Vor Biopharma Inc. ("Vor"), and Gelesis during 2019. We expect this trend to continue into the foreseeable future as our Controlled Founded Entities raise additional funding that reduces our ownership interest. Any deconsolidation affects our financials in the following manner:

- our ownership interest does not provide us with a controlling financial interest;
- we no longer control the Founded Entity's assets and liabilities and as a result we derecognize the assets, liabilities and non-controlling interests related to the Founded Entity from our Consolidated Statements of Financial Position;
- we record our non-controlling financial interest in the Founded Entity at fair value; and
- the resulting amount of any gain or loss is recognized in our Consolidated Statements of Comprehensive Income/(Loss).

We anticipate our expenses to continue to increase proportionally in connection with our ongoing development activities related mostly due to the advancement into late-stage studies of the clinical programs within our Wholly Owned Pipeline and Controlled Founded Entities. In addition, having completed our U.S. listing in November 2020, we have, and will continue, to incur additional costs associated with operating as a public company in the U.S. We also expect that our expenses and capital requirements will increase substantially in the near to mid-term as we:

- continue our research and development efforts;
- seek regulatory approvals for any therapeutic candidates that successfully complete clinical trials;
- add clinical, scientific, operational financial and management information systems and personnel, including personnel to support our therapeutic development and potential future commercialization claims; and
- operate as a U.S. public company.

In addition, our internal research and development spend will increase in the foreseeable future as we may initiate additional clinical studies for LYT-100, LYT-200 and LYT-300, and advance LYT-210, LYT-510 and LYT-500 into the clinic and continue to progress our Glyph™, Orasome™ and Alivio™ technology platforms as well as our meningeal lymphatics research program.

In addition, with respect to our Founded Entities' programs, we anticipate that we will continue to fund a small portion of development costs

by strategically participating in such companies' financings when it is in the best interests of our shareholders. The form of any such participation may include investment in public or private financings, collaboration and partnership arrangements and licensing arrangements, among others. Our management and strategic decision makers consider the future funding needs of our Founded Entities and evaluate the needs and opportunities for returns with respect to each of these Founded Entities routinely and on a case-by-case basis.

As a result, we may need substantial additional funding in the future, following the assessment period described above, to support our continuing operations and pursue our growth strategy until such time as we can generate sufficient revenue from product sales to support our operations, if ever. Until such time we expect to finance our operations through a combination of monetization of our interests in our Founded Entities, collaborations with third parties and also potentially from public or private equity or debt financings or other sources. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we are unable to raise capital or enter into such agreements as, and when needed, we may have to delay, scale back or discontinue the development and commercialization of one or more of our wholly-owned therapeutic candidates.

Measuring Performance

The Financial Review discusses our operating and financial performance, our cash flows and liquidity as well as our financial position and our resources. The results for each year are compared primarily with the results of the preceding year.

Reported Performance

Reported performance considers all factors that have affected the results of our business, as reflected in our Consolidated Financial Statements.

Core Performance

Core performance measures are alternative performance measures (APM) which are adjusted and non-IFRS measures. These measures cannot be derived directly from our Consolidated Financial Statements. We believe that these non-IFRS performance measures, when provided in combination with reported performance, will provide investors, analysts and other stakeholders with helpful complementary information to better understand our financial performance and our financial position from period to period. The measures are also used by management for planning and reporting purposes. The measures are not substitutable for IFRS results and should not be considered superior to results presented in accordance with IFRS.

Cash flow and liquidity

PureTech Level Cash and Cash Equivalents	**Measure type:** Core performance. **Definition:** Cash and cash equivalents held at PureTech Health plc and only wholly-owned subsidiaries as noted (PureTech LYT, PureTech LYT-100, PureTech Management, Inc., PureTech Health LLC,and other inactive entities in which we have no current operations. During the year ended December 31, 2021, the Company acquired the non controlling interest in Alivio Therapeutics, Inc. and since then Alivio Therapeutics, Inc. is wholly owned by the Company and the related cash and cash equivalents are included in the PureTech Level Cash and Cash Equivalents as of December 31, 2021. The cash and cash equivalents of Alivio Therapeutics, Inc. were not included in the PureTech Level Cash and Cash Equivalents as of December 31, 2020 as during that period, the subsidiary was not wholly owned by the Company. **Why we use it:** PureTech Level Cash and Cash Equivalents is a measure that provides valuable additional information with respect to cash and cash equivalents available to fund the Wholly Owned Programs and make certain investments in Founded Entities.

The Company no longer presents in the reported periods Consolidated Cash Reserves or PureTech Level Cash Reserves as the Company does not have short-term investments in addition to its cash and cash equivalents in all reported periods.

COVID-19

In March 2020, the World Health Organization declared the COVID-19 outbreak a pandemic. The pandemic has since caused widespread and significant disruption to daily life and the global economy as governments have taken actions, including the issuance of stay-at-home orders and social distancing guidelines, and businesses have adjusted their activities. While our business, operations and financial condition and results have not been significantly impacted in 2020 or 2021, as a result of the COVID-19 pandemic, we have taken swift action to ensure the safety of our employees and other stakeholders. We continue to monitor the latest developments regarding the COVID-19 pandemic on our business, operations, and financial condition and results and cannot predict the impact, including as a result of variations of the virus, that the pandemic may have on our business, operations, and financial condition and results.

Recent Developments (subsequent to December 31, 2021)

On January 13, 2022 Gelesis completed its business combination with Capstar Special Purpose Acquisition Corp ("Capstar"). As part of the business combination all shares held in Gelesis, common and preferred, were exchanged for common shares of the merged entity. In addition, PureTech invested $15.0 million in the class A common shares of Capstar as part of the PIPE transaction that took place immediately prior to the closing of the business combination and an additional approximately $5.0 million, as part of the Backstop agreement signed with Capstar on December 30, 2021. Pursuant to the business combination, Gelesis became a wholly-owned subsidiary of Capstar and Capstar changed its name to Gelesis Holdings, Inc., which began trading on the New York Stock Exchange under the ticker symbol "GLS" on January 14, 2022. Following the closing of the business combination, PureTech holds 16,727,582 shares of Gelesis Holdings Inc. common stock, which is equal to approximately 23.2% of Gelesis Holdings Inc's outstanding common shares.

On January 26, 2022 Akili Interactive and Social Capital Suvretta Holdings Corp a special purpose acquisition company announced they had entered into a definitive business combination agreement. Upon completion of the transaction, the combined company's securities are expected to be traded on the Nasdaq Stock Market under the ticker symbol "AKLI". The transaction is expected to close in mid-2022. As part of this transaction the Akili Interactive shares held by the Company will be exchanged for the combined company's securities and the Company's interest in the combined public entity is expected to decrease from its current voting interest in Akili of 26.4%.

Financial Highlights

Following is the reconciliation of the amounts appearing in our Statement of Financial Position to the Alternative Performance Measure described above:

	As of:	
(in thousands)	December 31, 2021	December 31, 2020
Consolidated Cash and cash equivalents	465,708	403,881
Less: Cash and cash equivalents held at non-wholly owned subsidiaries	(46,856)	(54,473)
PureTech Level Cash and Cash Equivalents	$418,851	$349,407

Basis of Presentation and Consolidation

Our Consolidated Financial Information consolidates the financial information of PureTech Health plc, as well as its subsidiaries, and includes our interest in associates and investments held at fair value, and is reported in four operating segments as described below.

Basis for Segmentation

Our Directors are our strategic decision-makers. Our operating segments are based on the financial information provided to our Directors periodically for the purposes of allocating resources and assessing performance. We have determined that each Founded Entity is representative of a single operating segment as our Directors monitor the financial results at this level. When identifying the reportable segments we have determined that it is appropriate to aggregate multiple operating segments into a single reportable segment given the high level of operational and financial similarities across the entities. We have identified multiple reportable segments which are outlined below. Substantially all of our revenue and profit generating activities are generated within the United States and, accordingly, no geographical disclosures are provided.

There was no change to reportable segments in 2021, except the change in the composition of the segments with respect to Alivio, as explained below.

During the year ended December 31, 2021, the Company acquired the non controlling interest in Alivio and since then Alivio is wholly owned by the Company and is managed within the Internal segment. The Company has revised in this report the prior period segment financial information to conform to the presentation as of and for the period ending December 31, 2021. This change in segments reflects how the Company's Board of Directors reviews the Group's results, allocates resources and assesses performance of the Group at this time.

Following is the description of our reportable segments:

Internal

The Internal segment is advancing Wholly Owned Programs, which is focused on immunological, fibrotic and lymphatic system disorders and builds upon validated biologic pathways and proven pharmacology. The Internal segment is comprised of the technologies that are wholly owned and will be advanced through either PureTech Health funding or non-dilutive sources of financing in the near-term. The operational management of the Internal segment is conducted by the PureTech Health team, which is responsible for the strategy, business development, and research and development. As of December 31, 2021, this segment included PureTech LYT, Inc. (formerly Ariya Therapeutics Inc.), PureTech LYT-100, Inc and Alivio Therapeutics, Inc.

Controlled Founded Entities

The Controlled Founded Entities segment is comprised of our subsidiaries that are currently consolidated operational subsidiaries that either have, or have plans to hire, independent management teams and have previously raised, or are currently in the process of raising, third-party dilutive capital. These subsidiaries have active research and development programs and either have entered into or plan to seek a strategic partnership with an equity or debt investment partner, who will provide additional industry knowledge and access to networks, as well as additional funding to continue the pursued growth of the company. As of December 31, 2021, this segment included Entrega, Inc., Follica, Incorporated, Sonde Health, Inc. and Vedanta Biosciences, Inc.

Non-Controlled Founded Entities

The Non-Controlled Founded Entities segment is comprised of the entities in respect of which PureTech Health (i) no longer holds majority voting control as a shareholder and (ii) no longer has the right to elect a majority of the members of the entity's Board of Directors. Upon deconsolidation of an entity the segment disclosure is restated to reflect the change on a retrospective basis, as this constitutes a change in the composition of its reportable segments. The Non-Controlled Founded Entities segment included Akili Interactive Labs, Inc. ("Akili"), Vor Biopharma, Inc. ("Vor"), Karuna Therapeutics, Inc. ("Karuna"), and Gelesis, Inc. ("Gelesis").

The Non-Controlled Founded Entities segment incorporates the operational results of the aforementioned entities to the date of deconsolidation.

Following the date of deconsolidation, we account for our investment in each entity at the parent level, and therefore the results associated with investment activity following the date of deconsolidation is included in the Parent Company and Other segment (the "Parent Company and Other segment").

Parent Company and Other

Parent Company and Other includes activities that are not directly attributable to the operating segments, such as the activities of the Parent, corporate support functions and certain research and development support functions that are not directly attributable to a strategic business segment as well as the elimination of intercompany transactions. Parent Company and Other also captures the accounting for our holdings in entities for which control has been lost, which is inclusive of the following items: gain on deconsolidation, gain or loss on investments held at fair value, gain on loss of significant influence, and the share of net loss of associates accounted for using the equity method. As of December 31, 2021, this segment included PureTech Health plc, PureTech Health LLC, PureTech Management, Inc., PureTech Securities Corp., and PureTech Securities II Corp. as well as certain other dormant, inactive and shell entities.

The table below summarizes the entities that comprised each of our segments as of December 31, 2021:

Internal Segment	
PureTech LYT	100.0%
PureTech LYT-100, Inc.	100.0%
Alivio Therapeutics, Inc.	100.0%
Controlled Founded Entities	
Entrega, Inc.	77.3%
Follica, Incorporated	85.4%
Sonde Health, Inc.	51.8%
Vedanta Biosciences, Inc.	48.6%
Non-Controlled Founded Entities	
Akili Interactive Labs, Inc.	26.7%
Gelesis, Inc.	24.5%
Karuna Therapeutics, Inc.	5.6%
Vor Biopharma Inc.	8.6%
Parent Segment[1]	
Puretech Health plc	100.0%
PureTech Health LLC	100.0%
PureTech Securities Corporation	100.0%
PureTech Securities II Corporation	100.0%
PureTech Management, Inc.	100.0%

1 Includes dormant, inactive and shell entities that are not listed here.

Components of Our Results of Operations

Revenue

To date, we have not generated any meaningful revenue from product sales and we do not expect to generate any meaningful revenue from product sales for the near term future. We derive our revenue from the following:

Contract revenue

We generate revenue primarily from licenses, services and collaboration agreements, including amounts that are recognized related to upfront payments, milestone payments, royalties and amounts due to us for research and development services. In the future, revenue may include additional milestone payments and royalties on any net product sales under our collaborations. We expect that any revenue we generate will fluctuate from period to period as a result of the timing and amount of license, research and development services and milestone and other payments.

Grant Revenue

Grant revenue is derived from grant awards we receive from governmental agencies and non-profit organizations for certain qualified research and development expenses. We recognize grants from governmental agencies as grant income in the Consolidated Statement of Comprehensive Income/(Loss), gross of the expenditures that were related to obtaining the grant, when there is reasonable assurance that we will comply with the conditions within the grant agreement and there is reasonable assurance that payments under the grants will be received. We evaluate the conditions of each grant as of each reporting date to ensure that we have reasonable assurance of meeting the conditions of each grant arrangement and it is expected that the grant payment will be received as a result of meeting the necessary conditions.

For proceeds from sale of our investments held at fair value, please see our Consolidated Cash flow Statements, Net cash provided by investing activities.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our discovery efforts, and the development of our wholly-owned and our Controlled Founded Entities' therapeutic candidates, which include:

- employee-related expenses, including salaries, related benefits and equity-based compensation;
- expenses incurred in connection with the preclinical and clinical development of our wholly-owned and our Founded Entities' therapeutic candidates, including our agreements with contract research organizations, or CROs;
- expenses incurred under agreements with consultants who supplement our internal capabilities;
- the cost of lab supplies and acquiring, developing and manufacturing preclinical study materials and clinical trial materials;
- costs related to compliance with regulatory requirements; and
- facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other operating costs.

We expense all research costs in the periods in which they are incurred and development costs are capitalized only if certain criteria are met. For the periods presented, we have not capitalized any development costs since we have not met the necessary criteria required for capitalization. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and third-party service providers.

Research and development activities are central to our business model. Therapeutic candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will continue to increase for the foreseeable future in connection with our planned preclinical and clinical development activities in the near term and in the future. The successful development of our wholly-owned and our Founded Entities' therapeutic candidates is highly uncertain. As such, at this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the remainder of the development of these therapeutic candidates. We are also unable to predict when, if ever, material net cash inflows will commence from our wholly-owned or our Founded Entities' therapeutic candidates. This is due to the numerous risks and uncertainties associated with developing therapeutics, including the uncertainty of:

- progressing research and development of our Wholly Owned Pipeline, including LYT-100, LYT-200, LYT-210, LYT-300, LYT-510, LYT-500 and continue to progress our Glyph™, Orasome™ and Alivio™ technology platforms as well as our meningeal lymphatics research program and other potential therapeutic candidates based on previous human efficacy and clinically validated biology within our Wholly Owned Programs;
- establishing an appropriate safety profile with investigational new drug application enabling studies to advance our preclinical programs into clinical development;
- the success of our Founded Entities and their need for additional capital;
- identifying new therapeutic candidates to add to our Wholly Owned Pipeline;
- successful enrollment in, and the initiation and completion of, clinical trials;
- the timing, receipt and terms of any marketing approvals from applicable regulatory authorities;
- commercializing our wholly-owned and our Founded Entities' therapeutic candidates, if approved, whether alone or in collaboration with others;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- addressing any competing technological and market developments, as well as any changes in governmental regulations;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter and performing our obligations under such arrangements;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how, as well as obtaining and maintaining regulatory exclusivity for our wholly-owned and our Founded Entities' therapeutic candidates;
- continued acceptable safety profile of our therapeutics, if any, following approval; and
- attracting, hiring and retaining qualified personnel.

A change in the outcome of any of these variables with respect to the development of a therapeutic candidate

could mean a significant change in the costs and timing associated with the development of that therapeutic candidate. For example, the FDA, the EMA, or another comparable foreign regulatory authority may require us to conduct clinical trials beyond those that we anticipate will be required for the completion of clinical development of a therapeutic candidate, or we may experience significant trial delays due to patient enrollment or other reasons, in which case we would be required to expend significant additional financial resources and time on the completion of clinical development. In addition, we may obtain unexpected results from our clinical trials and we may elect to discontinue, delay or modify clinical trials of some therapeutic candidates or focus on others. Identifying potential therapeutic candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our wholly-owned and our Founded Entities' therapeutic candidates, if approved, may not achieve commercial success.

General and Administrative Expenses
General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in our executive, finance, corporate and business development and administrative functions. General and administrative expenses also include professional fees for legal, patent, accounting, auditing, tax and consulting services, travel expenses and facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

We expect that our general and administrative expenses will increase in the future as we increase our general and administrative headcount to support our continued research and development and potential commercialization of our portfolio of therapeutic candidates. We also expect to incur increased expenses associated with being a public company in the United States, including costs of accounting, audit, information systems, legal, regulatory and tax compliance services, director and officer insurance costs and investor and public relations costs.

Total Other Income/(Loss)

Gain on Deconsolidation
Upon losing control of a subsidiary, the assets and liabilities are derecognized along with any related non-controlling interest ("NCI"). Any interest retained in the former subsidiary is measured at fair value when control is lost. Any resulting gain or loss is recognized as profit or loss in the Consolidated Statements of Comprehensive Income/(Loss).

Gain/(Loss) on Investments Held at Fair Value
Investments held at fair value include both unlisted and listed securities held by us, which include investments in Akili, Gelesis, Karuna, Vor and certain insignificant investments. Our ownership in Akili is in preferred shares. Our ownership in Vor was in preferred shares until February 2021 at which time the preferred shares were converted into common shares as part of Vor Initial Public Offering. Preferred shares form part of our ownership in Gelesis and such preferred shares investment is accounted for as Investments Held at Fair value while the investment in common stock is accounted for under the equity method. When the investment in common stock is reduced to zero by equity method losses, subsequent equity method losses are applied to the preferred share investment, which is considered to be a Long-term Interest. Our ownership in Karuna was in preferred shares until its IPO in June 2019 when such shares were converted into common shares. When Karuna's preferred shares converted into common shares, our equity interest in Karuna investment was removed from Investments Held at Fair Value and accounted for under the equity method as we still retained significant influence in Karuna at such time. On December 2, 2019 we lost significant influence in Karuna and, beginning on that date, we accounted for our investment in Karuna in accordance with IFRS 9 as an Investment Held at Fair Value. We account for investments in preferred shares of our associates in accordance with IFRS 9 as Investments Held at Fair Value when the preferred shares do not provide access to returns underlying ownership interests.

Loss Realized on Investments Held at Fair Value
Loss realized on investments held at fair value relates to realized differences in the per share disposal price of a listed security as compared to the per share exchange quoted price at the time of disposal. The difference is attributable to a block sale discount, attributable to a variety of market factors, primarily the number of shares being transacted was significantly larger than the daily trading volume of a given security.

Gain on Loss of Significant Influence
Gain on loss of significant influence relates to the assessment related to the loss of our ability to exert significant influence over an investment in a Non-Controlled Founded Entity that is accounted for under the equity method. For the year ended December 31, 2019, we recognized gain on loss of significant influence in Karuna.

Other Income (Expense)
Other income (expense) consists primarily of gains and losses related to the sale of an asset and certain investments as well as sub-lease income.

Finance Costs/Income
Finance costs consist of loan interest expense and the changes in the fair value of certain liabilities associated with financing transactions, mainly preferred share liabilities in respect of preferred shares issued by our non wholly owned subsidiaries to third parties. Finance income consists of interest income on funds invested in money market funds and U.S. treasuries.

Share of Net Gain (Loss) of Associates Accounted for Using the Equity Method, and Impairment of Investment in Associate
Associates are accounted for using the equity method (equity accounted investees) and are initially recognized at cost, or if recognized upon deconsolidation they are initially recorded at fair value at the date of deconsolidation. The consolidated financial statements include our share of the total comprehensive income and equity movements of equity accounted investees, from the date that significant influence commences until the date that significant influence ceases. When the share of losses exceeds the net investment in the investee, including the investment in preferred shares that are considered Long-term Interests, the carrying amount is reduced to nil and recognition of further losses is discontinued except to the extent that we have incurred legal or constructive obligations or made payments on behalf of an investee.

We compare the recoverable amount of the investment to its carrying amount on a go-forward basis and determine the need for impairment. We recorded an impairment in the common stock investment in Gelesis in the year ended December 31, 2019.

Income Tax

We must make certain estimates and judgments in determining income tax expense for financial statement purposes. The amount of taxes currently payable or refundable is accrued, and deferred tax assets and liabilities are recognized for the estimated future tax consequences attributable to differences between the financial statement carrying amount of existing assets and liabilities and their respective tax bases. Deferred tax assets are also recognized for realizable loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using substantively enacted tax rates in effect for the year in which those temporary differences are expected to be recovered or settled. Net deferred tax assets are not recorded if we do not assess their realization as probable. The effect on deferred tax assets and liabilities of a change in income tax rates is recognized in our financial statements in the period that includes the substantive enactment date.

Results of Operations

The following table, which has been derived from our audited financial statements for the years ended December 31, 2021, 2020 and 2019, included herein, summarizes our results of operations for the periods indicated, together with the changes in those items in dollars:

	Year Ended December 31,				
(in thousands)	**2021**	2020	2019	Change (2020 to 2021)	Change (2019 to 2020)
Contract revenue	**$9,979**	$8,341	$8,688	$1,638	$(347)
Grant revenue	**7,409**	3,427	1,119	3,982	2,308
Total revenue	**17,388**	11,768	9,807	5,621	1,961
Operating expenses:					
General and administrative expenses	**(57,199)**	(49,440)	(59,358)	(7,760)	9,918
Research and development expenses	**(110,471)**	(81,859)	(85,848)	(28,612)	3,988
Operating income/(loss)	**(150,282)**	(119,531)	(135,399)	(30,751)	15,868
Other income/(expense):					
Gain/(loss) on deconsolidation	**—**	—	264,409	—	(264,409)
Gain/(loss) on investments held at fair value	**179,316**	232,674	(37,863)	(53,358)	270,537
Loss realized on sale of investment	**(20,925)**	(54,976)	—	34,051	(54,976)
Gain/(loss) on disposal of assets	**—**	—	—	—	—
Gain on loss of significant influence	**—**	—	445,582	—	(445,582)
Other income/(expenses)	**1,592**	1,035	39	557	996
Other income/(loss)	**159,983**	178,732	672,167	(18,749)	(493,434)
Net finance income/(costs)	**5,050**	(6,115)	(46,147)	11,164	40,032
Share of net gain/(loss) of associates accounted for using the equity method	**(73,703)**	(34,117)	30,791	(39,587)	(64,908)
Impairment of investment in associate	**—**	—	(42,938)	—	42,938
Income/(loss) before income taxes	**(58,953)**	18,969	478,474	(77,922)	(459,504)
Taxation	**(3,756)**	(14,401)	(112,409)	10,645	98,008
Net income/(loss) including non-controlling interest	**(62,709)**	4,568	366,065	(67,277)	(361,497)
Net (loss)/income attributable to the Company	**$(60,558)**	$5,985	$421,144	$(66,543)	$(415,159)

Comparison of the Years Ended December 31, 2021 and 2020

Total Revenue

	Year Ended December 31,		
(in thousands)	**2021**	2020	Change
Contract Revenue:			
Internal Segment	**$8,129**	$5,297	$2,833
Controlled Founded Entities	**1,615**	990	625
Non-Controlled Founded Entities	**—**	—	—
Parent Company and other	**235**	2,054	(1,819)
Total Contract Revenue	**$9,979**	$8,341	$1,638
Grant Revenue:			
Internal Segment	**$1,253**	$1,563	$(310)
Controlled Founded Entities	**6,156**	1,864	4,292
Non-Controlled Founded Entities	**—**	—	—
Parent Company and other	**—**	—	—
Total Grant Revenue	**$7,409**	$3,427	$3,982
Total Revenue	**$17,388**	$11,768	$5,621

Our total revenue was $17.4 million for the year ended December 31, 2021, an increase of $5.6 million, or 47.8 percent compared to the year ended December 31, 2020. The increase was primarily attributable to an increase of $2.8 million in contract revenue in the Internal segment, which was primarily driven by a $6.5 million increase in revenue due to payment

from Imbrium Therapeutics, Inc. following the exercise of the option to acquire an exclusive license for the Initial Product Candidate. The increase was partially offset by a decrease in contract revenue of $3.7 million recognized under IFRS 15 due to the completion of development activities related to revenues associated with multiple collaborations in the year ended December 31, 2021. The increase was also driven by an increase of $4.3 million in grant revenue in the Controlled Founded Entities segment for the year ended December 31, 2021, which was driven primarily by Vedanta's grant revenue earned pursuant to its CARB-X and BARDA agreements. The aforementioned increases were partially offset by the a non-recurrent milestone payment of $2.0 million received from Karuna (and included in Parent Company and Other) in the year ended December 31, 2020.

Research and Development Expenses

	Year Ended December 31,		
(in thousands)	**2021**	2020	Change
Research and Development Expenses:			
Internal Segment	**$(65,444)**	$(45,346)	$20,098
Controlled Founded Entities	**(43,783)**	(36,279)	7,504
Non-Controlled Founded Entities	**—**	—	—
Parent Company and other	**(1,244)**	(234)	1,010
Total Research and Development Expenses:	**$(110,471)**	$(81,859)	$28,612

Our research and development expenses were $110.5 million for the year ended December 31, 2021, an increase of $28.6 million, or 35.0 percent compared to the year ended December 31, 2020. The change was primarily attributable to an increase of $20.1 million in research and development expenses incurred by the Internal segment due to the advancement of programs in clinical testing. This was primarily driven by an increase in clinical trial and clinical research organization expenditures of $14.0 million, an increase in research and development related consulting and professional fees of $2.5 million and an increase in research and development related salaries and stock compensation of $2.6 million. We progressed our ongoing clinical trials of LYT-100 and LYT- 200 in multiple indications and initiated clinical trials with respect to LYT 300, as well as advanced pre-clinical studies and research related to multiple candidates and research platforms. The increase was further attributable to an increase of $7.5 million in research and development expenses incurred by the Controlled Founded Entities segment, primarily attributable to Vedanta as they progressed their therapeutic candidates VE202, VE303, VE416 and VE800 towards meaningful milestones.

General and Administrative Expenses

	Year Ended December 31,		
(in thousands)	**2021**	2020	Change
General and Administrative Expenses:			
Internal Segment	**$(8,673)**	$(3,482)	$5,191
Controlled Founded Entities	**(20,729)**	(13,691)	7,038
Non-Controlled Founded Entities	**—**	—	—
Parent Company and other	**(27,797)**	(32,267)	(4,470)
Total General and Administrative Expenses	**$(57,199)**	$(49,440)	$7,760

Our general and administrative expenses were $57.2 million for the year ended December 31, 2021, an increase of $7.8 million, or 15.7 percent compared to the year ended December 31, 2020. The increase was primarily attributable to an increase of $7.0 million in the Controlled Founded Entities segment, which was primarily driven by non-cash increases of $2.9 million in stock based compensation expense, $1.4 million increase in payroll-related costs due to increased personnel, an increase in professional fees of $1.1 million, and an increase in legal fees of $0.9 million. The increase was further attributable to an increase of $5.2 million in the Internal segment, which was primarily driven by an increase in the management fee charged by the Parent company of $6.2 million which was partially offset by a decrease in depreciation expense of $0.5 million for the year ended December 31, 2021. The decrease in the Parent Company and other of $4.5 million was primarily attributable to the allocation of management fee charged to other segments of $7.0 million which was partially offset by an increase in professional and recruiting fees of $0.9 million and an increase in business insurance of $1.7 million for the year ended December 31, 2021.

Total Other Income (Loss)

Total other income was $160.0 million for the year ended December 31, 2021, a decrease of $18.7 million, compared to the year ended December 31, 2020. The decline in other income was primarily attributable to a decrease in gains from investments held at fair value of $53.4 million, primarily driven by the change in the fair value of the investment in Karuna. These gains from investments held at fair value were partially offset by losses realized on sale of certain investments held at fair value, as a result of the block sale discount included in the sale. The losses realized on sale of certain investments held at fair value for the year ended December 31, 2021 decreased $34.1 million compared to the year ended December 31, 2020.

Net Finance Income (Costs)

Net finance Income was $5.0 million for the year ended December 31, 2021, a change of $11.2 million, compared to net finance cost of $6.1 million for the year ended December 31, 2020. The change was primarily attributable to a $14.0 million change leading to increased income in respect of the change in the fair value of our preferred shares, warrant and convertible note liabilities held by third parties, partially offset by a $1.8 million increase in contractual finance costs, mainly in our controlled founded entity, Vedanta, and a $1.0 million decline in interest income from financial assets for the year ended December 31, 2021.

Share of Net Gain (Loss) in Associates Accounted for Using the Equity Method

For the year ended December 31, 2021, the share in net loss of associates reported under the equity method was $73.7 million as compared to the share of net loss of $34.1 million for the year ended December 31, 2020. The change was primarily attributable to an increase in Gelesis losses reported under IFRS for the year ended December 31, 2021 as compared to the losses reported for the year ended December 31, 2020, due to an increase in the fair value of Gelesis financial instrument liabilities that are accounted for at Fair Value Through Profit and Loss (FVTPL).

Taxation

Income tax expense was $3.8 million for the year ended December 31, 2021, as compared to income tax expense of $14.4 million for the year ended December 31, 2020. The decrease in income tax expense was primarily attributable to the decrease in profit before tax in entities in the U.S. Federal and Massachusetts consolidated return groups of the Company. For information on the change in the tax rate, see Note 25 in the consolidated financial statements.

Comparison of the Years Ended December 31, 2020 and 2019

Total Revenue

	Year Ended December 31,		
(in thousands)	2020	2019	Change
Contract Revenue:			
Internal Segment	$5,297	$7,077	$(1,780)
Controlled Founded Entities	990	1,474	(484)
Non-Controlled Founded Entities	—	—	—
Parent Company and other	2,054	137	1,917
Total Contract Revenue	$8,341	$8,688	$(347)
Grant Revenue:			
Internal Segment	$1,563	$928	$635
Controlled Founded Entities	1,864	191	1,673
Non-Controlled Founded Entities	—	—	—
Parent Company and other	—	—	—
Total Grant Revenue	$3,427	$1,119	$2,308
Total Revenue	$11,768	$9,807	$1,961

Our total revenue was $11.8 million for the year ended December 31, 2020, an increase of $2.0 million, or 20.0 percent compared to the year ended December 31, 2019. The increase was primarily attributable to an increase of $2.3 million in grant revenue in the Controlled Founded Entities segment for the year ended December 31, 2020, which was driven primarily by Vedanta's grant revenue earned pursuant to its CARB-X and BARDA agreements. The increase was further attributable to an increase of $1.9 million in contract revenue in the Parent segment for the year ended December 31, 2020, which was primarily driven by a $2.0 million milestone payment received from Karuna for initiation of its KarXT Phase 3 clinical study pursuant to the Exclusive Patent License Agreement between PureTech and Karuna. The increases were partially offset by a decline of $1.8 million in contract revenue in the Internal segment, which was primarily drive by the Orasome collaboration and license agreement with Roche, which concluded during the year ended December 31, 2020.

Research and Development Expenses

	Year Ended December 31,		
(in thousands)	2020	2019	Change
Research and Development Expenses:			
Internal Segment	$(45,346)	$(28,874)	$16,472
Controlled Founded Entities	(36,279)	(39,883)	(3,603)
Non-Controlled Founded Entities	—	(15,555)	(15,555)
Parent Company and other	(234)	(1,536)	(1,302)
Total Research and Development Expenses:	$(81,859)	$(85,848)	$(3,988)

Our research and development expenses were $81.9 million for the year ended December 31, 2020, a decline of $4.0 million, or 4.6 percent compared to the year ended December 31, 2019. The change was attributable to a decline of $15.6 million in the Non-Controlled Founded Entities segment owing to the deconsolidation of Vor, Karuna and Gelesis during year ended December 31, 2019. The decline was further attributable to declines of $3.6 million in the Controlled Founded Entities segment and $1.3 million in the Parent segment for the year ended December 31, 2020. The declines were partially offset by an increase of $16.5 million in research and development expenses incurred by the Internal segment for the year ended December 31, 2020. In 2020 we progressed our wholly-owned therapeutic candidates to key milestones. We completed a Phase 1 multiple ascending dose and food effect study for LYT-100. We also initiated a Phase 2a proof-of-concept study of LYT-100 in patients with breast cancer-related, upper limb secondary lymphedema as well as initiated a Phase 2 trial of LYT-100 in Long COVID respiratory complications and related sequelae, which is also known as post-acute COVID-19 syndrome (PACS). Finally, we initiated a Phase 1 clinical trial of LYT-200 for the potential treatment of metastatic solid tumors that are difficult to treat and have poor survival rates.

General and Administrative Expenses

(in thousands)	Year Ended December 31, 2020	2019	Change
General and Administrative Expenses:			
Internal Segment	$(3,482)	$(3,252)	$230
Controlled Founded Entities	(13,691)	(13,569)	122
Non-Controlled Founded Entities	—	(10,439)	(10,439)
Parent Company and other	(32,267)	(32,098)	168
Total General and Administrative Expenses	$(49,440)	$(59,358)	$(9,918)

Our general and administrative expenses were $49.4 million for the year ended December 31, 2020, a decrease of $9.9 million, or 16.7 percent compared to the year ended December 31, 2019. The decrease was primarily attributable to a decline of $10.4 million in the Non-Controlled Founded Entities segment, owing to the deconsolidation of Vor, Karuna and Gelesis during the year ended December 31, 2019.

Total Other Income (Loss)

Total other income was $178.7 million for the year ended December 31, 2020 a decrease of $493.4 million, compared to the year ended December 31, 2019. We recognized a gain on loss of significant influence of $445.6 million with respect to Karuna for the year ended December 31, 2019. No loss of significant influence of associates occurred during the year ended December 31, 2020. The decline was further attributable to a decline of $264.4 million in gain on deconsolidation as no deconsolidation of subsidiaries occurred during the year ended December 31, 2020, as compared to a gain of $264.4 million recognized for the deconsolidation of Vor, Karuna and Gelesis during the year ended December 31, 2019. The decline was further attributable to a loss of $55.0 million realized on the sale of certain investments held at fair value during year ended December 31, 2020. The declines were partially offset by an increase of $270.5 million on gain on investments held at fair value for the year ended December 31, 2020, which was primarily driven by Karuna.

Net Finance Income (Costs)

Net finance costs were $6.1 million for the year ended December 31, 2020, a decline of $40.0 million, or 86.7 percent compared to net finance costs of $46.1 million for the year ended December 31, 2019. The change was primarily attributable to a $42.1 million decline in the change in the fair value of our preferred shares, warrant and convertible note liabilities held by third parties for the year ended December 31, 2020.

Share of Net Gain (Loss) in Associates Accounted for Using the Equity Method, and Impairment of Investment in Associate

The share of net loss in associates was $34.1 million for the year ended December 31, 2020, a decrease of $64.9 million, or 210.8 percent as compared to net gain of $30.8 million for the year ended December 31, 2019. The change in share of net gain/(loss) in associates was primarily attributable to the financial results of Gelesis for the year ended December 31, 2020. Additionally, we allocated a share of our net loss in Gelesis for the year ended December 31, 2020, totaling $23.0 million, to our long-term interest in Gelesis as of December 31, 2020. We recorded equity method income of $37.1 million with respect to Gelesis, which was partially offset by our share of net loss in Karuna of $6.3 million for the year ended December 31, 2019. Additionally, we recorded an impairment charge of $42.9 million for the year ended December 31, 2019, related to our investment in common shares held in Gelesis. See Note 6 to our consolidated financial statements included elsewhere in this annual report.

Taxation

Income tax expense was $14.4 million for the year ended December 31, 2020, a decline of $98.0 million, or 87.2 percent as compared to the year ended December 31, 2019. The decline in income tax expense was primarily attributable to the gains realized on the loss of significant influence on Karuna for the year ended December 31, 2019 and the gains recognized on deconsolidation of Vor, Karuna and Gelesis during the year ended December 31, 2019.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with international accounting standards in conformity with the requirements of the Companies Act 2006 and International Financial Reporting Standards (IFRSs) as adopted for use in the UK. The Consolidated Financial Statements also comply fully with IFRS as issued by the International Accounting Standards Board (IASB). In the preparation of these financial statements, we are required to make judgments, estimates and assumptions about the carrying amounts of assets and liabilities that are not readily apparent from other sources. The estimates and associated assumptions are based on historical experience and other factors that are considered to be relevant. Actual results may differ from these estimates under different assumptions or conditions.

Our estimates and assumptions are reviewed on an ongoing basis. Revisions to accounting estimates are recognized in the period in which the estimate is revised if the revision affects only that period or in the period of the revisions and future periods if the revision affects both current and future periods.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing at the end of this report, we believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our financial statements. See Note 1 to our consolidated financial statements for a further detailed description of our significant accounting policies.

Financial instruments
We account for our financial instruments according to IFRS 9. As such, when issuing preferred shares in our subsidiaries we determine the classification of financial instruments in terms of liability or equity. Such determination involves significant judgement. These judgements include an assessment of whether the financial instruments include any embedded derivative features, whether they include contractual obligations upon us to deliver cash or other financial assets or to exchange financial assets or financial liabilities with another party at any point in the future prior to liquidation, and whether that obligation will be settled by exchanging a fixed amount of cash or other financial assets for a fixed number of the Group's equity instruments.

In accordance with IFRS 9 we carry certain investments in equity securities at fair value as well as our subsidiary preferred share, convertible notes and warrant liabilities, all through profit and loss (FVTPL). Valuation of the aforementioned financial instruments (assets and liabilities) includes making significant estimates, specifically determining the appropriate valuation methodology and making certain estimates of the future earnings potential of the subsidiary businesses, appropriate discount rate and earnings multiple to be applied, marketability and other industry and company specific risk factors.

Consolidation:
The consolidated financial statements include the financial statements of the Company and the entities it controls. Based on the applicable accounting rules, the Company controls an investee when it is exposed, or has rights, to variable returns from its involvement with the investee and has the ability to affect those returns through its power over the investee. Therefore an assessment is required to determine whether the Company has (i) power over the investee; (ii) exposure, or rights, to variable returns from its involvement with the investee; and (iii) the ability to use its power over the investee to affect the amount of the investor's returns. Judgement is required to perform such assessment and it requires that the Company considers, among others, activities that most significantly affect the returns of the investee, its voting shares, representation on the board, rights to appoint board members and management, shareholders agreements, de facto power, investee dependence on the Company and other contributing factors.

Investment in Associates
When we do not control an investee but maintain significant influence over the financial and operating policies of the investee the investee is an associate. Significant influence is presumed to exist when we hold 20 percent or more of the voting power of an entity, unless it can be clearly demonstrated that this is not the case. We evaluate if we maintain significant influence over associates by assessing if we have the power to participate in the financial and operating policy decisions of the associate.

Associates are accounted for using the equity method (equity accounted investees) and are initially recognized at cost, or if recognized upon deconsolidation they are initially recorded at fair value at the date of deconsolidation. The consolidated financial statements include our share of the total comprehensive income and equity movements of equity accounted investees, from the date that significant influence commences until the date that significant influence ceases. When our share of losses exceeds the net investment in an equity accounted investee, including preferred share investments that are considered to be Long-Term Interests, the carrying amount is reduced to zero and recognition of further losses is discontinued except to the extent that we have incurred legal or constructive obligations or made payments on behalf of an investee. To the extent we hold interests in associates that are not providing access to returns underlying ownership interests, the instrument held by PureTech is accounted for in accordance with IFRS 9.

Judgement is required in order to determine whether we have significant influence over financial and operating policies of investees. This judgement includes, among others, an assessment whether we have representation on the Board of Directors of the investee, whether we participate in the policy making processes of the investee, whether there is any interchange of managerial personnel, whether there is any essential technical information provided to the investee and if there are any transactions between us and the investee.

Judgement is also required to determine which instruments we hold in the investee form part of the investment in the associate, which is accounted for under IAS 28 and scoped out of IFRS 9, and which instruments are separate financial instruments that fall under the scope of IFRS 9. This judgement includes an assessment of the characteristics of the financial instrument of the investee held by us and whether such financial instrument provides access to returns underlying an ownership interest.

Where the company has other investments in an equity accounted investee that are not accounted for under IAS 28, judgement is required in determining if such investments constitute Long-Term Interests for the purposes of IAS 28 (please refer to Notes 5 and 6). This determination is based on the individual facts and circumstances and characteristics of each investment, but is driven, among other factors, by the intention and likelihood to settle the instrument through redemption or repayment in the foreseeable future, and whether or not the investment is likely to be converted to common stock or other equity instruments

Recent Accounting Pronouncements
For information on recent accounting pronouncements, see our consolidated financial statements and the related notes found elsewhere in this report.

Cash Flow and Liquidity

Our cash flows may fluctuate and are difficult to forecast and will depend on many factors, including:

- the expenses incurred in the development of wholly-owned and Controlled Founded Entity therapeutic candidates;
- the revenue, if any, generated by wholly-owned and Controlled-Founded Entity therapeutic candidates;
- the revenue, if any, generated from licensing and royalty agreement with Founded Entities;
- the financing requirements of the Internal segment, Controlled-Founded Entities segment and Parent segment; and
- the investment activities in the Internal, Controlled-Founded Entities, and Non-Controlled Founded Entities and Parent segments.

As of December 31, 2021, we had consolidated cash and cash equivalents of $465.7 million. As of December 31, 2021, we had PureTech Level cash and cash equivalents of $418.9 million (for a definition of PureTech Level cash and cash equivalents, see paragraph "Cash flow and cash equivalents" earlier in this Financial review).

Cash Flows

The following table summarizes our cash flows for each of the periods presented:

	Year Ended December 31,		
(in thousands)	**2021**	2020	2019
Net cash used in operating activities	**$(158,274)**	$(131,827)	$(98,156)
Net cash provided by investing activities	**197,375**	364,478	63,659
Net cash provided by financing activities	**22,727**	38,869	49,910
Effect of exchange rates on cash and cash equivalents	**—**	—	(104)
Net increase in cash and cash equivalents	**$61,827**	$271,520	$15,309

Operating Activities

Net cash used in operating activities was $158.3 million for the year ended December 31, 2021, as compared to $131.8 million for the year ended December 31, 2020. The increase in outflows is primarily attributable to our higher operating loss and higher income taxes paid of $7.0 million, and to a lesser extent the timing of receipts and payments in the normal course of business.

Net cash used in operating activities was $131.8 million for the year ended December 31, 2020, as compared to $98.2 million for the year ended December 31, 2019. The increase in outflows was primarily attributable to estimated income taxes of $20.7 million paid for our disposals of Karuna common shares during the year ended December 31, 2020. The increase was further attributable to a decrease of $4.5 million in payments received with respect to contract revenue for the year ended December 31, 2020. We received a $2.0 million milestone payment from Karuna for initiation of its KarXT Phase 3 clinical study pursuant to the Exclusive Patent License Agreement between PureTech and Karuna during the year ended December 31, 2020. We received $3.5 million from Imbrium Therapeutics LP for the execution of a Research Collaboration Option and License Agreement and $3.0 million from Boehringer Ingelheim for the execution of a Collaboration and License Agreement during the year ended December 31, 2019. The increase in outflows was further attributable to reduced interest income and the timing of payments in the normal course of business for the year ended December 31, 2020.

Investing Activities

Net cash provided by investing activities was $197.4 million for the year ended December 31, 2021, as compared to inflows of $364.5 million for the year ended December 31, 2020, resulting in a decrease of $167.1 million in net cash provided by investing activities. The decrease in the net cash provided by investing activities was primarily attributed to the decrease in proceeds from the sale of investments held at fair value of $132.5 million (proceeds from such sales were $218.1 million for the year ended December 31, 2021 vs. $350.6 million for the year ended December 30, 2020) and the fact that for the year ended December 31, 2020 the Company had proceeds of $30.1 million from maturity of short term investments while for the year ended December 31, 2021, there were no such cash inflows.

Net cash provided by investing activities was $364.5 million for the year ended December 31, 2020, as compared to inflows of $63.7 million for the year ended December 31, 2019. The inflow was primarily attributable to the sale of Karuna and resTORbio common shares for aggregate proceeds of $350.6 million during the year ended December 31, 2020. The inflow was further attributable to cash provided by the maturity of short-term investments totaling $30.1 million. The inflows were offset by purchases of Gelesis and Vor preferred shares totaling $11.1 million and the purchase of fixed assets totaling $5.2 million.

Financing Activities

Net cash provided by financing activities was $22.7 million for the year ended December 31, 2021, as compared to $38.9 million for the year ended December 31, 2020, resulting in a decrease of $16.1 million in the net cash provided by financing activities. The decrease in the net cash provided by financing activities was primarily attributable to the decrease in proceeds from issuance of convertible notes in subsidiaries of $22.8 million and the fact that for the year ended December 31, 2020 the Company had proceeds from the issuance of a long term loan of $14.7 million, while for the year ended December 31, 2021, there was no such cash inflow. Such decreases were partially offset by an increase in proceeds from issuance of preferred shares in subsidiaries of $23.9 million

Net cash provided by financing activities was $38.9 million for the year ended December 31, 2020, as compared to $49.9 million for the year ended December 31, 2019. The net inflow was primarily attributable to the issuances by Vedanta of a $25.0 million convertible promissory note and a long-term loan with net proceeds of $14.7 million. The inflow was further attributable to $13.8 million received from the Vedanta Series C-2 and Sonde Series A-2 preferred share financings. The inflows were partially offset by the $12.9 million settlement of 2017 RSU awards granted to certain executives.

Funding Requirements

We have incurred operating losses since inception. Based on our current plans, we believe our existing cash and cash equivalents at December 31, 2021, will be sufficient to fund our operations and capital expenditure requirements into the first quarter of 2025. We expect to incur substantial additional expenditures in the near term to support our ongoing activities. We anticipate to continue to incur net operating losses for the foreseeable future as is typical for pre-revenue biotechnology companies. Our ability to fund our therapeutic development and clinical operations as well as commercialization of our wholly-owned therapeutic candidates, will depend on the amount and timing of cash received from planned financings and potential business development activities. Our future capital requirements will depend on many factors, including:

- the costs, timing and outcomes of clinical trials and regulatory reviews associated with our wholly-owned therapeutic candidates;
- the costs of commercialization activities, including product marketing, sales and distribution;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims;
- the emergence of competing technologies and products and other adverse marketing developments;
- the effect on our therapeutic and product development activities of actions taken by the U.S. Food and Drug Administration ("FDA"), the European Medicines Agency ("EMA") or other regulatory authorities;
- our degree of success in commercializing our wholly-owned therapeutic candidates, if and when approved; and
- the number and types of future therapeutics we develop and commercialize.

A change in the outcome of any of these or other variables with respect to the development of any of our wholly-owned therapeutic candidates could significantly change the costs and timing associated with the development of that therapeutic candidate.

Further, our operating plans may change, and we may need additional funds to meet operational needs and capital requirements for clinical trials and other research and development activities. We currently have no credit facility or other committed sources of capital. Because of the numerous risks and uncertainties associated with the development and commercialization of our wholly-owned therapeutic candidates, we have only a general estimate of the amounts of increased capital outlays and operating expenditures associated with our current and anticipated therapeutic development programs and these may change in the future.

Financial Position

Summary Financial Position

	As of December 31,		
(in thousands)	**2021**	2020	Change
Investments held at fair value (*)	**397,179**	530,161	(132,982)
Other non-current assets	**47,018**	45,484	1,534
Non-current assets	**444,197**	575,645	(131,448)
Cash and cash equivalents	**465,708**	403,881	61,827
Other current assets	**36,101**	10,468	25,634
Current assets	**501,809**	414,348	87,461
Total assets	**946,006**	989,994	(43,988)
Lease Liability	**29,040**	32,088	(3,048)
Deferred tax liability	**89,765**	108,626	(18,861)
Other non-current liabilities	**16,921**	14,818	2,103
Non-current liabilities	**135,725**	155,531	(19,806)
Trade and other payables	**35,760**	20,566	15,194
Notes payable	**3,916**	26,455	(22,539)
Warrant liability	**6,787**	8,206	(1,419)
Preferred shares	**174,017**	118,972	55,045
Other current liabilities	**5,654**	6,724	(1,069)
Current liabilities	**226,135**	180,924	45,211
Total liabilities	**361,859**	336,455	25,405
Net assets	**584,147**	653,539	(69,392)
Total equity	**584,147**	653,539	(69,392)

(*) Fair value of investments accounted for at fair value, does not take into consideration contribution from milestones that occurred after December 31, 2021, the value of our consolidated Founded Entities (Vedanta, Follica, Sonde, Alivio, and Entrega), our Wholly Owned Programs, or our cash.

Investments Held at Fair Value

Investments held at fair value decreased $133.0 million to $397.2 million as of December 31, 2021. Investments held at fair value consists primarily of our common share investment in Karuna and Vor (from February 2021) and our preferred share investments in Akili, Gelesis and Vor (until February 2021). See Note 5 to our consolidated financial statements included elsewhere in this annual report for details regarding the change in investments held at fair value.

Cash and Cash Equivalents

Consolidated cash, cash equivalents increased $61.8 million to $465.7 million as of December 31, 2021, while we had PureTech Level cash and cash equivalents of $418.9 million. The increase reflected primarily the disposals of Karuna common shares during the year ended December 31, 2021. On February 9, 2021, PureTech sold 1,000,000 shares of Karuna common shares for aggregate proceeds of $118.0 million. On November 9, 2021, PureTech sold an additional 750,000 Karuna common shares for aggregate proceeds of $100.1 million. The inflows from the disposals were primarily offset by our operating loss of $150.3 million for the year ended December 31, 2021.

Non-Current Liabilities

Non-current liabilities decreased $19.8 million to $135.7 million as of December 31, 2021. The decrease was driven by declines of $3.0 million and $18.9 million in our long-term lease and deferred tax liabilities, respectively as of December 31, 2021.

Trade and Other Payables

Trade and other payables increased $15.2 million to $35.8 million as of December 31, 2021. The increase reflected primarily the timing of payments as of December 31, 2021.

Notes Payable

Notes payable decreased $22.5 million to $3.9 million as of December 31, 2021. The decrease reflected the conversion of the Vedanta $25.0 million convertible promissory note to a third party investor during the execution of the Series D financing round. This decrease was partially offset by a $2.2 million note issuance by Sonde.

Preferred Shares

Preferred share liability increased $55.0 million to $174.0 million as of December 31, 2021. The increase reflected the issuance by Vedanta of Series D preferred shares and the conversion of Vedanta notes into Series D preferred shares, increasing the liability by $63.4 million. This increases was partially offset by a decrease in fair value of the preferred share liability by $8.4 million during the year ended December 31, 2021.

Quantitative and Qualitative Disclosures about Financial Risks

Interest Rate Sensitivity

As of December 31, 2021, we had consolidated cash and cash equivalents of $465.7 million, while we had PureTech Level cash and cash equivalents of $418.9 million. Our exposure to interest rate sensitivity is impacted by changes in the underlying U.K. and U.S. bank interest rates. We have not entered into investments for trading or speculative purposes. Due to the conservative nature of our investment portfolio, which is predicated on capital preservation and investments in short duration, high-quality U.S. Treasury Bills and U.S. debt obligations and related money market accounts we do not believe change in interest rates would have a material effect on the fair market value of our portfolio, and therefore we do not expect our operating results or cash flows to be significantly affected by changes in market interest rates.

Foreign Currency Exchange Risk

We maintain our consolidated financial statements in our functional currency, which is the U.S. dollar. Monetary assets and liabilities denominated in currencies other than the functional currency are translated into the functional currency at rates of exchange prevailing at the balance sheet dates. Non-monetary assets and liabilities denominated in foreign currencies are translated into the functional currency at the exchange rates prevailing at the date of the transaction. Exchange gains or losses arising from foreign currency transactions are included in the determination of net income (loss) for the respective periods. Such foreign currency gains or losses were not material for all reported periods.

We recorded foreign currency losses in respect of foreign operations of $0.0 million, $0.5 million and $0.0 million for the years ended December 31, 2021, December 31, 2020, and December 31, 2019, respectively, which are included in Other comprehensive income/(loss) in the Consolidated Statements of Comprehensive Income/(Loss).

We do not currently engage in currency hedging activities in order to reduce our currency exposure, but we may begin to do so in the future. Instruments that may be used to hedge future risks include foreign currency forward and swap contracts. These instruments may be used to selectively manage risks, but there can be no assurance that we will be fully protected against material foreign currency fluctuations.

Controlled Founded Entity Investments

We maintain investments in certain Controlled Founded Entities. Our investments in Controlled Founded Entities are eliminated as intercompany transactions upon financial consolidation. We are however exposed to a preferred share liability owing to the terms of existing preferred shares and the ownership of Controlled Founded Entities preferred shares by third parties. The liability of preferred shares is maintained at fair value through the profit and loss. Our strong cash position, budgeting and forecasting processes, as well as decision making and risk mitigation framework enable us to robustly monitor and support the business activities of the Controlled Founded Entities to ensure no exposure to credit losses and ultimately dissolution or liquidation. Accordingly, we view exposure to third party preferred share liability as low. Please refer to Note 16 to our consolidated financial statements for further information regarding our exposure to Controlled Founded Entity Investments.

Non-Controlled Founded Entity Investments

We maintain certain investments in Non-Controlled Founded Entities which are deemed either as investments and accounted for as investments held at fair value or associates and accounted for under the equity method (please refer to Note 1 to our consolidated financial statements). Our exposure to investments held at fair value was $397.2 million as of December 31, 2021, and we may or may not be able to realize the value in the future. Accordingly, we view the risk as high. Our exposure to investments in associates in limited to the carrying amount of the investment. We are not exposed to further contractual obligations or contingent liabilities beyond the value of initial investment. As of December 31, 2021, Gelesis was the only associate. The carrying amount of the investment in Gelesis as an associate was zero. Accordingly, we do not view this as a risk. Please refer to Notes 5, 6 and 16 to our consolidated financial statements for further information regarding our exposure to Non-Controlled Founded Entity Investments.

Equity Price Risk

As of December 31, 2021, we held 1,656,564 common shares of Karuna and 3,207,200 common shares of Vor. The fair value of our investment in the common shares of Karuna was $217.0 million and common shares of Vor was $37.3 million.

The investments in Karuna and Vor are exposed to fluctuations in the market price of these common shares. The effect of a 10.0 percent adverse change in the market price of Karuna common shares and Vor common shares as of December 31, 2021, would have been a loss of approximately $21.7 million and $3.7 million, respectively, recognized as a component of Other income (expense) in our Consolidated Statements of Comprehensive Income/(Loss).

Subsequent to December 31, 2021 our investment in Gelesis was converted into shares of common stock of Gelesis (after the combination with Capstar), which are publicly traded on the New York Stock Exchange.

Liquidity Risk

We do not believe we will encounter difficulty in meeting the obligations associated with our financial liabilities that are settled by delivering cash or another financial asset. While we believe our cash and cash equivalents do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes or decline in value based on market conditions.

Credit Risk

We maintain an investment portfolio in accordance with our investment policy. The primary objectives of our investment policy are to preserve principal, maintain proper liquidity and to meet operating needs. Although our investments are subject to credit risk, our investment policy specifies credit quality standards for our investments and limits the amount of credit exposure from any single issue, issuer or type of investment. Also, due to the conservative nature of our investments and relatively short duration, interest rate risk is mitigated. We do not own derivative financial instruments. Accordingly, we do not believe that there is any material market risk exposure with respect to derivative or other financial instruments.

Credit risk is also the risk of financial loss if a customer or counterparty to a financial instrument fails to meet its contractual obligations. We assess the credit quality of customers on an ongoing basis, taking into account its financial position, past experience and other factors. The credit quality of financial assets that are neither past due nor impaired can be assessed by reference to credit ratings (if available) or to historical information about counterparty default rates. We are also potentially subject to concentrations of credit risk in accounts receivable. Concentrations of credit risk with respect to receivables is owed to the limited number of companies comprising our customer base. However, our exposure to credit losses is currently de minimis due to the credit quality of our receivables, which are primarily from the US government and large funds with respect to grants.

Foreign Private Issuer Status

Owing to our U.S. listing, we report under the Securities Exchange Act of 1934, as amended, or the Exchange Act, as a non-U.S. company with foreign private issuer status. As long as we qualify as a foreign private issuer under the Exchange Act, we will be exempt from certain provisions of the Exchange Act that are applicable to U.S. domestic public companies, including:

- the sections of the Exchange Act regulating the solicitation of proxies, consents or authorizations in respect of a security registered under the Exchange Act;
- sections of the Exchange Act requiring insiders to file public reports of their stock ownership and trading activities and liability for insiders who profit from trades made in a short period of time;
- the rules under the Exchange Act requiring the filing with the SEC of quarterly reports on Form 10-Q containing unaudited financial and other specified information, or current reports on Form 8-K, upon the occurrence of specified significant events; and
- Regulation FD, which regulates selective disclosures of material information by issuers.

Chair's overview

"We believe that good corporate governance is essential for building a successful and sustainable business."

Dear Shareholder

I am pleased to introduce our Corporate Governance Report. This section sets out our governance framework and the work of the Board and its committees.

As a Board, we are responsible for ensuring there is an effective governance framework in place. This includes setting the Company's strategic objectives, ensuring the right leadership and resources are in place to achieve these objectives, monitoring performance, ensuring that sufficient internal controls and protections are in place and reporting to shareholders. An effective governance framework is also designed to ensure accountability, fairness and transparency in the Company's relationships with all of its stakeholders, whether shareholders, employees, partners, the government or the wider patient community. We believe that good corporate governance is essential for building a successful and sustainable business.

The Board is committed to the highest standards of corporate governance and undertakes to maintain a sound framework for our control and management. In this report, we provide details of that framework.

The key constituents necessary to deliver a robust structure are in place and, accordingly, this report includes a description of how the Company has applied the principles and provisions of the Governance Code and how it intends to apply those principles in the future.

The Board looks forward to being able to discuss these matters with our shareholders in connection with our AGM or indeed at any other time during the year.

Christopher Viehbacher
Chair

April 25, 2022

Board of Directors

(alphabetically)*

PureTech Health is led by a seasoned and accomplished Board of Directors and management team with extensive experience in maximising shareholder value, discovering scientific breakthroughs, and delivering therapeutics to market.

Sharon Barber-Lui
Independent Non-Executive Director

Sharon Barber-Lui has served as a member of our Board since March 2022. Ms. Barber-Lui has been the Senior Vice President of Finance at EQRx since January 2022. Prior to joining EQRx, Ms. Barber-Lui worked at Merck for over twenty years in roles of advancing responsibility, including most recently as the Head of Portfolio Market Strategy, Operations and Business Analytics from 2019 through 2021 and Chief Financial Officer from 2014 through 2018 for Merck's U.S. oncology business. Prior to that Ms. Barber-Lui held a number of other roles with Merck including Treasurer of U.S. Region, Head of U.S. Treasury Operations, and Head of Legal Entity Integration and Global Treasury Services, among others. Ms. Barber-Lui began her career as an accountant for KPMG LLP, and she received her bachelor's degree as well as her M.B.A. from Lehigh University. Ms. Barber-Lui is a member of the American Institute of Certified Public Accountants.

Raju Kucherlapati, Ph.D.
Independent Non-Executive Director, R&D Committee Member

Raju Kucherlapati, Ph.D., has served as a member of our Board since 2014. He has been the Paul C. Cabot professor of Genetics and a professor of medicine at Harvard Medical School since 2001. Dr. Kucherlapati currently serves on the board of directors of Gelesis, Inc. and KEW Inc. He was a founder and former board member of Abgenix, Cell Genesys and Millennium Pharmaceuticals. He is a fellow of the American Association for the Advancement of Science and a member of the National Academy of Medicine. Dr. Kucherlapati received his Ph.D. from the University of Illinois. He trained at Yale and has held faculty positions at Princeton University, University of Illinois College of Medicine and the Albert Einstein College of Medicine. He served on the editorial board of the New England Journal of Medicine and was Editor in Chief of the journal Genomics. His laboratory at Harvard Medical School is involved in cloning and characterization of human disease genes with a focus on human syndromes with a significant cardiovascular involvement, use of genetic/genomic approaches to understand the biology of cancer and the generation and characterization of genetically modified mouse models for cancer and other human disorders.

John LaMattina, Ph.D.
Independent Non-Executive Director, R&D Committee Member

John LaMattina, Ph.D., has served as a member of our Board since 2009. Dr. LaMattina previously worked at Pfizer in different roles from 1977 to 2007, including vice president of U.S. Discovery Operations in 1993, senior vice president of worldwide discovery operations in 1998, senior vice president of worldwide development in 1999 and president of global research and development from 2003 to 2007. Dr. LaMattina serves on the board of directors of Ligand Pharmaceuticals, Immunome Inc. and Vedanta. Dr. LaMattina previously served on the board of Zafgen, Inc. until April 2020. He also serves on the Scientific Advisory Board of Frequency Therapeutics and is a trustee associate of Boston College. During Dr. LaMattina's leadership tenure, Pfizer discovered and/or developed a number of important new medicines including Tarceva, Chantix, Zoloft, Selzentry and Lyrica, along with a number of other medicines currently in late stage development for cancer, rheumatoid arthritis and pain. He is the author of numerous scientific publications and U.S. patents. Dr. LaMattina received the 1998 Boston College Alumni Award of Excellence in Science and the 2004 American Diabetes Association Award for Leadership and Commitment in the Fight Against Diabetes. He was awarded an Honorary Doctor of Science degree from the University of New Hampshire in 2007. In 2010, he was the recipient of the American Chemical Society's Earle B. Barnes Award for Leadership in Chemical Research Management. He is the author of *"Devalued and Distrusted—Can the Pharmaceutical Industry Restore its Broken Image," "Drug Truths: Dispelling the Myths About Pharma R&D"* and an author of the Drug Truths blog at Forbes.com. Dr. LaMattina received a B.S. in Chemistry from Boston College and received a Ph.D. in Organic Chemistry from the University of New Hampshire. He then moved on to Princeton University as a National Institutes of Health postdoctoral fellow in the laboratory of professor E. C. Taylor.

* Biographies for executive directors, Daphne Zohar and Bharatt Chowrira, can be found on pages 115 to 116.

Robert Langer, Sc.D.
Co-Founder and Non-Executive Director, R&D Committee Member

Robert S. Langer, Sc.D., has served as a member of our Board since our founding and is our co-founder. Dr. Langer has served as the David H. Koch Institute professor at MIT since 2005. He served as a member of the FDA's science board from 1995 to 2002 and as its chairman from 1999 to 2002. Dr. Langer serves on the board of directors of Seer Bio, Abpro Bio, Frequency Therapeutics, Entrega, Inc. and Moderna, Inc. Dr. Langer has received over 220 major awards, including the 2006 U.S. National Medal of Science, the Charles Stark Draper Prize in 2002 and the 2012 Priestley Medal. He is also the first engineer to ever receive the Gairdner Foundation International Award. Dr. Langer has received the Dickson Prize for Science, Heinz Award, Harvey Prize, John Fritz Award, General Motors Kettering Prize for Cancer Research, Dan David Prize in Materials Science, Breakthough Prize in Life Sciences, National Medal of Science, National Medal of Technology and Innovation, Kyoto Prize, Wolf Prize, Albany Medical Center Prize in Medicine and Biomedical Research and the Lemelson-MIT prize. In 2006, he was inducted into the National Inventors Hall of Fame. In January 2015, Dr. Langer was awarded the 2015 Queen Elizabeth Prize for Engineering. Dr. Langer received his bachelor's degree in Chemical Engineering from Cornell University and his Sc.D. in Chemical Engineering from MIT.

Kiran Mazumdar-Shaw
Independent Non-Executive Director

Kiran Mazumdar-Shaw has served as a member of our Board since September 2020. Ms. Mazumdar-Shaw has been the executive chairperson of Biocon Limited, which she founded in 1978, since April 2020, and she served as managing director of Biocon Limited from 1995 to 2020. Ms. Mazumdar-Shaw holds key positions in various industry, educational, government and professional bodies globally. She has been elected as a full-term member of the board of trustees of Massachusetts Institute of Technology. She has been elected as a member of the prestigious U.S.-based National Academy of Engineering. She also serves as the lead independent member of the board of Infosys Ltd, a director on the board of United Breweries Limited, and non-executive director on the board of Narayana Health. Ms. Mazumdar-Shaw has received two of India's highest civilian honors, the Padma Shri in 1989 and the Padma Bhushan in 2005. She was also honored with the Order of Australia, Australia's highest civilian honor in January 2020. In 2016, she was conferred with the highest French distinction – Knight of the Legion of Honour – and in 2014 received the Othmer Gold Medal in 2014 from the U.S.-based Chemical Heritage Foundation for her pioneering efforts in biotechnology. Ms. Mazumdar-Shaw has been ranked as one of the world's top 20 inspirational leaders in the field of biopharmaceuticals by The Medicine Maker Power List 2020, and she was the winner of EY World Entrepreneur of the Year™ 2020 Award. She was the first woman business leader from India to sign the Giving Pledge, an initiative of the Gates Foundation, committing to give the majority of her wealth to philanthropic causes. She received a bachelor's degree in science, Zoology Hons., from Bangalore University and a master's degree in malting and brewing from Ballarat College, Melbourne University. She has been awarded several honorary degrees from other universities globally.

Dame Marjorie Scardino
Senior Independent Director

Dame Marjorie Scardino has served as a member of our Board since 2015. She served for 28 years as the chief executive officer of Pearson, a large education company that included The Economist, The Financial Times and Penguin Books. She was on the board of the MacArthur Foundation for 12 years, five as chairman, and left in 2017. She was a member of the board of Twitter from 2013 to 2018 and International Airlines Group from 2014 to 2019. Dame Scardino has received a number of honorary degrees, and in 2003 was dubbed a dame of the British Empire. She is also a member of the Royal Society of the Arts in the UK and the American Association of Arts and Sciences.

Christopher Viehbacher
Chair

Chris Viehbacher has served as a member of our Board since 2015 and as chairman since September 2019. He has been the managing partner of Gurnet Point Capital since October 2014. Immediately prior to joining Gurnet Point Capital, Mr. Viehbacher served as the chief executive officer and member of the board of directors of Sanofi from December 2008 to October 2014. From 1993 to 2008, Mr. Viehbacher worked at GlaxoSmithKline in different roles, including ultimately President of its North American pharmaceutical division. Mr. Viehbacher began his career with PricewaterhouseCoopers LLP and qualified as a chartered accountant. Mr. Viehbacher currently serves on the board of directors of Vedanta Biosciences as chairman, BEFORE Brands, Crossover Health, Boston Pharmaceuticals, Zikani and Gurnet Point Capital LLC. Mr. Viehbacher previously served on the board of directors of Axcella Health Inc. and Corium International, Inc. Mr. Viehbacher also serves on the Board of Trustees of Northeastern University and the Board of Fellows of Stanford Medical School. Mr. Viehbacher has co-chaired the Chief Executive Officer Roundtable on Neglected Diseases with Bill Gates and formerly chaired the chief executive officer Roundtable on Cancer. He was the chairman of the board of the Pharmaceutical Research and Manufacturers of America as well as president of the European Federation of Pharmaceutical Industries and Associations. At the World Economic Forum at Davos, Mr. Viehbacher was a chair of the Health Governors and co-chaired an initiative to create a Global Charter for Healthy Living. He was also a member of the International Business Council. Mr. Viehbacher has received the Pasteur Foundation Award for outstanding commitment to safeguarding and improving health worldwide. He has also received France's highest civilian honor, the Légion d'honneur. Mr. Viehbacher received his bachelor's degree in Commerce from Queen's University in Ontario, Canada in 1983.

Dennis Ausiello, M.D.**
Board Advisor, R&D Committee Member

Dennis Ausiello, M.D., is a board advisor and member of the PureTech R&D Committee. He is the Jackson Distinguished Professor of Clinical Medicine and was previously director, emeritus of the M.D./Ph.D. Program at Harvard Medical School. Dr. Ausiello is chairman of medicine, emeritus and director of the Center for Assessment Technology and Continuous Health (CATCH) at Massachusetts General Hospital (MGH). This center is a partnership among MGH, MIT and Harvard University with a mission to develop real-time assessment of human traits in wellness and disease. In partnership with industry, it is creating tools for measurements of traditional and novel phenotypes. Understanding the need for partnerships between the academy and industry, Dr. Ausiello served on the board of directors of Pfizer Pharmaceuticals, where he was their former lead director. He currently serves as a member of the board of directors of Seres Health and Alnylam. Dr. Ausiello is also a member of the board of directors of several non-public biotech companies and is a consultant to Verily (formerly Google Life Sciences) and Pfizer Pharmaceuticals. Dr. Ausiello is a nationally recognized leader in academic medicine who was elected to the National Academy of Medicine in 1999 and the American Academy of Arts and Sciences in 2003. He has published numerous articles, book chapters and textbooks and has served as an editor of Cecil's Textbook of Medicine. Dr. Ausiello received his BA from Harvard College and an M.D. from the University of Pennsylvania.

H. Robert Horvitz, Ph.D.**
Board Advisor, R&D Committee Chair

H. Robert Horvitz, Ph.D., is a board observer and Chair of the R&D Committee at PureTech. He received the Nobel Prize in Physiology or Medicine and is the David H Koch Professor of Biology at Massachusetts Institute of Technology, an investigator of the Howard Hughes Medical Institute, neurobiologist (Neurology) at Massachusetts General Hospital, a member of the MIT McGovern Institute for Brain Research and the MIT Koch Institute for Integrative Cancer Research. He is cofounder of multiple life science companies, including Epizyme (EPZM), Mitobridge (acquired by Astellas) and Idun Pharmaceuticals (acquired by Pfizer) and was a member of the Scientific Advisory Board of the Novartis Institutes for BioMedical Research.

Dr. Horvitz was a member of the board of trustees of the Massachusetts General Hospital. He also previously served as Chairman of the Board of Trustees of the Society for Science and the Public and as President of the Genetics Society of America. Dr. Horvitz is a member of the U.S. National Academy of Sciences, the U.S. National Academy of Medicine and the American Philosophical Society and is a foreign member of the Royal Society of London. He is a fellow of the American Academy of Arts and Sciences and of the American Academy of Microbiology.

Dr. Horvitz received the U.S. National Academies of Science Award in Molecular Biology; the Charles A. Dana Award for Pioneering Achievements in Health; the Ciba-Drew Award for Biomedical Science; the General Motors Cancer Research Foundation Alfred P. Sloan, Jr. Prize; the Gairdner Foundation International Award; the March of Dimes Prize in Developmental Biology; the Genetics Society of America Medal; the Bristol-Myers Squibb Award for Distinguished Achievement in Neuroscience; the Wiley Prize in the Biomedical Sciences; the Peter Gruber Foundation Genetics Prize; the American Cancer Society Medal of Honor; the Alfred G. Knudson Award of the National Cancer Institute; and the UK Genetics Society Mendel Medal. He has received honorary doctoral degrees from the University of Rome, Cambridge University, Pennsylvania State University and the University of Miami.

Bennett Shapiro, M.D.**
Board Advisor, R&D Committee Member

Bennett Shapiro, M.D., is a PureTech co-founder, a board advisor, a member of PureTech's R&D Committee. He also served as member of the Board from the Company's founding through June 2020. Dr. Shapiro was previously Executive Vice President at Merck Research Laboratories of Merck & Co. where he initially led Worldwide Basic Research and was responsible for all the basic and preclinical research activities at Merck. He later led Worldwide Licensing and External Research and was responsible for Merck's relationships with the academic and industrial biomedical research community. His leadership resulted in the discovery, development and registration of approximately 25 drugs and vaccines. Previously, he was professor and chairman of the Department of Biochemistry at the University of Washington and is the author of over 120 papers on the molecular regulation of cellular behavior. Following an internship in Medicine at the University of Pennsylvania Hospital, he was a Research Associate at the NIH, then a Visiting Scientist at the Institut Pasteur in Paris and returned to the NIH as Chief-Section on Cellular Differentiation in the Laboratory of Biochemistry prior to joining the University of Washington. Dr. Shapiro has been a Guggenheim Fellow, a Fellow of the Japan Society for the Promotion of Science and a Visiting Professor at the University of Nice. He currently serves as a member of the board of directors of Vedanta Biosciences and VBL Therapeutics. Dr. Shapiro previously served as a director of Celera Corporation, the Drugs for Neglected Diseases initiative and the Mind and Life Institute. Dr. Shapiro received a B.S. in Chemistry from Dickinson College and his M.D. from Jefferson Medical College.

** Dr. Horvitz, Dr. Ausiello and Dr. Shapiro are not members of the PureTech Board. As a Board Observer, Dr. Horvitz attends the majority of Board meetings. As Board Advisors, Dr. Ausiello and Dr. Shapiro attend select Board meetings. All three are also members of PureTech's R&D Committee, of which Dr. Horvitz is the Chair.

Management team

(alphabetically)

Joseph Bolen, Ph.D.
Chief Scientific Officer

Joseph Bolen, Ph.D., first joined PureTech in October 2015 and has served as PureTech's chief scientific officer since October 2016. Prior to joining PureTech, Dr. Bolen oversaw all aspects of research and development, or R&D, for Moderna, Inc. as president and chief scientific officer from July 2013 to October 2015. Previously, he was chief scientific officer and global head of oncology research at Millennium: The Takeda Oncology Company. Prior to joining Millennium in 1999, Dr. Bolen held senior positions at Hoechst Marion Roussel, Schering-Plough and Bristol-Myers Squibb. Dr. Bolen began his career at the National Institutes of Health, where he contributed to the discovery of a class of proteins known as tyrosine kinase oncogenes as key regulators of the immune system. Dr. Bolen received a B.S. in Microbiology & Chemistry and a Ph.D. in Immunology from the University of Nebraska and conducted his postdoctoral training in Molecular Virology at the Kansas State University Cancer Center.

Bharatt Chowrira, Ph.D., J.D.
President and Chief Business, Legal and Operating Officer, Member of the Board of Directors

Bharatt Chowrira, Ph.D., J.D., has been our president and chief business, legal and operating officer since January, 2022 and was our president and chief of business and strategy from March 2017 through December 2021. Dr. Chowrira has also served as a member of PureTech's Board since February 1, 2021. Prior to joining PureTech, Dr. Chowrira was the president of Synlogic, Inc., a biopharmaceutical company focused on developing synthetic microbiome-based therapeutics, from September 2015 to February 2017, where he oversaw and managed corporate and business development, alliance management, financial, human resources, intellectual property and legal operations. Prior to that, Dr. Chowrira was the chief operating officer of Auspex Pharmaceuticals, Inc. from October 2013 to July 2015, which was acquired by Teva Pharmaceuticals Ltd. in the spring of 2015. Previously, he was president and chief executive officer of Addex Therapeutics Ltd., a biotechnology company publicly-traded on the SIX Swiss Exchange, from August 2011 to July 2013. Prior to that Dr. Chowrira held various leadership and management positions at Nektar Therapeutics (chief operating officer), Merck & Co, or Merck (vice president), Sirna Therapeutics (general counsel; acquired by Merck) and Ribozyme Pharmaceuticals (chief patent counsel). Dr. Chowrira is currently a member of the board of directors of Vedanta Biosciences, Inc. and Akili Interactive Labs, Inc., and, he previously served on the board of directors of Karuna Therapeutics, Inc. from August of 2017 to December 2019. Dr. Chowrira received a J.D. from the University of Denver's Sturm College of Law, a Ph.D. in Molecular Biology from the University of Vermont College of Medicine, an M.S. in Molecular Biology from Illinois State University and a B.S. in Microbiology from the UAS, Bangalore, India.

Eric Elenko, Ph.D.
Chief Innovation and Strategy Officer

Eric Elenko, Ph.D., has served as our chief innovation officer since June 2015 and held various other positions at PureTech prior thereto. While at PureTech, Dr. Elenko has led the development of a number of programs, including Akili Interactive Labs, Gelesis, Karuna Therapeutics and Sonde Health. Dr. Elenko serves on the board of directors of Sonde. Prior to joining PureTech, Dr. Elenko was a consultant with McKinsey and Company from February 2002 to September 2005, where he advised senior executives of both Fortune 500 and specialty pharmaceutical companies on a range of issues such as product licensing, mergers and acquisitions, research and development strategy and marketing. Dr. Elenko received a B.A. in Biology from Swarthmore College and his Ph.D. in Biomedical Sciences from University of California, San Diego.

George Farmer, Ph.D.
Chief Financial Officer

George Farmer, Ph.D., has served as our chief financial officer since January 1, 2021. Dr. Farmer joined PureTech from BMO Capital Markets, where he completed a 15-year career as a senior biotechnology equity analyst providing in-depth sector research for institutional investor clients. Prior to this role, Dr. Farmer served as chief executive officer of Cortice Biosciences, a privately held biotechnology company focused on the clinical development of therapies for brain malignancies and neurodegenerative diseases. He also served as vice president of corporate development at Synta Pharmaceuticals, a publicly traded company developing cancer therapeutics. Dr. Farmer serves on the board of directors of Sonde Health, Inc. and Follica, Inc. Dr. Farmer was a postdoctoral fellow at Sloan Kettering Cancer Center and University of California San Francisco after receiving his Ph.D. in biological sciences from Columbia University and a BA from Dartmouth College.

Julie Krop, M.D.
Chief Medical Officer

Julie Krop, MD, is the chief medical officer at PureTech, where she is responsible for all clinical development, regulatory, CMC, and medical affairs for PureTech's clinical-stage Wholly Owned Pipeline. Prior to PureTech, Dr. Krop served as Chief Medical Officer at Freeline Therapeutics, a clinical-stage gene therapy company. She also previously served as Chief Medical Officer of AMAG Pharmaceuticals (acquired by Covis group for $647 million), where she oversaw clinical development, regulatory affairs, clinical operations, medical affairs, program management and pharmacovigilance. During her time at AMAG, Dr. Krop was responsible for the oversight of three FDA approvals. Earlier in her career, she held leadership positions at Vertex Pharmaceuticals, Stryker Regenerative Medicine, Peptimmune, Millennium Pharmaceuticals and Pfizer and also served on the board of directors of Aquestive Bio, Inc. Dr. Krop received her M.D. from Brown University School of Medicine and completed an internal medicine residency at Georgetown University Hospital. Additionally, she completed fellowships in epidemiology, clinical trial design and endocrinology as a Robert Wood Johnson Foundation Clinical Scholar at the Johns Hopkins School of Medicine.

Daphne Zohar
Founder and Chief Executive Officer, Member of the Board of Directors

Daphne Zohar is the founder of PureTech and has served as our chief executive officer and a member of our board of directors since our formation and UK main market listing in 2015 and served as the founding chief executive officer of a number of our Founded Entities. A successful entrepreneur, Ms. Zohar created PureTech, assembling a leading team and scientific network to help implement her vision for the company, and was a key participant in fundraising, business development and establishing the underlying programs and platforms that have resulted in PureTech's substantial pipeline which is comprised of 26 therapeutics and therapeutic candidates to date, including two therapeutics that have been cleared by the U.S. Food and Drug Administration for marketing and granted marketing authorization in the European Economic Area, or EEA. Ms. Zohar has been recognized as a top leader and innovator in biotechnology by a number of sources, including EY, BioWorld, MIT's Technology Review, the Boston Globe, and Scientific American. Ms. Zohar serves on the board of directors of Follica, Inc. Previously, Ms. Zohar has served on a number of private company boards including Karuna Therapeutics, Inc. and served on the board of resTORbio, Inc. (now Adicet Bio, Inc.) from December 2017-November 2018. Ms. Zohar received a B.S. from Northeastern University.

The Board

Roles and responsibilities of the Board

The Board is responsible to shareholders for our overall management as a whole. The main roles of the Board are:

- creating value for shareholders;
- providing business and scientific leadership;
- approving our strategic objectives;
- ensuring that the necessary financial and human resources are in place to meet strategic objectives;
- overseeing our system of risk management; and
- setting the values and standards for both our business conduct and governance matters.

The Directors are also responsible for ensuring that obligations to shareholders and other stakeholders are understood and met and that communication with shareholders is maintained. The responsibility of the Directors is collective, taking into account their respective roles as Executive Directors and Non-Executive Directors. All Directors are equally accountable to the Company's shareholders for the proper stewardship of its affairs and our long-term success.

The Board reviews strategic issues on a regular basis and exercises control over our performance by agreeing on budgetary and operational targets and monitoring performance against those targets. The Board has overall responsibility for our system of internal controls and risk management. Any decisions made by the Board on policies and strategy to be adopted by us or changes to current policies and strategy are made following presentations by the Executive Directors and other members of management, and only after a detailed process of review and challenge by the Board. Once made, the Executive Directors and other members of management are fully empowered to implement those decisions.

Except for a formal schedule of matters which are reserved for decision and approval by the Board, the Board has delegated our day-to-day management to the Chief Executive Officer who is supported by other members of the senior management team. The schedule of matters reserved for Board decision and approval are those significant to us as a whole due to their strategic, financial or reputational implications.

The Company's schedule of matters reserved for the Board includes the following matters:

- approval and monitoring of our strategic aims and objectives;
- approval of the annual operating and capital expenditure budget;
- changes to our capital structure, the issue of any of our securities and material borrowings;
- approval of the annual report and half-year results statement, accounting policies and practices or any matter having a material impact on our future financial performance;
- ensuring a sound system of internal control and risk management;
- approving Board appointments and removals, and approving policies relating to directors' remuneration;
- strategic acquisitions;
- major disposals of our assets or subsidiaries;
- approval of all circulars, prospectuses and other documents issued to shareholders governed by the Financial Conduct Authority's (FCA) Listing Rules, Disclosure Guidance and Transparency Rules or the City Code on Takeovers and Mergers;
- approval of terms of reference and membership of Board committees;
- considering and, where appropriate, approving directors' conflicts of interest; and
- approval, subject to shareholder approval, of the appointment and remuneration of the auditors.

The schedule of matters reserved to the Board is available on request from the Company Secretary or within the Investors section of our website at www.puretechhealth.com.

The Board delegates specific responsibilities to certain committees that assist the Board in carrying out its functions and ensure independent oversight of internal control and risk management. The three principal Board committees (Audit, Remuneration and Nomination) play an essential role in supporting the Board in fulfilling its responsibilities and ensuring that we maintain the highest standards of corporate governance. Each committee has its own terms of reference which set out the specific matters for which delegated authority has been given by the Board.

The terms of reference for each of the committees are fully compliant with the provisions of the Governance Code. All of these are available on request from the Company Secretary or within the Investors section of our website at www.puretechhealth.com.

Board size and composition

As of December 31, 2021, there were eight Directors on the Board: the Non-Executive Chair, two Executive Directors and five Non-Executive Directors. The biographies of these Directors are provided on pages 112 to 116. One of the Company's former Executive Directors, Mr. Stephen Muniz, retired from the Board and as Chief Operating Officer of the Company in May 2021. Dr. Bharatt Chowrira was appointed as an Executive Director in February 2021. There were no other changes to the composition of the Board during 2021. On March 24, 2022, Ms. Sharon Barber-Lui joined the Board as a non-Executive Director.

The Company's policy relating to the terms of appointment and the remuneration of both Executive and Non-Executive Directors is detailed in the Directors' Remuneration Report on pages 131 to 146.

The size and composition of the Board is regularly reviewed by the Nomination Committee to ensure there is an appropriate and diverse mix of skills and experience on the Board.

The Board may appoint any person to serve as a Director, either to fill a vacancy or as an addition to the existing Board. Any Director so appointed by the Board shall hold office only until the following AGM and then shall be eligible for election by the shareholders. In accordance with the Governance Code, all of the Directors will be offering themselves for election at the AGM to be held on June 15, 2022, full details of which are set out in the notice of meeting accompanying this Annual Report.

Non-Executive Directors

The Company's Non-Executive Directors are Mr. Christopher Viehbacher (Chair), Ms. Sharon Barber-Lui, Dr. Raju Kucherlapati, Dr. John LaMattina, Dr. Robert Langer, Ms. Kiran Mazumdar-Shaw and Dame Marjorie Scardino.

The Non-Executive Directors provide us with a wide range of skills and experience. Each Non-Executive Director has significant senior level experience as well as an extensive network in each of their own fields, an innovative mindset and independent judgement on issues of strategy, performance and risk, and is well placed to constructively challenge and scrutinize the performance of management. In addition, certain of our Non-Executive Directors also serve as members of one or more boards of directors of our Founded Entities and are key drivers for our Wholly Owned Pipeline.

Senior Independent Director

The Company's Senior Independent Director is Dame Marjorie Scardino. A key responsibility of the Senior Independent Director is to be available to shareholders in the event that they may feel it inappropriate to relay views through the Chair or Chief Executive Officer. In addition, the Senior Independent Director serves as an intermediary between the rest of the Board and the Chair where necessary. Further, the Senior Independent Director will lead the Board in its deliberations on any matters on which the Chair is conflicted.

The roles of Chair and Chief Executive Officer

The Company's Chair is Mr. Christopher Viehbacher. There is a clear division of responsibilities between the Chair and the Chief Executive Officer. Mr. Viehbacher was appointed Chair in September 2019.

The Chair is responsible for the leadership and conduct of the Board and for ensuring effective communication with shareholders.

The Chair facilitates the full and effective contribution of Non-Executive Directors at Board and Committee meetings, ensures that they are kept well informed and ensures a constructive relationship between the Executive Directors and Non-Executive Directors. The Chair also ensures that the Board committees carry out their duties, including reporting back to the Board either orally or in writing following their meetings at the next Board meeting.

The role of the Chief Executive Officer, Ms. Daphne Zohar, is to lead the execution of the Company's strategy and the executive management of PureTech. She is responsible, among other things, for the development and implementation of strategy and processes which enable us to meet the requirements of shareholders, for delivering the operating plans and budgets for our businesses, for monitoring business performance against key performance indicators (KPIs) and reporting on these to the Board and for providing the appropriate environment to recruit, engage, retain and develop the high-quality personnel needed to deliver our strategy.

Independence

The Governance Code requires that at least 50 percent of the Board of a UK premium listed company, excluding the Chair, consists of Non-Executive Directors determined by the Board to be independent in character and judgement and free from relationships or circumstances which may affect, or could appear to affect, the Directors' judgement. The Board regards Ms. Barber-Lui, Dr. Kucherlapati, Dr. LaMattina, Ms. Mazumdar-Shaw and Dame Marjorie Scardino as Independent Non-Executive Directors for the purposes of the Governance Code. In reaching this determination, the Board duly considered (i) their directorships and links with other Directors through their involvement in other subsidiary companies; (ii) their equity interests in PureTech and/or the Founded Entities, including equity grants of restricted stock units made to Non-Executive Directors by the Company under its Performance Share Plan; and (iii) in respect of Dr. LaMattina, the length of his tenure as a Director of the Company. The Board is satisfied that the judgement, experience and challenging approach adopted by each of these Directors should ensure that they each make a significant contribution to the work of the Board and its committees. Therefore, the Board has determined that Ms. Barber-Lui, Dr. Kucherlapati, Dr. LaMattina, Ms. Mazumdar-Shaw and Dame Marjorie Scardino are of independent character and judgement, notwithstanding the circumstances described at (i), (ii) and (iii) above.

Board support, indemnity and insurance

The Company Secretary, Dr. Bharatt Chowrira, is responsible to the Board for ensuring Board procedures are followed, applicable rules and regulations are complied with and that the Board is advised on governance and relevant regulatory matters. All Directors have access to the impartial advice and services of the Company Secretary.

There is also an agreed procedure for Directors to take independent professional advice at the Company's expense. In accordance with the Company's Articles of Association and a contractual Deed of Indemnity, the Directors have been granted an indemnity issued by the Company to the extent permitted by law in respect of liabilities incurred to third parties as a result of their office. The indemnity would not provide any coverage where a Director is proved to have acted fraudulently or with wilful misconduct. The Company has also arranged appropriate insurance cover in respect of legal action against its Directors and officers.

Board meetings and decisions

The Board meets regularly during the year, as well as on an ad hoc basis as required by business need. The Board had 4 scheduled meetings in 2021, and details on attendance are set forth in the table below:

Director	Number of Board Meetings Attended
Christopher Viehbacher	4/4
Raju Kucherlapati	4/4
John LaMattina	4/4
Robert Langer	4/4
Kiran Mazumdar-Shaw	4/4
Dame Marjorie Scardino	4/4
Bharatt Chowrira	4/4
Stephen Muniz	1/1
Daphne Zohar	4/4

While each director was able to attend every meeting in 2021, in the event of any unavoidable absence, the impacted Director would review with management the topics and materials to be discussed at the meeting, and provide appropriate feedback to be conveyed at such meeting.

The Board also acted by unanimous written consent five times in 2021. On occasion it was more expedient for the board to approve matters, especially administrative matters, by unanimous written consent rather than to convene a board meeting for the purpose. However, Directors were provided opportunity to discuss any concerns they had with the written resolution before its issue for signature.

At each meeting of the Board, there was a closed session held in which only the Chair and the other Non-Executive Directors participated.

The schedule of Board and Committee meetings each year is, so far as is possible, determined before the commencement of that year and all Directors or, if applicable, all Committee members, are expected to attend each meeting.

Supplementary meetings of the Board and/or the Committees are held as and when necessary. Each member of the Board receives in advance of each scheduled meeting detailed Board packages, which include an agenda based upon matters to be addressed and appropriate presentation and background materials. If a Director is unable to attend a meeting due to exceptional circumstances, he or she will nonetheless receive the meeting materials and discuss the materials with the Chief Executive Officer.

The Chair, Chief Executive Officer and senior management team work together to ensure that the Directors receive relevant information to enable them to discharge their duties and that such information is accurate, timely and clear. This information includes quarterly management accounts containing analysis of performance against budget as well as a summary of the operational performance of each of our businesses against its goals. Additional information is provided as appropriate for the topics being addressed at the meeting. At each meeting, the Board receives presentations from the Chief Executive Officer and, by invitation, other members of senior management as required. This ensures that all Directors are in a position to monitor effectively our overall performance, and to contribute to the development and implementation of its strategy.

The majority of Board meetings are held at our offices in Boston, Massachusetts, U.S., which gives members of the Company's senior management team, as well as the senior management of the Founded Entities, the opportunity to formally present to the Board on new technology development and business strategies. However, since the onset of the COVID-19 pandemic, for the safety of the Board and the Company's employees, all board meetings have been held by videoconference.

Certain Directors also serve on the boards of directors of our Founded Entities. These Founded Entity boards of directors meet regularly during the year, as well as on an ad hoc basis as required by business need. This service enables the Directors to have deep understanding of the businesses and contribute significantly to the strategy and oversight of these businesses.

Directors' conflicts of interest

Each Director has a statutory duty under the Companies Act 2006 (the CA 2006) to avoid a situation in which he or she has or can have a direct or indirect interest that conflicts or may potentially conflict with the interests of the Company. This duty is in addition to the continuing duty that a director owes to the Company to disclose to the Board any transaction or arrangement under consideration by the Company in which he or she is interested. The Company's Articles of Association permit the Board to authorize conflicts or potential conflicts of interest. The Board has established procedures for managing and, where appropriate, authorizing any such conflicts or potential conflicts of interest. In deciding whether to authorize any conflict, the Directors must have regard to their general duties under the CA 2006 and their overriding obligation to act in a way they consider, in good faith, will be most likely to promote the Company's success. In addition, the Directors are able to impose limits or conditions when giving authorization to a conflict or potential conflict of interest if they think this is appropriate. The authorization of any conflict matter, and the terms of any authorization, may be reviewed by the Board at any time. The Board believes that the procedures established to deal with conflicts of interest are operating effectively.

Induction, awareness and development

In preparation for the Company's initial public offering (IPO), all Directors received an induction briefing from the Company's legal advisors on their duties and responsibilities as Directors of a publicly quoted company. The Directors also received presentations from the Company's corporate brokers prior to the IPO. In addition, in order to ensure that the Directors continue to further their understanding of the challenges facing our Founded Entities and Wholly Owned Pipeline, the Board periodically receives the presentations and reports covering the business and operations of each of our Founded Entities as well as its Wholly Owned Pipeline.

We have put in place a comprehensive induction plan for any new Directors. This program will be tailored to the needs of each individual Director and agreed with him or her so that he or she can gain a better understanding of us and our businesses. In addition, the Company facilitates sessions as appropriate with our advisers, as well as appropriate governance specialists, to ensure that any new Directors are fully aware of, and understand, their responsibilities and obligations of a publicly quoted company and of the governance framework within which they must operate.

Board effectiveness and performance evaluation

The Board periodically reviews its effectiveness and performance. The Board seeks the assistance of an independent third-party provider at least once every three years in its evaluation in compliance with the Governance Code, and will otherwise carry out an internally facilitated Board evaluation led by the Senior Independent Director, assisted by the Company Secretary, covering the effectiveness of the Board as a whole, its individual Directors and its Committees.

In addition to the above, the Non-Executive Directors, led by the Senior Independent Director, will periodically appraise the Chair's performance, following which the Senior Independent Director will provide any feedback to the Chair. The performance of each of the Directors on the Board and the performance of the committees of the Board will be reviewed by the Chair as deemed necessary. The performance of Executive Directors will be reviewed by the Board on an ongoing basis, as deemed necessary, in the absence of the Executive Director under review.

Committees of the Board

The Board has three principal committees: the Nomination Committee, the Audit Committee and the Remuneration Committee. The composition of the three principal committees of the Board and the attendance of the members throughout the year is set out in the respective committee reports contained in this Annual Report. The terms of reference of each committee are available on request from the Company Secretary and within the Investors section of our website at www.puretechhealth.com.

Internal Control

The Board fully recognizes the importance of the guidance contained in the Guidance on Risk Management, Internal Control and Related Financial and Business Reporting. Our internal controls were in place during the whole of 2021, with a material weakness related to our risk assessment process over the design and implementation of our management review controls over the valuation of financial instruments, the completeness and accuracy of related sensitivity disclosures, the valuation of share based payment liabilities and completeness and the accuracy of the tax provision. We concluded that a similar material weakness existed in the prior financial period. During the year ended December 31, 2021, the Company took certain steps in its remediation plan, including (i) designing and documenting management review controls to address the level of aggregation and criteria for investigation, and (ii) implementing more robust procedures over the documentation of the performance of these management review controls. The Company has made progress toward remediation and will continue to implement its remediation plan for the ongoing material weaknesses in internal control over financial reporting described. The material weaknesses will not be considered remediated until the applicable controls operate for a sufficient period of time and management has concluded, through testing, that the controls are operating effectively. Additionally, in connection with the audit of our consolidated financial statements as of and for the year ended December 31, 2020, one of the identified material weaknesses related to a lack of segregation of duties with regard to uploading and posting journal entries in our previous ERP system. We deployed a new ERP system that went live on January 1, 2021, and as of December 31, 2021, this material weakness was remediated.

The Board is responsible for establishing and monitoring internal control systems and for reviewing the effectiveness of these systems. The Board views the effective operation of a rigorous system of internal control as critical to our success; however, it recognizes that such systems are designed to manage rather than eliminate risk of failure and can provide only reasonable and not absolute assurance against material misstatement or loss. The key elements of our internal control system, all of which have been in place during the financial year and up to the date these financial statements were approved, are as follows:

Control environment and procedures

We have a clear organizational structure with defined responsibilities and accountabilities. It adopts the highest values surrounding quality, integrity and ethics, and these values are communicated clearly throughout the whole organization. Detailed written policies and procedures have been established covering key operating and compliance risk areas. These policies and procedures are reviewed and the effectiveness of the systems of internal control is assessed periodically by the Board.

Identification and evaluation of risks

The Board actively identifies and evaluates the risks inherent in the business and ensures that appropriate controls and procedures are in place to manage these risks. The Board obtains an update regarding our Wholly Owned Pipeline and all Founded Entities on a regular basis and reviews our performance and the performance of our Wholly Owned Pipeline and Founded Entities on a quarterly basis. However, the performance of business units may be reviewed more frequently if deemed appropriate.

The key risks and uncertainties we face, as well as the relevant mitigations, are set out on pages 90 to 93 and in the Additional Information section from pages 217 to 251.

Information and financial reporting systems

We evaluate and manage significant risks associated with the process for preparing consolidated accounts by having in place systems and internal controls that ensure adequate accounting records are maintained and transactions are recorded accurately and fairly to permit the preparation of financial statements in accordance with IFRS. The Board approves the annual operating budgets and regularly receives details of actual performance measured against the budget.

Principal risks and uncertainties

Our operations and the implementation of our objectives and strategy are subject to a number of key risks and uncertainties. Risks are formally reviewed by the Board at least annually and appropriate procedures are put in place to monitor and, to the extent possible, mitigate these risks.

A summary of the key risks affecting us and the steps taken to manage these risks is set out on pages 90 to 93 and in the Additional Information section from pages 217 to 251.

Political expenditure

It is the Board's policy not to incur political expenditure or otherwise make cash contributions to political parties and it has no intention of changing that policy.

2022 Annual General Meeting

The Notice of the AGM, which will be held at 11:00 am EDT (4:00 pm BST) on June 15, 2022 at the Company's headquarters at 6 Tide Street in Boston, Massachusetts, U.S. is enclosed with this report. Details of the resolutions and the explanatory notes thereto are included with the Notice. To ensure compliance with the Governance Code, the Board proposes separate resolutions for each issue and proxy forms allow shareholders who are unable to attend the AGM to vote for or against or to withhold their vote on each resolution. In addition, to encourage shareholders to participate in the AGM process, the Company proposes to offer electronic proxy voting through the Registrar's website and through the CREST service. The results of all proxy voting will be published on our website after the AGM.

Our website at www.puretechhealth.com is the primary source of information on us. The website includes an overview of our activities, details of our businesses, and details of all of our recent announcements.

Relations with Stakeholders – Section 172 Statement

The Board recognizes its duties under Section 172 of the Companies Act 2006 and continuously has regard to how the Company's activities and decisions will impact investors, employees, those with whom it has a business relationship, the community and environment and its reputation for high standards of business conduct. In weighing all of the relevant factors, the Board, acting in good faith and fairly between members, makes decisions and takes actions that it considers will best lead to the long- term success of the Company. In accordance with Section 172, it is the responsibility of the Board as a whole to ensure that a satisfactory dialogue takes place and that the Board considers the potential impact on the Company's key stakeholders when making decisions.

The Board is committed to understanding and engaging with shareholders and other key stakeholder groups of the Company in order to maximize value and promote long-term Company success in line with our strategic objectives, as well as to promote and ensure fairness between our stakeholders. The Board believes that appropriate steps and considerations have been taken during the year so that each Director has an understanding of the various key stakeholders of the Company. The Board recognizes its responsibility to contemplate all such stakeholder needs and concerns as part of its discussions, decision-making, and in the course of taking actions and will continue to make stakeholder engagement a top priority in the coming years.

During the year, the Board assessed its current activities between the Board and its stakeholders, which demonstrated that the Board actively engages with its stakeholders and takes their various objectives into consideration when making decisions.

Stakeholder	How we engage	Key matters identified	Further information
Investors	• Our shareholders are the owners and investors in our business. We make significant efforts to engage with our shareholders and understand their objectives. We engage with our shareholders through a number of mechanisms to ensure that shareholder views are brought into the boardroom and considered in our decision-making. • The Board's primary shareholder contact is through the Chief Executive Officer. The Chair, the Senior Independent Director and other Directors, as appropriate, make themselves available for contact with major shareholders and other stakeholders in order to understand their issues and concerns. • Stakeholder engagement will often take place by the Executive Directors and senior management through investor meetings and investor roadshows, including participation at healthcare conferences and participating in fireside chats at those events, with the Board receiving regular updates by way of analysis reports on stakeholder views. • Meetings were held throughout the year with institutional shareholders. Key shareholder publications including the annual report, the full year and half year results announcements and press releases and the information for investors are available on the Company's website: www.puretechhealth.com.	• Our Board keeps its Strategy and Business Model under regular review. During the past year, the Board has engaged to carefully consider its strategy for future growth and development, in particular devoting attention to the future prospects of its business model and its listing venues and the risks and opportunities this would give to the Company's stakeholders. • The company carefully manages its expenditure and anticipates future capital needs through careful capital management and capital allocation to its Wholly Owned Programs and clinical trials as well as opportunities to secure financing from third parties, for example the $110m Series D financing for Akili in May 2021 and the $68m Series D financing for Vedanta in July 2021. Our Board also carefully considers opportunities for disposal of shares held in its Founded Entities such as the disposals of shares in Karuna raising $118m in February 2021 and $100m in November 2021. • During 2021, the Board welcomed Bharatt Chowrira to the Board as an Executive Director and saw the retirement of Steve Muniz as an Executive Director. The Board seeks to ensure appropriate board structure suitable for a Company of PureTech's size. • The Board recognizes the importance of Diversity, Equity and Inclusion and is delighted to be one of the few FTSE250 companies with a female CEO.	• Governance Section of ARA (Pages 90 to 146) • ESG Report (Pages 73 to 89) • Karuna disposals (Page 94) • Remuneration Report (Pages 131 to 146) • Value for Investors Section (Pages 23 to 34)

Stakeholder	How we engage	Key matters identified	Further information
Our People	• Our employees are crucial to the success of our business and many key decisions made by our Board have an impact on them. It is important to understand the employee perspective and ensure that we maintain an engaged workforce, as we believe that this will lead to better business results. We engage with our employees in various ways to ensure that their voice is heard in the management of our business including: – The conduct of regular Town Hall Meetings, email briefings to employees on key events as well as communication through the company intranet site and an engagement survey – The implementation of regular appraisals and personal development programs	• The Board recognizes the importance of an incentivized and engaged workforce, especially in the competitive greater Boston area. The Board engages to ensure the remuneration and benefit packages are competitive. • The Board aims to attract and retain employees through an established personal management and development program, with a view to development of the individual in an inclusive environment where employees from diverse backgrounds can thrive. • We are proud to be a company dedicated to discovering, developing and commercializing highly differentiated medicines for devastating diseases where limited or no treatment options currently exist for patients and believe we have established a business where our employees are proud to work.	• ESG Report (Pages 73 to 89) • Remuneration Report (Pages 131 to 146) • Strategic Report (Pages 1 to 72)
Community & Environment	• We are committed to supporting the communities in which we operate and the wider public. To that end, we have developed various mechanisms for engagement including: – Internships/partnerships with local universities and programs – Charitable giving – Building Certifications – Therapeutic Focus	• We are committed to improving our practices to ensure our business operates on a sustainable basis. In particular we have created an ESG committee chaired by one of our Non-Executive Directors to guide our sustainability initiatives. Our business Is a low carbon emissions and we are committed to delivering long term environmental sustainability. • We partner with local universities and programs to offer paid internship and externship programs, generally within technical fields in our development organization. • The company engages with local community and supports charitable causes. In particular, in 2021 and through the January 2022 post-period, PureTech made charitable contributions to Life Sciences Cares, The Greater Boston Food Bank (GBFB), Lymphatic Education & Research Network (LE&RN), Langer Prize for Innovation & Entrepreneurial Excellence Fellowship, and Fred Hutchinson Cancer Research Center.	• ESG Report (Pages 73 to 89) • LYT-100 Long COVID Study (Page 26)
Suppliers/ Business Partners	• Our business model creates value through partnerships and relationships with various key collaborators, and we continually evaluate how to strengthen relationships and arrangements with these institutions and individuals. Our engagement in 2021 included: – Quality updates and quality audits – Meetings with key surgeons to understand/identify potential indications and applications for therapeutics – Partnerships – Imbrium, BeiGene, Eli Lilly	• We aim to build clear and reliable supply arrangements with our contract manufacturers for clinical product supply, in particular with an emphasis on quality, especially in relation to a clinical environment. • We seek partnerships with other life sciences organizations to secure non-dilutive funding, access to development opportunities, and access to materials for our clinical trials.	• Value for Investors (Pages 23 to 34) • LYT-503/IMB-150 (Page 50) • LYT-200 (Pages 41 to 43) • Entrega (Page 72)

Directors' Report for the year ended December 31, 2021

The Directors present their report and the audited consolidated financial statements for the financial year ended December 31, 2021.

Certain disclosure requirements for inclusion in this report have been incorporated by way of cross reference to the Strategic Report, the Directors' Remuneration Report and the ESG Report which should be read in conjunction with this report.

The Company was incorporated on May 8, 2015 as a public company limited by shares in the UK and has a registered office situated at 8th Floor, 20 Farringdon Street, London, EC4A 4AB, United Kingdom. The Company was admitted to the premium listing segment of the Official List of the UK Listing Authority and to trading on the main market of the London Stock Exchange on June 24, 2015. The Company's American Depository Shares, each representing 10 ordinary shares, began trading on the Nasdaq Global Market on November 16, 2020.

Directors

The membership of the Board can be found below, and biographical details of the directors can be found on pages 112 to 116 and are deemed to be incorporated into this report.

Descriptions of the terms of the directors' service contracts are set forth on page 137 and page 144 of this report.

All directors shall retire from office and will offer themselves for reappointment by the members at the Company's upcoming AGM.

Details of the interests of directors in the share capital of the Company as of December 31, 2021 are set out in the Annual Report on Remuneration on page 144 and Note 24 to the financial statements, located on page 207. There have been no changes in such interests from December 31, 2021 to March 31, 2022, except as specifically set forth in those sections.

Results and dividends

We generated a loss for the year ended December 31, 2021 of $62.7 million (2020: income of $4.5 million).

The Directors do not recommend the payment of a dividend for the year ended December 31, 2021 (2020: nil).

Share capital

As of December 31, 2021, the ordinary issued share capital of the Company stood at 287,796,585 shares of £0.01 each, including shares issuable upon conversion of outstanding ADSs. Details on share capital are set out in Note 14 to the financial statements, page 191.

The Company's issued ordinary share capital comprises a single class of ordinary shares. Details on movements in issued share capital can be found in Note 14 to the financial statements, page 191.

Rights of ordinary shares

All of the Company's issued ordinary shares are fully paid up and rank pari passu in all respects and there are no special rights with regard to control of the Company. There are no restrictions on the transfer of ordinary shares or on the exercise of voting rights attached to them, which are governed by the Articles of Association and relevant UK legislation. The Directors are not aware of any agreements between holders of the Company's shares that may result in restrictions on the transfer of securities or in voting rights.

The shares in the Company issued to former holders of Ariya Therapeutics Inc. securities were subject to lock up agreements with the Company and were not tradable until such restrictions lapsed on October 1, 2021.

Substantial shareholders

As of March 31, 2022, the Company had been advised that the shareholders listed on page 124 hold interests of 3 percent or more in its ordinary share capital (other than interests of the Directors which are detailed on page 144 of the Directors' Remuneration Report). Other than as shown, so far as the Company (and its Directors) are aware, no other person holds or is beneficially interested in a disclosable interest in the Company.

Powers of the Directors

Subject to the Company's Articles of Association, UK legislation and any directions given by special resolution, the business of the Company is managed by the Board of Directors. Details of the matters reserved for the Board can be found in the Corporate Governance Report on page 117.

Articles of Association

The Articles of Association of the Company can only be amended by special resolution at a general meeting of the shareholders. No amendments are proposed at The 2022 AGM.

Ms. Sharon Barber-Lui was appointed to the Board as a Non-Executive Director on March 24, 2022.
The following have served as Directors of the Company during the 2021 financial year.

Name	Role	Age (as of December 31, 2021)
Mr. Christopher Viehbacher	Non-Executive Chair	61
Ms. Daphne Zohar	Chief Executive Officer	51
Dame Marjorie Scardino	Senior Independent Director	74
Dr. Robert Langer	Non-Executive Director	73
Dr. Raju Kucherlapati	Independent Non-Executive Director	78
Dr. John LaMattina	Independent Non-Executive Director	71
Ms. Kiran Mazumdar-Shaw	Independent Non-Executive Director	68
Dr. Bharatt Chowrira	President; Chief Business, Legal and Operating Officer; Company Secretary (appointed February 2021)	56
Mr. Stephen Muniz	Chief Operating Officer (retired May 2021)	51

Directors' liabilities (Directors' indemnities)

As at the date of this report, the Company has granted qualifying third party indemnities to each of its Directors against any liability that attaches to them in defending proceedings brought against them, to the extent permitted by the Companies Act. In addition, Directors and officers of the Company and its Founded Entities have been and continue to be covered by directors' and officers' liability insurance.

See further description of indemnity and insurance on page 118.

Political donations

No political contributions/donations for political purposes were made by the Company or any of our affiliate companies to any political party, politician, elected official or candidate for public office during the financial year ended December 31, 2021 (2020: nil).

Significant agreements

There are no agreements between the Company or any of our affiliate companies and any of its employees or any Director which provide for compensation to be paid to an employee or a Director for loss of office as a consequence of a takeover of the Company.

Compliance with the UK Corporate Governance Code

The Directors are committed to a high standard of corporate governance and compliance with the best practice of the UK Corporate Governance Code (Governance Code) published in July 2018. The Governance Code is available at the Financial Reporting Council website at www.frc.org.uk.

The Directors consider that the Company has, throughout the year ended December 31, 2021, applied the main principles and complied with the provisions set out in the Governance Code with the following exception: contrary to provision 24 of the Governance Code, the Chair, Mr. Christopher Viehbacher, was also Chair of the Audit Committee in 2021. The Board believes that Mr. Viehbacher's professional background and experience, together with his past participation on such committee for the past five years, made him a valuable member of the Audit Committee and that his membership was in the best interests of the Company's shareholders. Mr. Viehbacher was appointed Chair in September 2019. Immediately following the publication of its Annual Report and Accounts for the year ended December 31, 2021, Ms. Sharon Barber-Lui will become the Chair of the Audit Committee, and Mr. Viehbacher will step down as the Chair of the Audit Committee but remain a member thereof.

Further explanation as to how the provisions set out in the Governance Code have been applied by the Company is provided in this Report, the Report of the Nomination Committee and the Report of the Audit Committee.

Financial instruments

The financial risk management and internal control processes and policies, and exposure to the risks associated with financial instruments can be found in Note 16 to the financial statements and the Corporate Governance section of the Annual Report on page 129.

Sustainable development and environmental matters

Details of the Company's policies and performance, as well as disclosures concerning GHG emissions, are provided in the ESG Report on pages 73 to 89.

Related party transactions

Details of related party transactions can be found in Note 24 of the financial statements on pages 206 to 207.

Issuances of equity by major subsidiary undertaking

In April 2021 and November 2021, Sonde issued convertible promissory notes in the principal aggregate amount of $4.3 million. PureTech Health LLC participated and invested $2.1 million in the notes.

In July 2021, Vedanta completed Its Series D financing round In which It Issued and sold an aggregate of 2,387,675 shares of preferred stock for aggregate proceeds of approximately $68 million, of which purchased 174,520 shares for an aggregate purchase price of $5.0 million.

Future business developments

Information on the Company and its Wholly Owned Pipeline and Founded Entities' future developments can be found in the Strategic Report on pages 35 to 72.

Risk and internal controls

The principal risks we face are set out on pages 90 to 93 and in the Additional Information section from pages 217 to 251. The Audit Committee's assessment of internal controls is laid out on page 129.

Subsequent Events

Research and Development
Information on our research and development activities can be found in the Strategic Report on pages 35 to 72.

Going concern

As of December 31, 2021, the directors had a reasonable expectation that we had adequate resources to continue in operational existence into the first quarter of 2025.

Shareholder	%
Invesco Asset Management Limited	22.51
Baillie Gifford & Co	10.28
Lansdowne Partners International Limited	8.66
M&G Investment Management, LTD	4.20
Miller Value Partners	3.66
Recordati SA	3.32

* Represents an entity that is not a major subsidiary undertaking of the Company.

Annual General Meeting

The Notice of the AGM, which will be held at 11:00 am EDT (4:00 pm BST) on June 15, 2022 at the Company's headquarters at 6 Tide Street in Boston, Massachusetts, U.S. is enclosed with this report. Details of the resolutions and the explanatory notes thereto are included with the Notice. To ensure compliance with the Governance Code, the Board proposes separate resolutions for each issue and proxy forms allow shareholders who are unable to attend the AGM to vote for or against or to withhold their vote on each resolution. In addition, to encourage shareholders to participate in the AGM process, the Company proposes to offer electronic proxy voting through the Registrar's website and through the CREST service. The results of all proxy voting will be published on our website after the AGM.

The Notice of the Meeting, together with an explanation of the items of business, will be contained in a circular to shareholders to be dated April 26, 2022.

Pension schemes

Information on the Company's 401K Plan can be found in the Annual Report on Remuneration on page 133.

Disclosure of information under Listing Rule 9.8.4R

For the purposes of LR 9.8.4R, the information required to be disclosed can be found in the sections of the Annual Report and Financial Statements listed in the table below.

Listing Rule Requirement	Location in Annual Report
A statement of the amount of interest capitalized during the period under review and details of any related tax relief.	N/A
Information required in relation to the publication of unaudited financial information.	N/A
Details of any long-term incentive schemes.	Directors' Remuneration Report, page 131
Details of any arrangements under which a Director has waived emoluments, or agreed to waive any future emoluments, from the Company.	N/A
Details of any non-pre-emptive issues of equity for cash.	N/A
Details of any non-pre-emptive issues of equity for cash by any unlisted major subsidiary undertaking.	Directors' Report, page 124
Details of parent participation in a placing by a listed subsidiary.	N/A
Details of any contract of significance in which a Director is or was materially interested.	N/A
Details of any contract of significance between the Company (or one of its subsidiaries) and a controlling shareholder.	N/A
Details of any provision of services by a controlling shareholder.	N/A
Details of waiver of dividends or future dividends by a shareholder.	N/A
Where a shareholder has agreed to waive dividends, details of such waiver, together with those relating to dividends which are payable during the period under review.	N/A
Board statements in respect of relationship agreement with the controlling shareholder.	N/A

Whistleblowing, anti-bribery and corruption

We seek at all times to conduct our business with the highest standards of integrity and honesty. We also have an anti-bribery and corruption policy which prohibits our employees from engaging in bribery or any other form of corruption. In addition, we have a whistleblowing policy under which staff are encouraged to report to the Chief Executive Officer or the President, any alleged wrongdoing, breach of a legal obligation or improper conduct by or on the part of us or any of our officers, Directors, employees, consultants or advisors.

Appointment of auditor

KPMG LLP, the external Auditor of the Company, was appointed in 2015 and a resolution proposing its reappointment will be proposed at the forthcoming AGM.

Disclosure of information to auditor

The Directors who held office at the date of approval of this Directors' report confirm that:

- so far as the Director is aware, there is no relevant audit information of which the Company's Auditor is unaware; and
- the Director has taken all steps that he/she ought to have taken as a Director in order to make himself/herself aware of any relevant audit information and to establish that the Company's Auditor is aware of that information.

This confirmation is given and should be interpreted in accordance with the provisions of Section 418 of the CA 2006.

Statement of Directors' responsibilities in respect of the Annual Report and the financial statements

The directors are responsible for preparing the Annual Report and the Group and parent Company financial statements in accordance with applicable law and regulations.

Company law requires the directors to prepare Group and parent Company financial statements for each financial year. Under that law they are required to prepare the Group financial statements in accordance with UK-adopted international accounting standards and applicable law and have elected to prepare the parent Company financial statements on the same basis. In addition, the Group financial statements are required under the UK Disclosure Guidance and Transparency Rules to be prepared in accordance with the UK-adopted international accounting standards.

Under company law the directors must not approve the financial statements unless they are satisfied that they give a true and fair view of the state of affairs of the Group and parent Company and of the Group's profit or loss for that period. In preparing each of the Group and parent Company financial statements, the directors are required to:

- select suitable accounting policies and then apply them consistently;
- make judgements and estimates that are reasonable, relevant and reliable;
- state whether they have been prepared in accordance with the UK-adopted international accounting standards;
- assess the Group and parent Company's ability to continue as a going concern, disclosing, as applicable, matters related to going concern; and
- use the going concern basis of accounting unless they either intend to liquidate the Group or the parent Company or to cease operations, or have no realistic alternative but to do so.

The directors are responsible for keeping adequate accounting records that are sufficient to show and explain the parent Company's transactions and disclose with reasonable accuracy at any time the financial position of the parent Company and enable them to ensure that its financial statements comply with the Companies Act 2006. They are responsible for such internal control as they determine is necessary to enable the preparation of financial statements that are free from material misstatement, whether due to fraud or error, and have general responsibility for taking such steps as are reasonably open to them to safeguard the assets of the Group and to prevent and detect fraud and other irregularities.

Under applicable law and regulations, the directors are also responsible for preparing a Strategic Report, Directors' Report, Directors' Remuneration Report and Corporate Governance Statement that complies with that law and those regulations.

The directors are responsible for the maintenance and integrity of the corporate and financial information included on the company's website. Legislation in the UK governing the preparation and dissemination of financial statements may differ from legislation in other jurisdictions.

Responsibility statement of the directors in respect of the annual financial report

We confirm that to the best of our knowledge:

- the financial statements, prepared in accordance with the applicable set of accounting standards, give a true and fair view of the assets, liabilities, financial position and profit or loss of the company and the undertakings included in the consolidation taken as a whole; and
- the strategic report includes a fair review of the development and performance of the business and the position of the issuer and the undertakings included in the consolidation taken as a whole, together with a description of the principal risks and uncertainties that they face.

We consider the annual report and accounts, taken as a whole, is fair, balanced and understandable and provides the information necessary for shareholders to assess the Group's position and performance, business model and strategy.

By Order of the Board

Daphne Zohar
Founder, Chief Executive Officer and Director

April 25, 2022

Report of the Nomination Committee

Dame Marjorie Scardino
Chair, Nomination Committee

Committee responsibilities

The Nomination Committee assists the Board in discharging its responsibilities relating to the composition and make-up of the Board and any Committees of the Board. It is also responsible for periodically reviewing the Board's structure and identifying potential candidates to be appointed as Directors or Committee members as the need may arise. The Nomination Committee is responsible for evaluating the balance of skills, knowledge and experience and the size, structure and composition of the Board and Committees of the Board, retirements and appointments of additional and replacement Directors and Committee members, and makes appropriate recommendations to the Board on such matters. A full copy of the Committee's Terms of Reference is available on request from the Company Secretary and within the Investor's section on Company's website at www.puretechhealth.com.

Committee membership

The Nomination Committee consisted of Dame Marjorie Scardino, who served as the committee's Chair, Dr. Robert Langer, and Ms. Kiran Mazumdar-Shaw. The biographies of the Nomination Committee members can be found on pages 112 to 113.

The Governance Code requires that a majority of the members of a nomination committee should be independent Non-Executive Directors.

In making their determination for the year 2021, the Board regarded Dame Marjorie Scardino, Dr. Langer and Ms. Mazumdar-Shaw as meeting the independence criteria set out in the Governance Code as it is applied to their service on the Nomination Committee. In reaching this determination, the Board duly considered (i) their directorships and links with other Directors through their involvement in other Founded Entities; (ii) their equity interests in PureTech Health and/or the Founded Entities; and (iii) the circumstance that Dr. Langer is a founding Director of the Company. The Board also duly considered the extent to which these matters may impact their service on the Nomination Committee. After such consideration, the Board has determined Dame Marjorie Scardino, Dr. Langer and Ms. Mazumdar-Shaw to be independent in character and judgement and free from relationships or circumstances which might affect, or appear to affect, the Directors' judgement in their service on the Nomination Committee.

The Nomination Committee meets as required to initiate the selection process of, and make recommendations to, the Board with regard to the appointment of new Directors. During 2021, the Nomination Committee met one time to review the structure, size and composition of the Board in light of the requirements of the Governance Code. Dame Marjorie Scardino and Dr. Langer participated in the meeting. The Chief Executive Officer and the President were invited to and attended the meeting.

Diversity policy

Diversity within the Company's Board is essential in maximizing its effectiveness, as it enriches debates, business planning and problem-solving. The Company approaches diversity in its widest sense so as to recruit the best talent available, based on merit and assessed against objective criteria of skills, knowledge, independence and experience as well as other criteria such as gender, age and ethnicity. The Company will adhere to a strategy of recruiting individuals who meet these criteria as it searches for additional independent Non-Executive Directors to the Board, as discussed below. The Committee's primary objective is to ensure that the Company maintains the strongest possible leadership.

Information regarding the Company's diversity efforts can be found in the ESG Report on pages 73 to 89.

Board and Committee evaluation

Information regarding the evaluation of the Board and its Committees can be found on page 119.

Report of the Audit Committee

Mr. Christopher Viehbacher
Chair, Audit Committee

Committee responsibilities

The Audit Committee monitors the integrity of our financial statements and reviews all proposed annual and half-yearly results announcements to be made by us with consideration being given to any significant financial reporting judgements contained in them. The Committee also advises the Board on whether it believes the annual report and accounts, taken as a whole, are fair, balanced and understandable and provide the information necessary for shareholders to assess the Company's position and performance, business model and strategy. The Committee also considers internal controls, compliance with legal requirements, the FCA's Listing Rules, Disclosure Guidance and Transparency Rules, and reviews any recommendations from the Group's Auditor regarding improvements to internal controls and the adequacy of resources within our finance function. A full copy of the Committee's Terms of Reference is available on request from the Company Secretary and within the Investor's section on the Company's website at www.puretechhealth.com.

Committee membership

The Committee consisted of three independent Non-Executive Directors, Mr. Christopher Viehbacher, Dr. Raju Kucherlapati and Dame Marjorie Scardino, until Ms. Sharon Barber-Lui joined the Committee upon her appointment to the Board on March 24, 2022. Mr. Viehbacher served as Chair of the Committee. Mr. Viehbacher has experience as a Chartered Accountant and has held numerous senior executive positions in his career. The Board has deemed this to be recent and relevant financial experience, qualifying him to be Chair of the Committee. The biographies of the Committee members can be found on pages 112 to 113. The Committee met four times during the year, with Mr. Viehbacher, Dr. Kucherlapati and Dame Marjorie Scardino each attending all four meetings. The Chief Financial Officer and the external Auditor were invited to and attended all of the meetings. The Chief Executive Officer and President also attended certain of the meetings. When appropriate, the Committee met with the Auditor without any members of the executive management team being present. Immediately following the Company's publication of Its Annual Report and Accounts for the year ended December 31, 2021, Ms. Barber-Lui will become the Chair of the Audit Committee, and Mr. Viehbacher will step down as the Chair of the Audit Committee but remain a member thereof. Ms. Barber-Lui has accounting experience, is currently the Senior Vice President of Finance at EQRx, Inc., a publicly-traded U.S. company (Nasdaq: EQRX), and has held a number of senior finance and executive leadership positions In her career. The Board has deemed this to be recent and relevant financial experience qualifying her to be Chair of the Committee.

Activities during the year

The activities undertaken by the Committee were the normal recurring items, the most important of which are noted below.

Significant issues considered in relation to the financial statements

The Committee considered, in conjunction with management and the external auditor, the significant areas of estimation, judgement and possible error in preparing the financial statements and disclosures, discussed how these were addressed and approved the conclusions of this work. The principal areas of focus in this regard were:

Valuation of investments and intercompany receivable balances held by the Parent Company

The significant issue is the recoverability of the investment by the Company, due to its materiality in the context of the total assets of the Company. The carrying value of investments in Founded Entities and intercompany receivables is supported by our underlying assets. The Committee was satisfied with the conclusion reached.

Valuation of financial instruments; investments in Gelesis and Akili preferred share financial assets, Vedanta and Follica preferred shares financial liabilities and Follica and Vedanta warrants financial liabilities

An area of material judgement in our financial statements and, therefore, audit risk relates to the valuation of third party held preferred shares classified as liabilities, convertible loan notes and warrants measured at fair value through profit/loss, which at year end had a carrying value totaling $183 million (2020 – $152 million), as well as investments held at fair value that do not have a quoted active market price which at year end had a carrying value totaling $240 million (2020 – $207 million). We considered the underlying economics of the valuations of the Founded Entities and the investees and sought external expertise in determining the appropriate valuation of the liabilities and investments. These valuations rely, in large part, on the valuation of our programs and values of recent transactions and determine the amount of gain (loss) on the financial instruments.

Classification of new preferred shares and convertible loan notes including identification and classification of any embedded derivatives

As part of our strategy to finance the Founded Entities, we issue financial instruments commensurate with the economics of each transaction. These financial instruments can include preferred shares, convertible notes, warrants and loans payable. Often these arrangements contain terms that can make it difficult to determine whether the financial instrument should be classified as debt or equity on our statement of financial position. We considered the pertinent terms and underlying economics of the financial instruments and have appropriately classified them as debt or equity. The Committee believes that we considered the pertinent terms and underlying economics of each of the financial instruments, as well as the advice of external experts, and has appropriately classified them as debt or equity.

Regulatory compliance

Ensuring compliance for FCA regulated businesses also represents an important control risk from the perspective of the Committee. We engage with outside counsel and other advisors on a regular basis to ensure compliance with legal requirements.

Review of Annual Report and Accounts and Half-yearly Report

The Committee carried out a thorough review of our 2021 Annual Report and Accounts and our 2021 Half-yearly Report resulting in the recommendation of both for approval by the Board. In carrying out its review, the Committee gave particular consideration to whether the Annual Report, taken as a whole, was fair, balanced and understandable, concluding that it was. It did this primarily through consideration of the reporting of our business model and strategy, the competitive landscape in which it operates, the significant risks it faces, the progress made against its strategic objectives and the progress made by, and changes in fair value of, its Founded Entities during the year.

Going concern

At least annually, the Committee considers the going concern principle on which the financial statements are prepared. As a business which seeks to fund the development of its Wholly Owned Pipeline, as well as support its Founded Entities with further capital, the business model is currently inherently cash consuming.

As of December 31, 2021, we had sufficient cash reserves to extend operations over a three-year period into the first quarter of 2025.

Therefore, while an inability of the Wholly Owned Pipeline and Founded Entities to raise funds through equity financings with outside investors, strategic arrangements, licensing deals or debt facilities may require us to modify our level of capital deployment into our Wholly Owned Pipeline and Founded Entities or to more actively seek to monetize one or more Founded Entities, it would not threaten our viability overall.

Compliance

The Committee has had a role in supporting our compliance with the Governance Code, which applies to us for the 2021 financial year. The Board has included a statement regarding our longer-term viability on page 94. The Committee worked with management and assessed that there is a robust process in place to support the statement made by the Board.

Similarly, the Committee worked with management to ensure that the current processes underpinning its oversight of internal controls provide appropriate support for the Board's statement on the effectiveness of risk management and internal controls.

Risk and internal controls

The principal risks we face are set out on pages 70 to 73 and in the Additional Information section from pages 217 to 251.

The Committee has directed that management engage in a continuous process to review internal controls around financial reporting and safeguarding of assets. Management has engaged external advisors to complete internal control testing on behalf of management for the 2021 financial year and the results were presented to the Committee. With the exception of the material weakness related to our risk assessment process over the design and implementation of our management review controls over the valuation of financial instruments, the completeness and accuracy of related sensitivity disclosures, the valuation of share based payment liabilities and completeness and the accuracy of the tax provision, the Committee believes that we have adequate controls and appropriate plans to evolve the control structure in anticipation of increased complexity of the business model and operations.

We have a formal whistleblowing policy. The Committee is satisfied that the policy has been designed to encourage staff to report suspected wrongdoing as soon as possible, to provide staff with guidance on how to raise those concerns, and to ensure staff that they should be able to raise genuine concerns without fear of reprisals, even if they turn out to be mistaken.

Internal audit

We do not maintain a separate internal audit function. This is principally due to our size, where close control over operations is exercised by a small number of executives. In assessing the need for an internal audit function, the Committee considered the risk assessment performed by management to identify key areas of assurance and the whole system of internal financial and operational controls. The Company achieves internal assurance by performing the risk assessment of the key areas of assurance and maintaining related key internal controls.

External audit

We have engaged KPMG LLP as our Auditor since 2015. The current audit partner is Robert Seale who has been our audit partner since June 2019.

The effectiveness of the external audit process is dependent on appropriate risk identification. In October 2021, the Committee discussed the Auditor's audit plan for 2021. This included a summary of the proposed audit scope and a summary of what the Auditor considered to be the most significant financial reporting risks facing us together with the Auditor's proposed audit approach to these significant risk areas. The main areas of audit focus for the year were (a) the valuation of investments and intercompany receivable balances held by the Parent Company, (b) Valuation of financial instruments; investments in Gelesis and Akili preferred share financial assets, Vedanta and Follica preferred shares financial liabilities and Follica and Vedanta warrants financial liabilities and (c) Classification of new preferred shares and convertible loan notes including identification and classification of any embedded derivatives.

Appointment and independence

The Committee advises the Board on the appointment of the external Auditor and on its remuneration both for audit and non-audit work, and discusses the nature, scope and results of the audit with the external Auditor. The Committee keeps under review the cost-effectiveness and the independence and objectivity of the external Auditor. Controls in place to ensure this include monitoring the independence and effectiveness of the audit, a policy on the engagement of the external Auditor to supply non-audit services, and a review of the scope of the audit and fee and performance of the external Auditor.

The Audit Committee ensures that at least once every ten years the audit services contract is put out to tender to enable us to compare the quality and effectiveness of the services provided by the incumbent auditor with those of other audit firms.

Non-audit work

The Committee approves all fees paid to the Auditor for non-audit work.

Where appropriate, the Committee sanctions the use of KPMG LLP for non-audit services in accordance with our non-audit services policy. During 2021 KPMG LLP did not provide any non-audit related services. Therefore the ratio of non-audit work to audit work was nil, which the committee is satisfied does not breach the independence of KPMG LLP.

Christopher Viehbacher
Chair of Audit Committee

April 25, 2022

Directors' Remuneration Report for the year ended December 31, 2021

Dr. John LaMattina
Chair,
Remuneration
Committee

The Directors' Remuneration Report is split into three sections, namely:

- This Annual Statement: summarizing and explaining the major decisions on Directors' remuneration in the year;
- The Directors' Remuneration Policy: setting out the framework for remuneration for our Directors in 2022 on pages 133 to 137; and
- The Annual Report on Remuneration: setting out the implementation of the Remuneration Policy in the year ended December 31, 2021 on pages 138 to 146.

The Company puts the Directors' Remuneration Policy to a binding vote of our shareholders every three years (sooner if changes are required to the Policy). The Annual Report on Remuneration is subject to an annual advisory vote of our shareholders.

The current Directors' Remuneration Policy was last approved at the 2021 AGM, and such approval is effective until the 2024 AGM. The Annual Report on Remuneration will be subject to an advisory shareholder vote at the forthcoming 2022 AGM.

Committee responsibilities

The Remuneration Committee's primary purpose is to assist the Board in determining the Company's remuneration policies. The Remuneration Committee has the responsibility for setting the remuneration policy for all Executive Directors and the Chairman of the Company, including pension rights and compensation payments, and in determining such policy must take into account all factors which it deems necessary including regulatory requirements, with the objective of attracting, retaining and motivating executive management having regard to views of shareholders and stakeholders and the risk appetite of the Company and alignment to the Company's long term goals and strategic plan. The Remuneration Committee also recommends and monitors the level and structure of remuneration for senior management.

The Remuneration Committee shall, in consultation with the Chairman and/or the Chief Executive Officer, determine the total individual remuneration package of each Executive Director, including share awards. The Remuneration Committee shall also have regard to current information for remuneration in other companies of comparable scale and complexity and can appoint remuneration consultants to assist in such process. The Remuneration Committee also has responsibility to review the design of all share incentive plans and determine awards under such plans. A full copy of the Remuneration Committee's Terms of Reference is available on request from the Company Secretary and within the Investors section of the Company's website at www.puretechhealth.com.

Committee membership

The Remuneration Committee consists of Dr. Kucherlapati, Dr. LaMattina and Ms. Mazumdar-Shaw, with Dr. LaMattina serving as Chair of the Committee. The biographies of the Committee members can be found on pages 112 to 113. The Committee met three times during the year, with each Committee member in attendance for all of the meetings. The Committee also acted by unanimous written consent five times during the year. The Chief Executive Officer and the Chief Operating Officer were invited to and attended all of the meetings, with Mr. Muniz attending each of the two meetings prior to his retirement in May 2021. Dr. Chowrira was invited to and attended the Committee meeting occurring after Mr. Muniz's retirement. However, no Executive Director was permitted to participate in discussions or decisions about his or her personal remuneration.

Our Remuneration Policy

The success of PureTech depends on the motivation and retention of our highly skilled workforce with significant expertise across a range of science and technology disciplines, as well as our highly-experienced management team and seasoned Directors. PureTech's Remuneration Policy is therefore an important part of our business strategy. Our guiding principle is to provide market competitive remuneration packages, including with respect to cash compensation in the form of base salary, annual bonuses and benefits as well as share based compensation, benchmarked against data generated from our local markets to enable us to put together and retain a top tier team.

The Directors' Remuneration Policy was approved by shareholders at the 2021 AGM with 89.3% support. Whilst the Committee was pleased with the support received, as part of the engagement process with shareholders for determining the policy, the Committee understood that some shareholders had concerns with the increase to quantum of the share based awards. Share based remuneration is a vital component of the remuneration packages of both executives and the Board of Directors and allows us to compete for, attract and retain talent in the U.S. market.

We remain committed to long-term performance-based remuneration delivered through our Performance Share Plan ("PSP") and believe that our current remuneration policy provides an appropriate framework to incentivize and motivate our senior management team with competitive U.S. remuneration packages, while also ensuring the structure of the PSP is aligned to UK practice.

All tables within the Directors' Remuneration Report are audited under the International Standards on Auditing (UK) ("ISAs (UK)") unless otherwise noted.

Objectives of the Remuneration Policy for our CEO and Senior Executives

In the construction of our senior executive Remuneration Policy, the Committee paid particular regard to the market practice of U.S. peer companies to ensure that packages are competitive, recognizing the predominantly U.S. market in which we compete for talent. At the same time, the structure of the packages was designed to be in line with the principles of the UK Corporate Governance Code and best practice.

The key aims of the Remuneration Policy and the Code principles to which they relate are as follows:

- promote our long-term success (Code principle: Proportionality);
- attract, retain and motivate high caliber senior management and focus them on the delivery of our long-term strategic and business objectives (Proportionality, alignment to culture and risk);
- be simple and understandable, both externally and internally (Clarity, simplicity, predictability and proportionality);

- achieve consistency of approach across senior management to the extent appropriate and informed by relevant market benchmarks (Clarity and alignment to culture); and
- encourage widespread equity ownership across the executive team to ensure a long-term focus and alignment of interest with shareholders (Alignment to culture, risk).

Performance and reward in 2021, and our response to the COVID-19 pandemic

One of our key business priorities during 2021 continued to be the health and well-being of our employees in light of the ongoing COVID-19 pandemic. We were pleased with the performance of our workforce under conditions that continued to require the development of new ways of working, in many cases from home, and we have supported our employees with several initiatives based around their welfare. These initiatives included extensive health protocols for those required to be onsite, flexible work from home arrangements, required vaccinations and a 100% company vaccination rate, assistance with safe transportation and a program to bring lunch into the office for those onsite, among others. As in 2020, we did not need to receive any Government support in 2021 and furthermore our operational and financial performance has not been significantly impacted by the pandemic.

During 2021, PureTech delivered exceptional execution and achievement of key strategic and financial goals, which has been reflected in the annual bonus and PSP outcomes. The Company delivered substantial growth and generated momentum to support future growth in the coming years as our balance sheet, Founded Entities equity and royalty stakes, and Wholly Owned programs position PureTech with the strength to build substantial value for shareholders in the current environment. This growth is due in large part to (i) significant development and advancement of our Wholly Owned Pipeline and activities initiated or progressed to potentially bring these innovative therapies to market, (ii) continued build out of our executive leadership team and creation of a world-class development organization to support increased operational activities, (iii) our Founded Entities raising in excess of $731 million and progressing their respective business, and (iv) generation of $218.1 million of non-dilutive cash income in 2021 from the sale of equity holdings in Founded Entities. This increase in value, together with management's operational performance at PureTech and within the Wholly Owned Pipeline and Founded Entities, resulted in the Remuneration Committee approving 100% of the target performance goals. In line with our standard approach, the Committee then reviewed the overall performance of the Company and the individual Executive Directors before determining the final bonus payout. The Committee considered operational performance, the overall growth of the business during the year, the extent to which the target performance goals had in some cases been exceeded and the individual contributions of the Executive Directors. As a result of the significant efforts of both Executive Directors in managing the organization in ways not captured by the performance goals set at the beginning of 2021, including taking on additional responsibilities as they managed the transition from the departure of two long-tenured senior leaders with minimal disruption to the business, the Committee determined that a number of additional critical objectives had also been achieved and decided that a bonus equal to 150% of target (or 75% of base salary) was to be awarded to the Executive Directors. The Committee is of the view that this is appropriate in recognizing the Executive Directors' achievements in strengthening the organization and its balance sheet in 2021 and entirely in line with the operational performance delivered during the year and the overall growth of the business. See highlights of 2021 on pages 1 to 9.

In relation to the PSP, PureTech's performance over the last three financial years was very strong with an increase in share price from 172 pence to 292 pence from December 31, 2018 to December 31, 2021 representing an average annual total shareholder return during the period of approximately 23.8%, significantly above the maximum target of 15% per annum set in the PSP awards. This, along with our relative total shareholder return performance and strong strategic performance over the three-year performance period, resulted in the vesting of 95.8 percent of the PSP awards granted to the executive management team, including the two Executive Directors, in 2019.

For the year ended December 31, 2021, the Committee believes the Remuneration Policy operated as intended and that remuneration outcomes are appropriate, taking into account remuneration outcomes throughout the business, company performance and the stakeholder experience. As mentioned above, the Committee determined that the final payout under the annual bonus plan for 2021 to the Executive Directors should be increased from 100% of target to 150% of target, reflective of the achievements during the year, and the individual contributions of the Executive Directors. No discretion has been exercised in relation to the PSP vesting outcome.

The year ahead

For 2022, the following key decisions have been made in relation to how the Policy will be implemented:

- Base salaries for the Executive Directors will be increased by 6 percent in line with the average increase for the general workforce taking into consideration a number of factors, including the current inflationary pressures in the United States;
- The annual bonus target and maximum will remain at 50 percent and 100 percent of base salary, respectively; and
- The grants of PSP awards in 2022 will be at levels of 500 percent of base salary for the Chief Executive Officer and 250 percent of salary for the President. These grant levels are lower than the maximum permitted under the Directors' Remuneration Policy, and lower than the grant levels in 2021. This takes into account the current share price and the resulting impact on the number of shares underlying each award.

Closing comments

The Committee is comfortable that the operation of the Policy for 2021 has demonstrated a robust link between performance and reward. The Committee believes the proposed operation of the Policy for 2022 is appropriate and takes into account the wider stakeholder experience.

The Committee looks forward to shareholders' support for the shareholder resolution for this Annual Statement and the Annual Report on Remuneration at the 2022 Annual General Meeting.

Directors' Remuneration Policy

This part of the Directors' Remuneration Report sets out the Remuneration Policy for the Executive Directors and has been prepared in accordance with the provisions of the Companies Act 2006, The Large and Medium Sized Companies and Groups (Accounts and Reports) (Amendment) Regulations 2008 and the subsequent amendments, and the UK Listing Authority Listing Rules. In addition, the report has been prepared on a "comply or explain" basis with regard to the UK Corporate Governance Code 2018.

This Directors' Remuneration Policy was approved by a binding shareholder vote at the Company's AGM on May 27, 2021. Unless the Company proposes changes to the policy, it will apply for a period of three years from that date. The approved Remuneration Policy can be found in the Director's Remuneration Report of our 2020 Annual Report and Accounts available in the Investor Relations portion of our website at www.puretechhealth.com.

All tables within this Directors' Remuneration Policy section are audited under the International Standards on Auditing (UK) ("ISAs (UK)") unless otherwise noted.

Decision making process for determination, review and implementation of Directors' Remuneration Policy

The Committee reviews the Policy and its operation to ensure it continues to support and align to the business strategy and appropriately reward the Executive Directors and takes into account relevant market practice, regulation and governance developments, institutional investor views and the views of our shareholders. The Committee also has regard to the remuneration arrangements, policies and practices of the workforce as a whole and takes this into account when reviewing Executive Director pay.

The Policy is reviewed annually by the Committee. If changes are required, a new policy will be put forward to shareholder vote prior to the normal triennial shareholder vote. The Committee consults with shareholders on remuneration proposals and will consider the feedback in finalizing the Policy.

Operation of the Policy is considered annually for the year ahead, including metrics for incentives, weightings and targets. The Committee reviews operation for the prior year and considers whether, in light of the strategy, changes are required for the year ahead or if remuneration remains appropriate for the year ahead. Shareholders' views may be sought depending on the changes proposed.

Element	How component supports corporate strategy	Operation	Maximum	Performance targets and recovery provisions
Base salary	To recognize the market value of the employee and the role.	Normally reviewed annually. Salaries are benchmarked periodically primarily against biotech, pharmaceutical and specialty finance companies listed in the U.S. and UK. The committee also considers UK-listed general industry companies of similar size to PureTech as a secondary point of reference.	There is no prescribed maximum base salary or annual salary increase. The Committee is guided by the general increase for the broader employee population but may decide to award a lower increase for Executive Directors or indeed exceed this to recognize, for example, an increase in the scale, scope or responsibility of the role and/or to take account relevant market movements. Current salary levels are set out in the Annual Report on Remuneration.	Not applicable.
Pension	To provide a market competitive level of contribution to pension.	The company operates a 401k Plan for its U.S. Executive Directors. The operation of the Plan is in line with the operation for all other employees.	Under the 401k Plan, Company contributions are capped at the lower of 3 percent of base salary or the maximum permitted by the U.S. IRS ($19,500 for 2021).	Not applicable.
Benefits	To provide a market competitive level of benefits.	Includes: private medical and dental cover, disability, life insurance. Additional benefits may also be provided in certain circumstances, such as those provided to all employees.	Cost paid by the company.	Not applicable.

Element	How component supports corporate strategy	Operation	Maximum	Performance targets and recovery provisions
Annual Bonus Plan (ABP)	To drive and reward annual performance of individuals, teams and PureTech.	Based on performance during the relevant financial year. Paid in cash. The Committee has discretion to adjust payout levels if it considers the formulaic outcome inappropriate taking into account the underlying financial performance of the Company, share price performance, the investment return to shareholders during the year, and such other factors as it considers appropriate.	Up to 100 percent of base salary.	Performance period: Normally one year. Payments are normally based on a scorecard of strategic and/or financial measures. Up to 0 percent of salary payable for threshold performance, 50 percent of base salary normally payable for the achievement of 'target' performance and 100 percent of base salary payable for the achievement of stretch performance. Recovery and withholding provisions are in place.
Long-term incentives	To drive and reward our sustained performance and to align the interests with those of shareholders.	The Company can make long-term incentive awards with the following features: • performance shares. • vesting is dependent on the satisfaction of performance targets and continued service. • performance and vesting periods are normally three years. Awards granted from 2019 onwards will be subject to a two-year post-vesting holding period during which vested shares cannot be sold other than to settle tax. This post-vesting period continues post-cessation of employment. The Committee also has the discretion to adjust vesting levels of performance-related awards to override formulaic outcomes, taking into account similar factors as apply in relation to annual bonus awards, but by reference to the performance period.	600 percent of salary for the Chief Executive Officer, 300 percent of base salary for the other Executive Directors. Participants may benefit from the value of dividends paid over the vesting period to the extent that awards vest. This benefit is delivered in the form of cash or additional shares at the time that awards vest.	Performance period: Normally three years. Up to 25 percent of an award vests at threshold performance (0 percent vests below this), increasing to 100 percent pro-rata for maximum performance. Normally at least half of any award will be measured against TSR targets with the remainder measured against relevant financial or strategic measures. Recovery and withholding provisions are in place.
Share ownership/ Holding Period	Further aligns executives with investors, while encouraging employee share ownership.	The Committee requires that Executive Directors who participate in a long-term incentive plan operated by the Company retain half of the net shares vesting under any long-term incentive plan until a shareholding requirement is met.	Minimum of 400 percent of base salary for the Chief Executive Officer and a minimum of 200 percent of base salary for the other Executive Directors.	None.
Post-cessation holding period	Aligns executives with investors and promotes long-term decision making	Executive Directors must hold shares for two years after the date of termination of their employment.	Lower of (i) 400 percent of base salary for the Chief Executive Officer and 200 percent of base salary for the other Executive Directors and (ii) the Executive Director's shareholding at the date that notice is served.	None.

Element	How component supports corporate strategy	Operation	Maximum	Performance targets and recovery provisions
Non-Executive Directors	To provide fee levels and structure reflecting time commitments and responsibilities of each role, in line with those provided by similarly-sized companies and companies operating in our sector.	Remuneration provided to Non-Executive Directors is operated in line with the terms set out in the Articles of Association. Cash fees, normally paid on a quarterly basis, are comprised of the following elements: • Base fee. • Additional fees. Beginning in 2021, a portion of the compensation to our Non-Executive Directors was in the form of our ordinary shares. Additional remuneration is payable for additional services to PureTech such as the Chairship of a Committee or membership on a Committee. Additional remuneration is also payable for services provided beyond those services traditionally provided as a director, and can be provided for a material increase in time commitment. Fees are reviewed annually and take into account: • the median level of fees for similar positions in the market; and • the time commitment each Non-Executive Director makes to us. Taxable benefits may be provided and may be grossed up where appropriate.	Any remuneration provided to a Non-Executive Director will be in line with the limits set out in the Articles of Association.	None.

Notes:

1 In the event that the Company elects any non-U.S. Executive Directors, the 401k Plan may not be an appropriate pension arrangement. In such cases an alternative pension arrangement may be offered. Any such arrangement would not be higher than the pension rate operated for the majority of employees in that jurisdiction.

2 For those below Board level, a lower annual bonus opportunity and PSP award size may apply. In general, these differences arise from the development of remuneration arrangements that are market competitive for the various categories of individuals, together with the fact that remuneration of the Executive Directors and senior executives typically has a greater emphasis on performance-related pay.

3 The choice of the performance metrics for the annual bonus scheme reflects the Committee's belief that incentive compensation should be appropriately challenging and linked to the delivery of the Company's strategy. Further information on the choice of performance measures and targets is set out in the Annual Report on Remuneration.

4 The performance conditions applicable to the PSP (see Annual Report on Remuneration) are selected by the Remuneration Committee on the basis that they reward the delivery of long-term returns to shareholders and are consistent with the Company's objective of delivering superior levels of long-term value to shareholders while providing the Company with tools to successfully recruit and retain employees in the U.S.

5 For the avoidance of doubt, the Company reserves the right to honour any commitments entered into in the past with current or former Directors (such as the vesting/exercise of share awards) notwithstanding that these may not be in line with this Remuneration Policy. Details of any payments to former Directors will be set out in the Annual Report on Remuneration as they arise.

Recovery and withholding provisions

Recovery and withholding provisions ("clawback and malus") may be operated at the discretion of the Remuneration Committee in respect of awards granted under the Performance Share Plan and in certain circumstances under the Annual Bonus Plan (including where there has been a material misstatement of accounts, or in the event of fraud, gross misconduct or conduct having a materially detrimental effect on the Company's reputation).

The issue giving rise to the recovery and withholding must be discovered within three years of vesting and there is flexibility to recover overpayments by withholding future incentive payments and recovering the amount directly from the employee.

Discretions in the policy

To ensure the efficient administration of the variable incentive plans outlined above, the Committee will apply certain operational discretions. These include the following:

- selecting the participants in the plans on an annual basis;
- determining the timing of grants of awards and/or payments;
- determining the quantum of awards and/or payments (within the limits set out in the Policy table above);
- reviewing performance against LTI performance metrics;
- determining the extent of vesting based on the assessment of performance;
- making the appropriate adjustments required in certain circumstances, for instance for changes in capital structure;
- deciding how to settle awards made under the plans, e.g. in cash, shares, nil-cost options or as otherwise permitted under the plan rules;
- overriding formulaic outcomes of incentive plans if determined by the Committee not to be reflective of company performance;

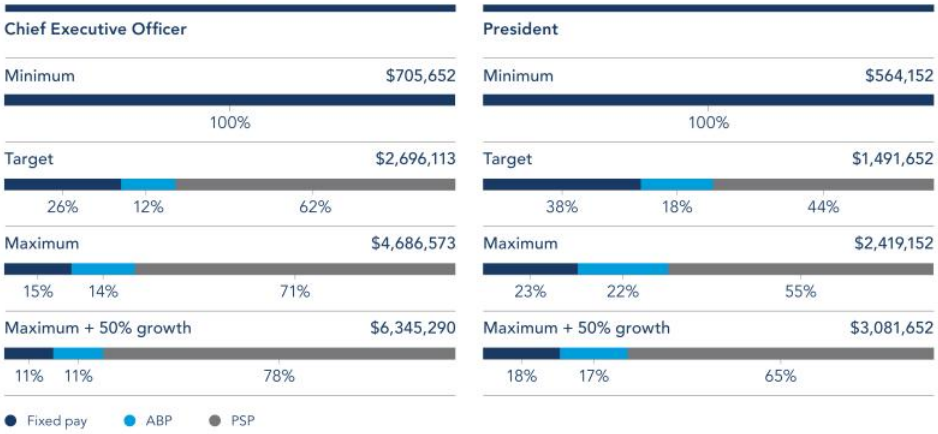
- determining "good leaver" status for incentive plan purposes and applying the appropriate treatment; further details on the discretion applicable in relation to leavers are set out on page 137;
- undertaking the annual review of weighting of performance measures and setting targets for the annual bonus plan and other incentive schemes, where applicable, from year to year; and
- discretion, in the event of a change in control of the Company, to determine that time pro-rating shall not apply to outstanding awards.

If an event occurs which results in the annual bonus plan or PSP performance conditions and/or targets being deemed no longer appropriate (e.g. material acquisition or divestment), the Committee will have the ability to adjust appropriately the measures and/or targets and alter weightings, provided that the revised conditions are not materially less challenging than the original conditions.

Reward scenarios

The charts below show how the composition of 2022 remuneration for the Chief Executive Officer and the President varies at different levels of performance under the Policy set out above, as a percentage of total remuneration opportunity and as a total value.

Executive Director compensation (unaudited)



Notes:

1 The minimum performance scenario comprises the fixed elements of remuneration only, including:
- Salary for FY2022 as set out in the Annual Report on Remuneration.
- Pension in line with policy and benefits as disclosed for FY2021 in the Annual Report on Remuneration.

2 The On-Target level of bonus is taken to be 50 percent of the maximum bonus opportunity (50 percent of salary), and the On-Target level of PSP vesting is assumed to be 50 percent of the face value of the PSP award (i.e. 250 percent of base salary for the CEO and 125 percent of base salary for the President). These values are included in addition to the components/values of Minimum remuneration.

3 Maximum assumes full bonus pay-out (100 percent of base salary only) and the full face value of the proposed PSP awards (i.e. 500 percent of base salary for the CEO and 250 percent of base salary for the President), in addition to fixed components of Minimum remuneration.

4 No share price growth has been factored into the calculations of minimum, target and maximum compensation. An additional maximum scenario has been shown which assumes 50% share price appreciation for the PSP during the performance period.

Approach to recruitment and promotions

The remuneration package for a new Executive Director would be set in accordance with the terms of the Company's prevailing approved Remuneration Policy at the time of appointment and take into account the skills and experience of the individual, the market rate for a candidate of that experience and the importance of securing the relevant individual.

Salary would be provided at such a level as required to attract the most appropriate candidate and may be set initially at or above mid-market level.

Additionally, salary may be provided at a below mid-market level on the basis that it may progress towards the mid-market level once expertise and performance has been proven and sustained. The annual bonus and long-term incentive awards would be limited in line with the policy. Depending on the timing of the appointment, the Committee may deem it appropriate to set annual bonus performance conditions for such appointee that are different than those applicable to the incumbent Executive Directors. A PSP award can be made shortly following an appointment.

In addition, the Committee may offer additional cash and/or share-based elements to replace deferred or incentive pay forfeited by an executive leaving a previous employer if required in order to facilitate, in exceptional circumstances, the recruitment of the relevant individual. It would seek to ensure, where possible, that these awards would be consistent with awards forfeited in terms of vesting periods, expected value, performance conditions and delivery mechanism.

For appointment of an Executive Director who was employed by the Company prior to the appointment, any variable pay element awarded in respect of the prior role may be allowed to pay out according to its terms. In addition, any other ongoing remuneration obligations existing prior to appointment may continue.

For any Executive Director appointment, the Committee may agree that the Company will meet certain relocation and/or incidental expenses as appropriate.

Service contracts

Executive Directors' service contracts do not provide for liquidated damages, longer periods of notice on a change of control of the Company or additional compensation on an Executive Director's cessation of employment with us, except as discussed below.

The Committee's Policy is to offer service contracts for Executive Directors with notice periods of no more than 12 months, and typically between 60 to 180 days.

Service contracts provide for severance pay following termination in the case that employment is terminated by the Company without 'cause', or by the employee for 'good reason'. In this case severance pay as set out in the contract is no greater than 12-months' base salary and is aligned to the duration of any restrictive covenants placed on the employee. Service contracts may also provide for the continuation of benefits but for no longer than a 12-month period post termination.

Service contracts also provide for the payment of international tax in non-U.S. jurisdictions if applicable to the Executive Director. They also can provide for garden leave and, if required by applicable law, the recovery and withholding of incentive payments.

Service contracts are available for inspection at the company's registered office.

Policy on termination of employment

The Policy on termination is that the Company does not make payments beyond its contractual obligations and the commitments entered into as part of any incentive plan operated by the Company. In addition, Executive Directors will be expected to mitigate their loss. The Committee ensures that there have been no unjustified payments for failure.

An Executive Director may be eligible for an annual bonus payment for the final year in which that Director served as an employee, provided that they are deemed to be a 'good leaver'. If so, any such annual bonus payment will be subject to performance testing and a pro-rata reduction will normally be applied based on the time served during the relevant financial year.

The default treatment for any share-based entitlements under the PSP is that any unvested outstanding awards lapse on cessation of employment. However, in certain prescribed circumstances, or at the discretion of the Remuneration Committee, 'good leaver' status can be applied. In these circumstances, a participant's awards will vest subject to the satisfaction of the relevant performance criteria and, ordinarily, on a time pro-rated basis, with the balance of the awards lapsing. The two-year post vest holding period will usually continue to apply. The Committee has discretion to permit the early vesting at the date of cessation of employment, again based on performance and ordinarily on a time pro-rated basis.

In addition, the Company can pay for any administrative expenses, legal expenses or outplacement services arising from the termination where considered appropriate.

External appointments

The Board can allow Executive Directors to accept appropriate outside commercial Non-Executive Director appointments provided that the duties and time commitment required are compatible with their duties and time commitment as Executive Directors.

Non-Executive Directors

Non-Executive Directors are appointed as a Non-Executive Director of the Company by a letter of appointment. These letters usually provide for a notice period of one month from the Company and the Non-Executive Director prior to termination.

Consideration of shareholder views

The Committee will carefully consider shareholder feedback received in relation to the AGM each year. This feedback, plus any additional feedback received during any meetings from time to time, is then considered as part of the annual review of the Remuneration Policy.

The Company will seek to engage directly with major shareholders and their representative bodies should any material changes be proposed to the Remuneration Policy or its implementation. Details of votes cast for and against the resolution to approve the prior year's remuneration report and any matters discussed with shareholders during the year will be set out in the Annual Report on Remuneration. The Company consulted with shareholders in 2021, as referenced on page 131, in relation to the proposed changes to the Remuneration Policy and we were pleased to receive support from those consulted.

Consideration of our employment conditions generally

To ensure a coherent cascade of the Remuneration Policy throughout the organization, no element of remuneration is operated solely for Executive Directors and all elements of remuneration provided to the Executive Directors are generally operated for other employees, including participation in stock-based incentive plans. In addition, the Committee considers the general base salary increase for the broader employee population when determining the annual salary increases for the Executive Directors. The Remuneration Committee has general responsibility for determining pay for senior management as well as Executive Directors. Employees (other than senior executives) have not been consulted in respect of the design of our Remuneration Policy, although the Committee will keep this under review.

Annual Report on Remuneration

Implementation of the Remuneration Policy for the year ending December 31, 2022

All tables within the Annual Report on Remuneration are audited under the International Standards on Auditing (UK) ("ISAs (UK)") unless otherwise noted.

Base salary
The Committee reviewed the base salary levels for the Executive Directors in early 2022 and an increase of 6 percent was awarded. This increase was in line with the increase for the general workforce, which was largely driven by cost of living considerations in the US.

		2021 Base salary	2022 Base salary
Daphne Zohar	Chief Executive Officer	$625,931	**$663,487**
Bharatt Chowrira	President, Chief Business, Legal and Operating Officer, Corporate Secretary ("President")	$500,000	**$530,000**

Pension
We will continue to contribute under the 401k Plan subject to the maximum set out in the Policy table.

Benefits
Benefits provided will continue to include private medical, disability and dental cover.

Annual bonus
For 2022, the operation of the annual bonus plan will be similar to that operated in 2021. The maximum annual bonus will continue to be 100 percent of base salary for all Executive Directors. The 2022 annual bonus will be based on clinical development milestones and internal program development, financial and strategic measures, and development of new strategic and investor relationships. The performance metrics and targets will be disclosed in the FY2022 Annual Report and Accounts.

Long-term incentives
Awards under the PSP will be made to the Executive Directors in 2022. The Chief Executive Officer will receive a PSP award with a face value of 500 percent of base salary, and the President will receive an award with a face value of 250 percent of base salary. These grant levels are lower than the maximum permitted under the Directors' Remuneration Policy, and lower than the grant levels in 2021. This takes into account the fall in the share price since the grant of the 2021 awards and the resulting impact on the number of shares underlying each award.

The PSP awards will be subject to the performance conditions described below. As a clinical-stage therapeutics company, the Company believes that TSR is an appropriate and objective measure of the Company's performance. In addition, measuring TSR on both an absolute and relative basis rewards our management team for absolute value creation for our shareholders whilst also incentivizing outperformance of the market. To provide a balance to the TSR performance conditions that is more directly based on Management's long term strategic performance, TSR is complemented by measures linked to strategic delivery. There will be a robust assessment of the achievement of the strategic targets over the three year period with full disclosure in the Directors' Remuneration Report following the end of the performance period.

Further detail of the performance conditions is set out below:

- 40 percent of the shares under award will vest based on the achievement of absolute TSR targets.
- 20 percent of the shares under award will vest based on the achievement of a relative TSR performance condition, 10 percent each against two benchmarks (explained below).
- 40 percent of the shares under award will vest based on the achievement of strategic targets.

The minimum performance target for the absolute TSR portion of the award will be TSR equal to 7 percent per annum, whilst the maximum target will be TSR equal to 15 percent per annum. Relative TSR will be measured against the constituent companies in the FTSE 250 Index (excluding Investment Trusts) and the MSCI Europe Health Care Index (for 10 percent of the award, respectively). The minimum performance target will be achievement of TSR equal to the median company in the Index and the maximum performance target will be achievement of upper quartile TSR performance. 25 percent of each element of the TSR targets will vest for threshold performance. Strategic measures will be based on the achievement of milestones and other qualitative measures of performance over the performance period. Strategic targets will be set at the outset based on financial achievements, including monetization of Founded Entities, clinical development progress, product pipeline growth, operational excellence and other shareholder value enhancing metrics in line with our strategic plan. Full disclosure of the measures, weightings and strategic targets will be made retrospectively.

The Committee believes that this combination of measures is appropriate. TSR measures the success of our management team in identifying and developing new therapeutics whilst strategic targets help incentivize our management team through the stages which ultimately result in successful therapeutics.

Non-Executive Directors

Fees for our Board of Directors were reviewed for 2022 and remain unchanged from 2021.

	FY2021 and FY2022
Chair fee	**$125,000**
Basic fee	**$75,000**
Equity-based Component	**$50,000**
Additional fees:	
Chair of a committee	**$10,000**
Membership of a committee	**$5,000**
Membership of a subsidiary board	**$0 to $10,000**

As our Board of Directors consists of leading experts with the experience of successfully developing technologies and bringing them to market, this gives rise to the possibility that the intellectual property we seek to acquire has been developed by one of our Non-Executive Directors and/or that our Non-Executive Directors provide technical or otherwise specialized advisory services to the Company above and beyond the services typically provided by a Non-Executive Director. In such exceptional circumstances, our Remuneration Policy provides us with the flexibility to remunerate them with equity in the relevant subsidiary company as we would any other inventor of the intellectual property or provider of technical advisory services. This practice is in line with other companies in the life sciences sector. If the Company is unable to offer market-competitive remuneration in these circumstances, it risks forfeiting opportunities to obtain intellectual property developed by our Non-Executive Directors and/or foregoing valuable advisory services. The Company believes foregoing such intellectual property and/or advisory services would not be in the long-term interest of our shareholders. Accordingly, subsidiary equity grants may be made to Non-Executive Directors upon the occurrence of the exceptional circumstances set out above.

Remuneration for the year ended December 31, 2021

Single total figure of remuneration for each Director (audited)

The table below sets out remuneration paid in relation to the 2021 financial year with a comparative figure for the 2020 financial year. There were no exercises of share options by Executive Directors or Non-Executive Directors in either of the 2021 or 2020 financial years.

	2021 and 2020 Remuneration									
	Year	Basic Salary/ Fees	Benefits[1]	Annual Bonus Plan	Performance Share Plan (Vested)[2]	Pension	Other payments[3]	Total Remuneration	Total Variable	Total Fixed
Executive Directors										
Daphne Zohar	**2021**	**$625,931**	**$33,465**	**$469,448**	**$2,693,882**	**$8,700**	**—**	**$3,831,426**	**$3,163,330**	**$668,096**
	2020	$607,700	$31,069	$607,700	$5,679,700[7]	$8,550	$260,122	$7,194,841	$6,287,400	$907,441
Bharatt Chowrira[4]	**2021**	**$500,000**	**$25,452**	**$375,000**	**$511,046**	**$8,700**	**—**	**$1,420,198**	**$886,046**	**$534,152**
Stephen Muniz[5]	**2021**	**$164,786**	**$11,396**	**—**	**—**	**$8,700**	**—**	**$184,882**	**—**	**$184,882**
	2020	$422,300	$28,919	$422,300	$1,901,101[7]	$8,550		$2,783,986	$2,323,401	$459,769
Non-Executive Directors										
Raju Kucherlapati	**2021**	**$145,000[8]**	**—**	**—**	**—**	**—**		**$145,000**		**$145,000**
	2020	$105,000	—	—	—	—		$105,000		$105,000
John LaMattina	**2021**	**$145,000[8]**	**—**	**—**	**—**	**—**		**$145,000**		**$145,000**
	2020	$125,000	—	—	—	—		$125,000		$125,000
Robert Langer	**2021**	**$145,000[8]**	**—**	**—**	**—**	**—**		**$145,000**		**$145,000**
	2020	$125,000	—	—	—	—		$125,000		$125,000
Kiran Mazumdar-Shaw[6]	**2021**	**$135,000[8]**	**—**	**—**	**—**	**—**		**$135,000**		**$135,000**
	2020	$21,250	—	—	—	—		$21,250		$21,250
Dame Marjorie Scardino	**2021**	**$140,000[8]**	**—**	**—**	**—**	**—**		**$140,000**		**$140,000**
	2020	$90,000	—	—	—	—		$90,000		$90,000
Christopher Viehbacher	**2021**	**$195,000[8]**	**—**	**—**	**—**	**—**		**$195,000**		**$195,000**
	2020	$155,000	—	—	—	—		$155,000		$155,000
TOTAL	**2021**	**$2,195,717**	**$70,313**	**$844,448**	**$3,204,928**	**$26,100**	**—**	**$6,341,506**	**$4,049,376**	**$2,292,130**
TOTAL	2020	$1,651,250	$59,988	$1,030,000	$7,580,801	$17,100	$260,122	$10,600,077	$8,610,801	$1,988,460

Notes:

1 Benefits comprise the following elements: private medical, disability and dental cover and parking.

2 The shares underlying the vested 2019 Performance Share Plan awards will be issued after the finalisation of this report. As a result, the share price on the date of issuance is not known at the date of this report and the figures shown above for the PSP awards have been valued using a share price of £3.236875, which was the average share price during the last three months of 2021, and an exchange rate of GBP 1 : USD 1.34809697, which was the average exchange rate over the last three months of 2021.

3 Other payments represent a one-time reimbursement to Ms. Zohar for costs associated with converting certain of her ordinary shares into ADSs, as required by Nasdaq prior to our listing on Nasdaq in November 2020.

4 Dr. Chowrira joined the Board in February 2021.

5 Mr. Muniz retired from the Board in May 2021.

6 Ms. Mazumdar-Shaw joined the Board in September 2020.

7 These amounts have been updated from those listed in the 2020 Annual Report and Accounts to reflect the actual values paid, which was not known at the date of publication of the 2020 Annual Report and Accounts.

8 These amounts include grants of share based remuneration on July 21, 2021 in the form 11,190 time-vesting restricted stock units with a face value of $50,000.

Annual bonus outcome for 2021

For the 2021 annual bonus, targets were set for a balanced scorecard at the beginning of the year. The 2021 targets were focused on (i) internal program development goals designed to incentivize the team to continue development of the Company's Wholly Owned Pipeline, generate valuable clinical data in support of the Company's programs and create innovative programs, (ii) strategic goals designed to incentivize the team to complete important deals and execute strategic partnerships, (iii) monetization and investor related goals designed to incentivize the team to generate non-dilutive cash and achieve enhanced analyst coverage of the Company's stock to support shareholder value generation, and (iv) Controlled Founded Entity program development goals designed to incentivize the team to take steps necessary to progress towards the potential commercial launch of therapeutics at our Founded Entities. In addition, the Remuneration Committee took into account other goals and other achievements by the management team in setting final achievement attainment and fixing bonus payouts. The table below sets out the performance assessment and associated bonus outcomes:

Target Goals – Maximum 100 percent Achievement

Performance Measures Category	Achievement	Percentage of Target Attained
Internal Program Development	The Internal Program Development Goals were 80% achieved in 2021. The management team's performance resulted in an achievement outcome of 40 percent out of a pre-specified cap of 50 percent for this category of the goals. A description of performance in 2021 is set out below: The Company's LYT 100 Long COVID study was fully enrolled, multiple clinical studies to demonstrate improved tolerability as compared to pirfenidone were completed, early-stage data was generated for LYT 200, the first human dose of LYT 300 was administered, proof of concept was achieved in rodents for the Orasome platform, and additional early-stage work was completed on certain other programs.	40%
Strategic Goals	The Strategic Goals were achieved in 2021. The management team's performance resulted in an achievement outcome of 20 percent which was equal to the pre-specified cap of 20 percent for this category of the goals. A description of performance in 2021 is set out below: The Company completed the acquisition of Alivio Therapeutics that added LYT 500 to the Company's Wholly Owned Pipeline, Gelesis announced that It would go public via a SPAC transaction (which closed In the January post-period), Akili progressed towards going public via a SPAC transaction (which was announced In the January post-period), Vedanta secured over $68 million in financing, and Karuna secured a partnership with Zai Lab with $35 million in upfront licensing fees and future potential milestone payments.	20%
Monetization and Investor Related Goals	The Monetization and Investor Related Goals were achieved in 2021. The management team's performance resulted in an achievement outcome of 20 percent which was equal to the pre-specified cap of 20 percent for this category of the goals. A description of performance in 2021 is set out below: The Company had $218 million of cash income in 2021 from the sale of equity holdings, and added a new analyst from a major investment bank.	20%
Controlled Founded Entity Program Development	The Controlled Entity Program Development Goals were achieved in 2021. The management team's performance resulted in an achievement outcome of 10 percent which was equal to the cap of 10 percent for this category of the goals. A description of performance in 2021 is set out below: Vedanta's phase 1 and 2 studies were completed with the phase 2 study for VE303 achieving its primary endpoint.	40%
Other Achievements	The management team evidenced further exceptional performance as described below: The Company recruited a seasoned chief medical officer and built a world-class development organization, operated within the pre-set budget, managed operations during the COVID-19 pandemic to execute all programs in accordance with the operating plan and achieved all core objectives, observed strict COVID-related protocols to minimize employee exposure and achieved a 100% vaccination rate among its employees, and managed the transition associated with two long-tenured senior executives with minimal disruption to the business.	10%
Pre-Specified Maximum Total		**100%**

Accordingly, determined that the Company had achieved 100 percent of its target goals for 2021.

Each of the above target categories are subject to maximum percentage achievement limits capped at 100 percent of the target bonus (i.e. 50 percent of salary). Payments beyond the target are determined by the Remuneration Committee taking into account the extent target goals have been exceeded, the overall quality of underlying performance, value created for shareholders and other relevant factors. In this case, the Company performed above the target maximum goals, including with respect to the other achievements described above related to operational performance and contribution to overall growth of the business during the year. The Committee also considered the additional responsibilities taken on by the Executive Directors during the year following the departure of certain senior executives and the need to ensure an appropriate level of continuity. In light of these achievements, the Committee determined that payouts at 150 percent of target (i.e. 75 percent of salary) are appropriate for the Executive Directors as explained earlier in this report. The Committee believes that such a bonus award is appropriate to reward and retain top management when such extraordinary performance is achieved.

Long-term incentive awards vesting in respect of the year (unaudited)

The 2019 PSP awards granted on December 20, 2019 were subject to three-year performance conditions covering the period from January 1, 2019 to December 31, 2021. Following an assessment of the performance conditions, the Remuneration Committee determined that the awards will vest at 95.8 percent of the maximum. Stephen Muniz's shares lapsed following his retirement in May 2021.

	Scheme	Basis of award granted	Shares awarded	Shares vested	Shares lapsed	Value of vested awards[1,2]
Daphne Zohar	PSP 2019	400% of salary	644,668	617,350	27,318	$2,693,882
Bharatt Chowrira	PSP 2019	100% of salary	122,924	117,715	5,209	$511,046

1 Shares have been valued using a share price of £3.236875, which was the average share price during the last three months of 2021, and an exchange rate of GBP 1 : USD 1.34809697, which was the average exchange rate over the last three months of 2021.
2 The value of the awards attributable to share price appreciation is $433,887 for Daphne Zohar and $80,115 for Bharatt Chowrira.

The outcome of the performance condition relating to these awards is set out below (unaudited):

Measure and weighting	Threshold	Maximum	Achievement	Vesting (% of each element)
Absolute TSR (50%)	7% p.a.	15% p.a.	23.8% p.a.	100%
Total return against FTSE Small Cap Index (12.5%)	At or above median	Upper quartile	83rd percentile	100%
Total return against MSCI Euro Healthcare Index (12.5%)	At or above median	Upper quartile	63rd percentile	66.4%
Strategic measures (25%)	See description below			100%

The strategic measures over the three-year period were focused on (i) financial goals (59 percent), (ii) clinical development goals (34 percent), and (iii) operational excellence (7 percent). The financial achievements resulting in satisfaction of 59 percent of the vesting of the strategic measures included obtaining $563 million for PureTech by monetizing certain Founded Entity equity, the closing of initial public offerings of two Founded Entities and the announcement of two SPAC transactions for Founded Entities, the execution of several partnership agreements which brought in non-dilutive funding, the raising of more than $1.58 billion into the Company's Founded Entities and the completion of PureTech's listing on the Nasdaq Global Market. The clinical development achievements resulting in satisfaction of 34 percent of the vesting of the strategic measures included the successful completion of several Phase 1 clinical studies for LYT-100 and the completion of enrollment In LYT-100 Long COVID phase 2 study, the advancement of other programs within our Wholly Owned Pipeline, the successful completion of Phase 2 clinical studies for the KarXT program, the completion of a Phase 2 clinical study for the VE303 program and the completion of Phase 1 clinical studies for the VE202 and VE416 programs, and successfully having two programs cleared for marketing by the U.S. Food and Drug Administration. The operational excellence achievements resulting in satisfaction of 7 percent of the vesting of the strategic measures include the operation of the Company's programs within projected timelines and budgets, successfully managing operations through the COVID-19 pandemic, building out a world-class development organization, the in-licensing and creation of new programs, the issuance of certain intellectual property, the advancement of certain pre-clinical programs, and the publication of validating data in top tier peer-reviewed academic journals.

Long-term incentive awards granted during the year (audited)

The following long-term Incentive awards were granted to Executive Directors during 2021:

	Scheme	Basis of award granted	Shares awarded (as conditional award of shares)	Share price at date of grant[1]	Face value of award	% of face value vesting at threshold performance	Vesting determined by performance over
Daphne Zohar	PSP 2021	600% of salary	683,652	282.33 pence	$2,430,800	20%	Three financial years to December 31, 2023
Bharatt Chowrira	PSP 2021	300% of salary	335,687	326.83 pence	$1,500,000	20%	

1 The share price at the date of grant is based on the 3-day average closing price immediately prior to the grant of the award.

The PSP awards granted in 2021 are subject to (i) achievement of absolute TSR targets (40 percent of the awards), (ii) achievement of TSR targets as compared to TSR performance of the constituent companies in the FTSE 250 Index (excluding Investment Trusts) and the MSCI Europe Health Care Index (20 percent of the awards, 10 percent against each benchmark) and (iii) achievement of targets based on strategic measures (40 percent of the awards), measured over the three year period to December 31, 2023.

The minimum performance target for the absolute TSR portion of the award is TSR equal to 7 percent per annum, whilst the maximum target is TSR equal to 15 percent per annum. The minimum performance target for the relative TSR portion of the award is TSR equal to the median of the index, whilst the maximum target will be TSR equal to the upper quartile of the index. Strategic measures are based on the achievement of project milestones and other qualitative measures of performance. Strategic targets have been set based on financial achievements, including monetization of Founded Entities, clinical development progress, product pipeline growth, operational excellence and other shareholder value enhancing metrics in line with our strategic plan. The Committee believes that this combination of measures and the equal weighting on TSR and strategic objectives is appropriate. TSR measures the success of our management team in identifying and developing new therapeutics whilst strategic targets help incentivize our management team through the stages which ultimately result in successful therapeutics.

Full disclosure of the strategic targets will be made retrospectively.

In addition, each Non-Executive Director was granted share based remuneration on July 21, 2021 in the form of 11,190 time-vesting restricted stock units. The equity awards granted to our Non-Executive Directors vest in their entirety immediately prior to Company's 2022 AGM, provided that the Non-Executive Directors continue their service through such date. This share based element is part of the annual fee for Non-Executive Directors and is not subject to performance (unaudited).

Non-Executive Directors	Shares awarded	Face value of award[1]	Vesting date
Raju Kucherlapati	11,190	$50,000	June 15, 2022
John LaMattina	11,190	$50,000	June 15, 2022
Robert Langer	11,190	$50,000	June 15, 2022
Kiran Mazumdar-Shaw	11,190	$50,000	June 15, 2022
Dame Marjorie Scardino	11,190	$50,000	June 15, 2022
Christopher Viehbacher	11,190	$50,000	June 15, 2022

Payments for Loss of Office (unaudited)

There were no payments for Loss of Office during 2021.

On March 18, 2021 the Company announced that Stephen Muniz would retire from the company and step down from the board on May 17, 2021. He continued to be paid base salary, benefits and pension until May 17, 2021, at which point payments ceased. There was no compensation payable for loss of office, no eligibility for 2021 bonus and all unvested PSP awards lapsed. Vested PSP awards remain subject to any applicable holding period and the post-employment shareholding policy applies, requiring a shareholding worth 200 percent of Mr. Muniz's final base salary level to be retained for two years.

Payments to past Directors (unaudited)

No payments to past Directors were made during 2021.

Directors' shareholdings (audited)

Executive Directors are required to maintain share ownership equal to a minimum of 400 percent of base salary for the Chief Executive Officer (subject to approval of the new policy) and a minimum of 200 percent of base salary for the other Executive Directors. The Chief Executive Officer and President both satisfy this requirement, and neither has disposed of any company shares since the Company's IPO. Post-employment shareholding requirements will apply.

The table below sets out current Directors' shareholdings which are beneficially owned or subject to a performance condition and interests of connected persons.

	Director Shareholdings					
	Total Share Awards not subject to Service Conditions		Share awards subject to performance conditions		Total	
Director	Dec 31, 2021	Dec 31, 2020	Dec 31, 2021	Dec 31, 2020	Dec 31, 2021	Dec 31, 2020
Daphne Zohar[1]	**12,197,307**[2]	12,197,307	**1,524,120**[3]	1,328,320[4]	**13,721,427**	13,525,627
Bharatt Chowrira[5]	**2,213,689**[6]	—	**1,158,902**[7]	—	**3,372,591**	—
Stephen Muniz[8]	**3,096,590**[8]	2,889,499	**—**	461,535	**3,096,590**[8]	3,351,034
Raju Kucherlapati	**2,459,831**	2,459,831	**11,190**[9]	—	**2,471,021**	2,459,831
John LaMattina[10]	**1,513,133**	1,495,332	**11,190**[9]	—	**1,524,323**	1,513,133
Robert Langer[11]	**2,944,134**	2,944,134	**11,190**[9]	—	**2,955,324**	2,944,134
Kiran Mazumdar-Shaw	**—**	—	**11,190**[9]	—	**11,190**	—
Dame Marjorie Scardino	**798,710**[12]	788,710	**11,190**[9]	—	**809,900**	788,710
Chris Viehbacher	**1,045,646**[13]	1,045,646	**11,190**[9]	—	**1,056,836**	1,045,646

1 A portion of Ms. Zohar's shareholding in the Company is indirect. As of December 31, 2020, an aggregate of 8,097,307 ordinary shares and 410,000 ADSs are held by (i) the Zohar Family Trust I, a U.S.-established trust of which Ms. Zohar is a beneficiary and trustee, (ii) the Zohar Family Trust II, a U.S.-established trust of which Ms Zohar is a beneficiary (in the event of her spouse's death) and trustee, (iii) Zohar LLC, a U.S.-established limited liability company, and (iv) directly by Ms. Zohar. Ms. Zohar owns or has a beneficial interest in 100 percent of the share capital of Zohar LLC.

2 ncludes 410,000 ADSs, which are convertible into 4,100,000 ordinary shares. Does not include 617, 350 shares which are issuable pursuant to the RSU award granted to Ms. Zohar covering the financial years 2019, 2020 and 2021 which have vested but not yet been issued.

3 Includes the following RSUs, which are subject to performance conditions: 683,652 (2020) and 840,468 (2021). Does not include 617, 350 shares which are issuable pursuant to the RSU award granted to Ms. Zohar covering the financial years 2019, 2020 and 2021 which have vested but not yet been issued.

4 Includes the following RSUs, which are subject to performance conditions: 644,668 (2019) and 683, 652 (2020).

5 Dr. Chowrira joined the board as an executive director in 2021.

6 Includes 826,189 shares of stock owned by Dr. Chowrira and 1,387,500 vested stock options, none of which have been exercised. Does not include 117,715 shares which are issuable pursuant to the RSU award granted to Dr. Chowrira covering the financial years 2019, 2020 and 2021 which have vested but not yet been issued.

7 Includes the following RSUs, which are subject to performance conditions: 260,715 (2020) and 335, 687 (2021), as well as 562,500 unvested stock options. Does not include 117,715 shares which are issuable pursuant to the RSU award granted to Dr. Chowrira covering the financial years 2019, 2020 and 2021 which have vested but not yet been issued.

8 Mr. Muniz retired on May 17, 2021. The values set forth for Mr. Muniz with reference to 2021 reflect Mr. Muniz's stock ownership immediately following his retirement, at which point Mr. Muniz forfeited any share based awards which had not yet vested.

9 Includes RSUs, which are subject to performance conditions, that were granted in July 2021 and vest immediately prior to the 2022 Annual General Meeting.

10 A portion of Dr. LaMattina's shareholding in the Company is indirect. As of December 31, 2021, an aggregate of 1,513,133 ordinary shares are held by (i) John L LaMattina Revocable Trust, (ii) John L LaMattina 2020-2 GRAT, and (iii) LaMattina Charitable Trust.

11 A portion of Dr. Langer's shareholding in the Company is indirect. As of December 31, 2021, an aggregate of 2,944,134 ordinary shares are held by (i) Langer Family 2020 Trust and (ii) directly by Dr. Langer.

12 Includes 100 ADSs, which are convertible into 1,000 ordinary shares.

13 Includes 2,000 ADSs, which are convertible into 20,000 ordinary shares.

Directors' service contracts (unaudited)

Detail of the service contracts of current Directors is set out below:

Executive Directors	Notice period	Contract date	Maximum potential termination payment	Potential payment on change of control/liquidation
Daphne Zohar	180 days	June 18, 2015	12 months' salary	Nil
Bharatt Chowrira	60 days	March 1, 2017	12 months' salary	Nil

Contracts for the above Executive Directors will continue until terminated by notice either by the Company or the Executive Director. Mr. Muniz terminated his service contract and his notice period ended on May 17, 2021.

Non-Executive Directors	Notice period	Contract date	Contract expiration date
Sharon Barber-Lui	30 days	March 24, 2022	March 24, 2025
Raju Kucherlapati	30 days	June 5, 2021	June 5, 2024
John LaMattina	30 days	June 5, 2021	June 5, 2024
Robert Langer	30 days	June 5, 2021	June 5, 2024
Kiran Mazumdar-Shaw	30 days	September 28, 2020	September 28, 2023
Marjorie Scardino	30 days	June 5, 2021	June 5, 2024
Christopher Viehbacher	30 days	June 5, 2021	June 5, 2024

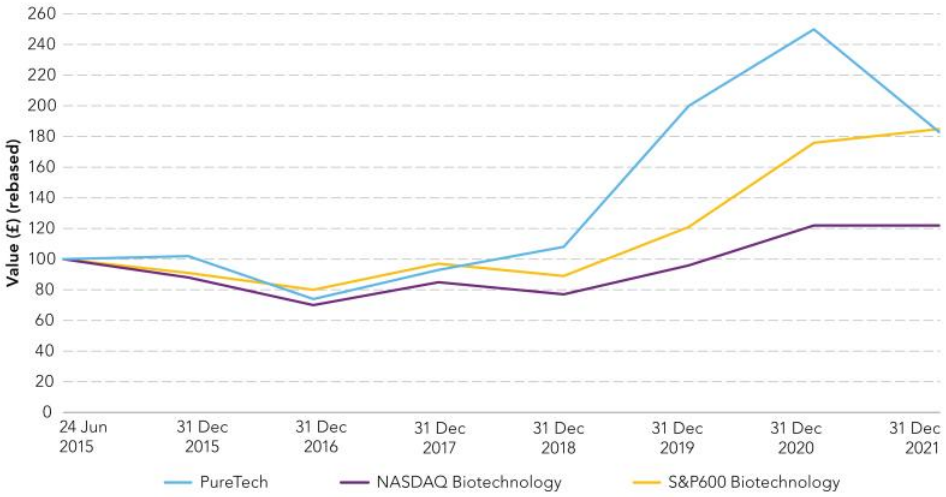
The Company and the Non-Executive Directors listed above intend to enter into new contracts prior to their expiration.

TSR performance graph (unaudited)

The graph shows the Company's performance, measured by total shareholder return (TSR), compared with the Nasdaq Biotechnology Index and S&P600 Biotechnology Index since the Company's IPO. The Committee considers these to be relevant indices for TSR comparison as they are broad-based measures of the performance of the biotechnology industry.

Total shareholder return (unaudited)

Source: Datastream (Thomson Reuters)



This graph shows the value, by December 31, 2021, of £100 invested in PureTech on the date of Admission (June 24, 2015), compared with the value of £100 invested in the Nasdaq Biotechnology and S&P600 Biotechnology indices on the same date.

The other points plotted are the values at intervening financial year-ends.

Chief Executive Officer's Remuneration History (unaudited)

Year	Incumbent	Role	Single figure of total remuneration	Annual bonus pay-out against maximum	PSP Vesting against maximum opportunity
2015	Daphne Zohar	Chief Executive Officer	$955,599	100%	n/a
2016	Daphne Zohar	Chief Executive Officer	$747,634	38.75%	n/a
2017	Daphne Zohar	Chief Executive Officer	$821,898	50%	n/a
2018	Daphne Zohar	Chief Executive Officer	$2,139,870	65%	50%
2019	Daphne Zohar	Chief Executive Officer	$5,783,682	100%	100%
2020	Daphne Zohar	Chief Executive Officer	$7,194,841	100%	100%
2021	**Daphne Zohar**	**Chief Executive Officer**	**$3,831,426**	**75%**	**95.8%**

Percentage change in remuneration of Directors and employees (unaudited)

The table below shows the change in the Directors' remuneration from 2020 to 2021 and 2019 to 2020 compared to the change in remuneration of all of our full-time employees who were employed throughout the same periods:

	2020 to 2021			2019 to 2020		
	Base salary[1]	Benefits	Annual bonus	Base Salary	Benefits	Annual Bonus
Daphne Zohar (CEO)	3%	6%	(23%)	3%	0%	3%
Bharatt Chowrira (President)[2]	N/A	N/A	N/A	N/A	N/A	N/A
Raju Kucherlapati	38.1%	N/A	N/A	11%	N/A	N/A
John LaMattina	16%	N/A	N/A	19%	N/A	N/A
Robert Langer	16%	N/A	N/A	13%	N/A	N/A
Kiran Mazumdar-Shaw[3]	635%	N/A	N/A	N/A	N/A	N/A
Marjorie Scardino	55%	N/A	N/A	0%	N/A	N/A
Christopher Viehbacher	26%	N/A	N/A	45%	N/A	N/A
Employees[4]	9%	7%	1%	8%	16%	14%

1 Base salary amounts for Non-Executive Directors in 2021 include grants of share based remuneration on July 21, 2021 in the form 11,190 time-vesting restricted stock units with a face value of $50,000.
2 Joined the Board effective February 2021.
3 Joined the Board effective September 2020. As a result, the increase in base salary reflects a full year of service in 2021 as opposed to Ms. Mazumdar-Shaw's more limited tenure in 2020.
4 Does not include employees of Founded Entities.

Relative importance of spend on pay (unaudited)

The following table sets out the percentage change in overall spend on pay and distributions to shareholders in 2021 compared to 2020:

	2021	2020	% change
Staff costs[1]	**$22,136,823**	$18,225,744	21%
Distributions to Shareholders	**—**	—	—

1 Excludes Founded Entities.

Details of the Remuneration Committee, advisors to the Committee and their fees

The Remuneration Committee consists of Dr. LaMattina, Ms. Mazumdar-Shaw and Dr. Kucherlapati, with Dr. LaMattina serving as the Chair of the Committee. In 2021 the Committee received independent remuneration advice from Aon plc. This independent advisor was appointed by and was accountable to the Committee and provided no other services to the Company. The terms of engagement between the Committee and Aon are available from the Company Secretary on request. The Remuneration Committee also received advice from Korn Ferry (UK) Limited, who was appointed by and is accountable to the Committee but also provides certain other candidate placement services to the Company. The terms of engagement between the Committee and Korn Ferry are available from the Company Secretary on request. The Committee also consults with the Chief Executive Officer and President, and historically consulted with Mr. Muniz when he was an Executive Director and our Chief Operating Officer. However, no Director is permitted to participate in discussions or decisions about their personal remuneration. During the year, fees in respect of remuneration advice from Aon amounted to $28,490 and from Korn Ferry £32,665. Each of Aon and Korn Ferry is a founder member of the Remuneration Consultants' Group and complies with its Code of Conduct which sets out guidelines to ensure that its advice is independent and free of undue influence.

Statement of voting at general meeting (unaudited)

The table below sets out the proxy results of the vote on our Remuneration Report at our 2021 AGM:

Resolutions	For	%	Against	%	Withheld	Total votes cast
To approve the Directors' Remuneration Report	200,319,991	89.74%	22,895,826	10.26%	2,309,748	223,215,817

The table below sets out the proxy results of the vote on our Remuneration Policy at our 2020 AGM:

Resolutions	For	%	Against	%	Withheld	Total votes cast
To approve the Directors' Remuneration Policy	187,285,809	83.90%	35,930,008	16.10%	2,309,748	223,215,817

2022 AGM

The Company's AGM will be held at 11:00 am EDT (4:00 pm BST) on June 15, 2022 at the Company's headquarters at 6 Tide Street, Boston, Massachusetts. Information regarding the voting outcome will be disclosed in next year's Annual Report on Remuneration.

This report has been prepared by the Remuneration Committee and has been approved by the Board. It complies with the CA 2006 and related regulations. This report will be put to shareholders for approval at the forthcoming AGM.

On behalf of the Board of Directors

Bharatt Chowrira
Company Secretary

April 25, 2022

[Pages 147-155 have been removed]

Consolidated Statements of Comprehensive Income/(Loss)

For the years ended December 31

	Note	2021 $000s	2020 $000s	2019 $000s
Contract revenue	3	**9,979**	8,341	8,688
Grant revenue	3	**7,409**	3,427	1,119
Total revenue		**17,388**	11,768	9,807
Operating expenses:				
General and administrative expenses	7	**(57,199)**	(49,440)	(59,358)
Research and development expenses	7	**(110,471)**	(81,859)	(85,848)
Operating income/(loss)		**(150,282)**	(119,531)	(135,399)
Other income/(expense):				
Gain on deconsolidation	5	**—**	—	264,409
Gain/(loss) on investments held at fair value	5	**179,316**	232,674	(37,863)
Loss realized on sale of investments	5	**(20,925)**	(54,976)	—
Gain on loss of significant influence	6	**—**	—	445,582
Other income/(expense)	6, 21	**1,592**	1,035	39
Other income/(expense)		**159,983**	178,732	672,167
Finance income/(costs):				
Finance income	9	**214**	1,183	4,362
Finance costs – contractual	9	**(4,771)**	(2,946)	(2,576)
Finance income/(costs) – fair value accounting	9	**9,606**	(4,351)	(46,475)
Finance income/(costs) – subsidiary preferred shares	9	**—**	—	(1,458)
Net finance income/(costs)		**5,050**	(6,115)	(46,147)
Share of net income/(loss) of associates accounted for using the equity method	6	**(73,703)**	(34,117)	30,791
Impairment of investment in associate	6	**—**	—	(42,938)
Income/(loss) before taxes		**(58,953)**	18,969	478,474
Taxation	25	**(3,756)**	(14,401)	(112,409)
Income/(Loss) for the year		**(62,709)**	4,568	366,065
Other comprehensive income/(loss):				
Items that are or may be reclassified as profit or loss				
Foreign currency translation differences		**—**	469	(10)
Total other comprehensive income/(loss)		**—**	469	(10)
Total comprehensive income/(loss) for the year		**(62,709)**	5,037	366,055
Income/(loss) attributable to:				
Owners of the Company		**(60,558)**	5,985	421,144
Non-controlling interests	18	**(2,151)**	(1,417)	(55,079)
		(62,709)	4,568	366,065
Comprehensive income/(loss) attributable to:				
Owners of the Company		**(60,558)**	6,454	421,134
Non-controlling interests	18	**(2,151)**	(1,417)	(55,079)
		(62,709)	5,037	366,055
		$	$	$
Earnings/(loss) per share:				
Basic earnings/(loss) per share	10	**(0.21)**	0.02	1.49
Diluted earnings/(loss) per share	10	**(0.21)**	0.02	1.44

The accompanying notes are an integral part of these financial statements.

Consolidated Statements of Financial Position

As of December 31,

	Note	2021 $000s	2020 $000s
Assets			
Non-current assets			
Property and equipment, net	11	**26,771**	22,777
Right of use asset, net	21	**17,166**	20,098
Intangible assets, net	12	**987**	899
Investments held at fair value	5, 16	**397,179**	530,161
Investments in associates	6	**—**	—
Lease receivable – long-term	21	**1,285**	1,700
Other non-current assets		**810**	11
Total non-current assets		**444,197**	575,645
Current assets			
Trade and other receivables	22	**3,174**	2,558
Income tax receivable	25	**4,514**	—
Prepaid expenses		**10,755**	5,405
Lease receivable – short-term	21	**415**	381
Other financial assets	13, 22	**2,124**	2,124
Short-term note from associate	16	**15,120**	—
Cash and cash equivalents	22	**465,708**	403,881
Total current assets		**501,809**	414,348
Total assets		**946,006**	989,994
Equity and liabilities			
Equity			
Share capital	14	**5,444**	5,417
Share premium	14	**289,303**	288,978
Merger reserve	14	**138,506**	138,506
Translation reserve	14	**469**	469
Other reserve	14	**(40,077)**	(24,050)
Retained earnings/(accumulated deficit)	14	**199,871**	260,429
Equity attributable to the owners of the Company		**593,515**	669,748
Non-controlling interests	14, 18	**(9,368)**	(16,209)
Total equity		**584,147**	653,539
Non-current liabilities			
Deferred tax liability	25	**89,765**	108,626
Lease liability, non-current	21	**29,040**	32,088
Long-term loan	20	**14,261**	14,818
Liability for share based awards	8	**2,659**	—
Total non-current liabilities		**135,725**	155,531
Current liabilities			
Deferred revenue	3	**65**	1,472
Lease liability, current	21	**3,950**	3,261
Trade and other payables	19	**35,817**	21,826
Subsidiary:			
Notes payable	16, 17	**3,916**	26,455
Warrant liability	16	**6,787**	8,206
Preferred shares	15, 16	**174,017**	118,972
Current portion of long-term loan	20	**857**	—
Other current liabilities		**726**	732
Total current liabilities		**226,135**	180,924
Total liabilities		**361,859**	336,455
Total equity and liabilities		**946,006**	989,994

Please refer to the accompanying Notes to the consolidated financial information. Registered number: 09582467.
The Consolidated Financial Statements were approved by the Board of Directors and authorized for issuance on April 25, 2022 and signed on its behalf by:

Daphne Zohar
Chief Executive Officer
April 25, 2022

The accompanying notes are an integral part of these financial statements.

Consolidated Statements of Changes in Equity

For the years ended December 31

	Share Capital									
	Shares	Amount $000s	Share premium $000s	Merger reserve $000s	Translation reserve $000s	Other reserve $000s	Retained earnings/ (accumulated deficit) $000s	Total Parent equity $000s	Non-controlling interests $000s	Total Equity $000s
Balance January 1, 2019	282,493,867	5,375	278,385	138,506	10	20,923	(166,693)	276,506	(108,535)	167,971
Net income/(loss)	—	—	—	—	—	—	421,144	421,144	(55,079)	366,065
Foreign currency exchange	—	—	—	—	(10)	—	—	(10)	—	(10)
Total comprehensive income/(loss) for the year	**—**	**—**	**—**	**—**	**(10)**	**—**	**421,144**	**421,134**	**(55,079)**	**366,055**
Deconsolidation of subsidiary	—	—	—	—	—	—	—	—	97,178	97,178
Subsidiary note conversion and changes in NCI ownership interest	—	—	—	—	—	(20,631)	—	(20,631)	23,049	2,418
Exercise of share-based awards	237,090	5	499	—	—	—	—	504	—	504
Purchase of subsidiary's non-controlling interest through issuance of shares	2,126,338	28	9,078	—	—	(33,145)	—	(24,039)	24,039	—
Revaluation of deferred tax assets related to share-based awards	—	—	—	—	—	3,061	—	3,061	—	3,061
Equity settled share-based payments	—	—	—	—	—	12,785	—	12,785	1,683	14,468
Vesting of restricted stock units (RSU)	513,324	—	—	—	—	(1,280)	—	(1,280)	—	(1,280)
Other	—	—	—	—	—	5	(7)	(2)	25	23
Balance December 31, 2019	**285,370,619**	**5,408**	**287,962**	**138,506**	**—**	**(18,282)**	**254,444**	**668,037**	**(17,639)**	**650,398**
Net income/(loss)	—	—	—	—	—	—	5,985	5,985	(1,417)	4,568
Foreign currency exchange	—	—	—	—	469	—	—	469	—	469
Total comprehensive income/(loss) for the year	**—**	**—**	**—**	**—**	**469**	**—**	**5,985**	**6,454**	**(1,417)**	**5,037**
Exercise of share-based awards	514,406	9	1,016	—	—	—	—	1,025	11	1,036
Revaluation of deferred tax assets related to share-based awards	—	—	—	—	—	(684)	—	(684)	—	(684)
Equity settled share-based awards	—	—	—	—	—	7,805	—	7,805	2,822	10,627
Settlement of restricted stock units	—	—	—	—	—	(12,888)	—	(12,888)	—	(12,888)
Other	—	—	—	—	—	—	—	—	13	13
As at December 31, 2020	**285,885,025**	**5,417**	**288,978**	**138,506**	**469**	**(24,050)**	**260,429**	**669,748**	**(16,209)**	**653,539**
Net income/(loss)	—	—	—	—	—	—	(60,558)	(60,558)	(2,151)	(62,709)
Foreign currency exchange	—	—	—	—	—	—	—	—	—	—
Total comprehensive income/(loss) for the year	**—**	**—**	**—**	**—**	**—**	**—**	**(60,558)**	**(60,558)**	**(2,151)**	**(62,709)**
Exercise of share-based awards	1,911,560	27	326	—	—	—	—	352	—	352
Revaluation of deferred tax assets related to share-based awards	—	—	—	—	—	615	—	615	—	615
Equity settled share-based awards	—	—	—	—	—	7,109	—	7,109	6,252	13,361
Settlement of restricted stock units	—	—	—	—	—	(10,749)	—	(10,749)	—	(10,749)
Reclassification of equity settled awards to liability awards	—	—	—	—	—	(6,773)	—	(6,773)	—	(6,773)
Vesting of share-based awards and net share exercise	—	—	—	—	—	(2,582)	—	(2,582)	—	(2,582)
Acquisition of subsidiary non-controlling interest	—	—	—	—	—	(9,636)	—	(9,636)	8,668	(968)
NCI exercise of share-based awards in subsidiaries	—	—	—	—	—	5,988	—	5,988	(5,922)	66
Distributions	—	—	—	—	—	—	—	—	(6)	(6)
Balance December 31, 2021	**287,796,585**	**5,444**	**289,303**	**138,506**	**469**	**(40,077)**	**199,871**	**593,515**	**(9,368)**	**584,147**

The accompanying notes are an integral part of these financial statements.

Consolidated Statements of Cash Flows

For the years ended December 31

	Note	2021 $000s	2020 $000s	2019 $000s
Cash flows from operating activities				
Income/(loss)		**(62,709)**	4,568	366,065
Adjustments to reconcile net operating loss to net cash used in operating activities:				
Non-cash items:				
Depreciation and amortization	11, 12	**7,287**	6,645	6,665
Impairment of investment in associate	6	**—**	—	42,938
Equity settled share-based payment expense	8	**13,950**	10,718	14,468
(Gain)/loss on investments held at fair value	5	**(179,316)**	(232,674)	37,863
Realized loss on sale of investments		**20,925**	54,976	—
Gain on deconsolidation	5	**—**	—	(264,409)
Gain on loss of significant influence	5	**—**	—	(445,582)
Loss on disposal of assets	11	**53**	66	140
Share of net (income)/loss of associates accounted for using the equity method	6	**73,703**	34,117	(30,791)
Fair value gain on derivative	6	**(800)**	—	—
Income taxes, net	25	**3,756**	14,402	112,077
Finance costs, net	9	**(5,050)**	6,114	46,229
Changes in operating assets and liabilities:				
Accounts receivable	22	**(617)**	(529)	747
Other financial assets	13	**—**	—	(48)
Prepaid expenses and other current assets		**(5,350)**	(3,371)	(25)
Deferred revenues	3	**(1,407)**	(5,223)	186
Trade and other payables	19	**8,338**	605	11,166
Other liabilities		**—**	(7)	3,002
Other		**(103)**	—	—
Income taxes paid		**(27,766)**	(20,737)	—
Interest received		**214**	1,155	3,648
Interest paid	20, 21	**(3,382)**	(2,651)	(2,495)
Net cash used in operating activities		**(158,274)**	(131,827)	(98,156)
Cash flows from investing activities:				
Purchase of property and equipment	11	**(5,571)**	(5,170)	(12,138)
Proceeds from sale of property and equipment		**30**	—	—
Purchases of intangible assets	12	**(90)**	(254)	(400)
Purchase of associate preferred shares held at fair value	5, 6	**—**	(10,000)	(13,670)
Purchase of investments held at fair value	5	**(500)**	(1,150)	(1,556)
Sale of investments held at fair value	5	**218,125**	350,586	9,294
Receipt of payment of sublease	21	**381**	350	191
Purchase of short-term note from associate	16	**(15,000)**	—	—
Purchase of convertible note	6	**—**	—	(6,480)
Cash derecognized upon loss of control over subsidiary		**—**	—	(16,036)
Purchases of short-term investments	22	**—**	—	(69,541)
Proceeds from maturity of short-term investments	22	**—**	30,116	173,995
Net cash provided by investing activities		**197,375**	364,478	63,659
Cash flows from financing activities:				
Receipt of PPP loan		**—**	68	—
Issuance of long term loan	20	**—**	14,720	—
Issuance of subsidiary preferred Shares	15	**37,610**	13,750	51,048
Proceeds from issuance of convertible notes in subsidiary	17	**2,215**	25,000	1,606
Payment of lease liability	21	**(3,375)**	(2,908)	(1,678)
Repayment of long-term debt		**—**	—	(178)
Distribution to Tal shareholders		**—**	—	(112)
Exercise of stock options		**352**	1,036	504
Settlement of RSU's		**(10,749)**	(12,888)	—
Vesting of restricted stock units and net share exercise		**(2,582)**	—	(1,280)
Issuance of shares to NCI in subsidiary	15	**66**	—	—
Issuance of warrants		**—**	92	—
Acquisition of a non-controlling Interest of a subsidiary		**(806)**	—	—
Other		**(5)**	—	—
Net cash provided by financing activities		**22,727**	38,869	49,910
Effect of exchange rates on cash and cash equivalents		**—**	—	(104)
Net increase in cash and cash equivalents		**61,827**	271,520	15,309
Cash and cash equivalents at beginning of year		**403,881**	132,360	117,051
Cash and cash equivalents at end of year		**465,708**	403,881	132,360
Supplemental disclosure of non-cash investment and financing activities:				
Purchase of non controlling interest in consideration for issuance of shares and options		**—**	—	9,106
Purchase of intangible asset and investment held at fair value in consideration for issuance of warrant liability and assumption of other long and short-term liabilities		**—**	—	15,894
Purchase of property, plant and equipment against trade and other payables	11	**1,841**	—	—
Leasehold improvements purchased through lease incentives (deducted from Right of Use Asset)	11	**1,010**	—	10,680
Conversion of subsidiary convertible note into preferred share liabilities	17	**25,797**	—	4,894
Conversion of subsidiary convertible note into subsidiary common stock (NCI)		**—**	—	2,418
Supplemental disclosure of cash paid for income taxes:				
Cash paid for income taxes		**27,766**	20,737	176

The accompanying notes are an integral part of these financial statements.

Notes to the Condensed Consolidated Financial Statements

1. Accounting policies

Description of Business

PureTech Health plc ("PureTech," the "Parent" or the "Company") is a public company incorporated, domiciled and registered in the United Kingdom ("UK"). The registered number is 09582467 and the registered address is 8th Floor, 20 Farringdon Street, London EC4A 4AB, United Kingdom.

PureTech's group financial statements consolidate those of the Company and its subsidiaries (together referred to as the "Group"). The Parent company financial statements present financial information about the Company as a separate entity and not about its Group.

The accounting policies set out below have, unless otherwise stated, been applied consistently to all periods presented in these group financial statements.

Basis of Presentation

The consolidated financial statements of the Group are presented as of December 31, 2021 and 2020, and for the years ended December 31, 2021, 2020 and 2019. The Group financial statements have been approved by the Directors on April 25, 2022, and are prepared in accordance with UK-adopted International Financial Reporting Standards (IFRSs). The Consolidated Financial Statements also comply fully with IFRSs as issued by the International Accounting Standards Board (IASB). UK-adopted IFRSs differs in certain respects from IFRS as issued by the IASB. However, the differences have no impact for the periods presented.

For presentation of the Consolidated Statements of Comprehensive Income/(Loss), the Company uses a classification based on the function of expenses, rather than based on their nature, as it is more representative of the format used for internal reporting and management purposes and is consistent with international practice.

Certain amounts in the Consolidated Financial Statements and accompanying notes may not add due to rounding. All percentages have been calculated using unrounded amounts.

Basis of Measurement

The consolidated financial statements are prepared on the historical cost basis except that the following assets and liabilities are stated at their fair value: investments held at fair value, short-term note from associate and liabilities classified as fair value through the profit or loss.

Use of Judgments and Estimates

In preparing these consolidated financial statements, management has made judgements, estimates and assumptions that affect the application of the Group's accounting policies and the reported amounts of assets, liabilities, income and expenses. Actual results may differ from these estimates. Estimates and underlying assumptions are reviewed on an on-going basis.

Significant estimation is applied in determining the following:

- Financial instruments valuations (Note 16): when estimating the fair value of subsidiary warrants, convertible notes and subsidiary preferred shares carried at fair value through profit and loss (FVTPL) as well as investments held at fair value, at initial recognition and upon subsequent measurement. This includes determining the appropriate valuation methodology and making certain estimates of the future earnings potential of the subsidiary businesses, appropriate discount rate, estimated time to exit, marketability and other industry and company specific risk factors. See Note 16 for the sensitivity analysis for key estimates used in these valuations.

Significant judgement is also applied in determining the following:

- Subsidiary preferred shares liability classification (Note 15): when determining the classification of financial instruments in terms of liability or equity. These judgements include an assessment of whether the financial instruments include any embedded derivative features, whether they include contractual obligations of the Group to deliver cash or other financial assets or to exchange financial assets or financial liabilities with another party, and whether that obligation will be settled by the Company exchanging a fixed amount of cash or other financial assets for a fixed number of its own equity instruments. Further information about these critical judgements and estimates is included below under Financial Instruments.
- When the power to control the subsidiaries exists (please refer to Notes 5 and 6 and accounting policy below Subsidiaries). This judgement includes an assessment of whether the Company has (i) power over the investee; (ii) exposure, or rights, to variable returns from its involvement with the investee; and (iii) the ability to use its power over the investee to affect the amount of the investor's returns. The Company considers among others its voting shares, shareholder agreements, ability to appoint board members, representation on the board, rights to appoint management, de facto control, investee dependence on the Company etc. If the power to control investees exists we consolidate the financial statements of such investee in the consolidated financial statements of the Group. Upon issuance of new shares in a subsidiary and a resulting change in any shareholders or governance agreements, the Group reassesses its ability to control the investee based on the revised board composition and revised subsidiary governance and management structure. When such new circumstances result in the Group losing its power to control the investee, the investee is deconsolidated.

1. Accounting policies — continued

- Whether the Company has significant influence over financial and operating policies of investees in order to determine if the Company should account for its investment as an associate based on IAS 28 or based on IFRS 9, Financial Instruments (please refer to Note 5). This judgement includes, among others, an assessment whether the Company has representation on the Board of Directors of the investee, whether the Company participates in the policy making processes of the investee, whether there is any interchange of managerial personnel, whether there is any essential technical information provided to the investee and if there are any transactions between the Company and the investee.
- Upon determining that the Company does have significant influence over the financial and operating policies of an investee, if the Company holds more than a single instrument issued by its equity-accounted investee, judgement is required to determine whether the additional instrument forms part of the investment in the associate, which is accounted for under IAS 28 and scoped out of IFRS 9, or it is a separate financial instrument that falls in the scope of IFRS 9 (please refer to Notes 5 and 6). This judgement includes an assessment of the characteristics of the financial instrument of the investee held by the Company and whether such financial instrument provides access to returns underlying an ownership interest.
- Where the company has other investments in an equity accounted investee that are not accounted for under IAS 28, judgement is required in determining if such investments constitute Long-Term Interests for the purposes of IAS 28 (please refer to Notes 5 and 6). This determination is based on the individual facts and circumstances and characteristics of each investment, but is driven, among other factors, by the intention and likelihood to settle the instrument through redemption or repayment in the foreseeable future, and whether or not the investment is likely to be converted to common stock or other equity instruments (please also refer to accounting policy with regard to Investments in Associates below). When considering the individual facts and circumstances of the Group's investment in its associate's preferred stock in the manner described above, including the long-term nature of such investment, the ability of the Group to convert its preferred stock investment to an investment in common shares and the likelihood of such conversion, as well the fact that there is no planned redemption or other settlement of the preferred stock by the investee in the foreseeable future, we concluded that such investment is considered a Long Term Interest.

As of December 31, 2021, the Group had cash and cash equivalents of $465.7 million. Considering the Group's and the Company's financial position as of December 31, 2021, and its principal risks and opportunities, a going concern analysis has been prepared for at least the twelve-month period from the date of signing the Consolidated Financial Statements ("the going concern period") utilizing realistic scenarios and applying a severe but plausible downside scenario. Even under the downside scenario, the analysis demonstrates the Group and the Company continue to maintain sufficient liquidity headroom and continue to comply with all financial obligations. The Directors believe the Group and the Company is adequately resourced to continue in operational existence for at least the twelve-month period from the date of signing the Consolidated Financial Statements, irrespective of uncertainty regarding the duration and severity of the COVID-19 pandemic and the global macroeconomic impact of the pandemic. Accordingly, the Directors considered it appropriate to adopt the going concern basis of accounting in preparing the Consolidated Financial Statements and the PureTech Health plc Financial Statements.

Basis of consolidation

The consolidated financial information as of December 31, 2021 and 2020, and for each of the years ended December 31, 2021, 2020 and 2019, comprises an aggregation of financial information of the Company and the consolidated financial information of PureTech Health LLC ("PureTech LLC"). Intra-group balances and transactions, and any unrealized income and expenses arising from intra-group transactions, are eliminated.

Subsidiaries

As used in these financial statements, the term subsidiaries refers to entities that are controlled by the Group. Financial results of subsidiaries of the Group as of December 31, 2021, are reported within the Internal segment, Controlled Founded Entities segment or the Parent Company and Other section (please refer to Note 4). Under applicable accounting rules, the Group controls an entity when it is exposed to, or has the rights to, variable returns from its involvement with the entity and has the ability to affect those returns through its power over the entity. In assessing control, the Group takes into consideration potential voting rights, board representation, shareholders' agreements, ability to appoint Directors and management, de facto control and other related factors. The financial statements of subsidiaries are included in the consolidated financial statements from the date that control commences until the date that control ceases. Losses applicable to the non-controlling interests in a subsidiary are allocated to the non-controlling interests even if doing so causes the non-controlling interests to have a deficit balance.

A list of all current and former subsidiaries organized with respect to classification as of December 31, 2021, and the Group's total voting percentage, based on outstanding voting common and preferred shares as of December 31, 2021, 2020 and 2019, is outlined below. All current subsidiaries are domiciled within the United States and conduct business activities solely within the United States.

1. Accounting policies — continued

	Voting percentage at December 31, through the holdings in					
	2021		2020		2019	
Subsidiary	**Common**	**Preferred**	Common	Preferred	Common	Preferred
Subsidiary operating companies						
Alivio Therapeutics, Inc.[1,2]	**—**	**100.0**	—	91.9	—	91.9
Entrega, Inc. (indirectly held through Enlight)[1,2]	**—**	**77.3**	—	83.1	—	83.1
Follica, Incorporated[1,2,5]	**28.7**	**56.7**	28.7	56.7	28.7	56.7
PureTech LYT (formerly Ariya Therapeutics, Inc.)	**—**	**100.0**	—	100.0	—	100.0
PureTech LYT-100	**—**	**100.0**	—	100.0	—	100.0
PureTech Management, Inc.[3]	**100.0**	**—**	100.0	—	100.0	—
PureTech Health LLC[3]	**100.0**	**—**	100.0	—	100.0	—
Sonde Health, Inc.[1,2]	**—**	**51.8**	—	51.8	—	64.1
Vedanta Biosciences, Inc.[1,2]	**—**	**48.6**	—	59.3	—	61.8
Vedanta Biosciences Securities Corp. (indirectly held through Vedanta)[1,2]	**—**	**48.6**	—	59.3	—	61.8
Deconsolidated former subsidiary operating companies						
Akili Interactive Labs, Inc.[2]	**—**	**26.7**	—	41.9	—	41.9
Gelesis, Inc.[1,2,7,10]	**4.8**	**19.7**	4.9	20.2	5.7	20.2
Karuna Therapeutics, Inc.[1,2,8]	**5.6**	**—**	12.6	—	28.4	—
Vor Biopharma Inc.[1,2,9]	**8.6**	**—**	—	16.4	—	47.5
Nontrading holding companies						
Endra Holdings, LLC (held indirectly through Enlight)[2]	**86.0**	**—**	86.0	—	86.0	—
Ensof Holdings, LLC (held indirectly through Enlight)[2]	**86.0**	**—**	86.0	—	86.0	—
PureTech Securities Corp.[2]	**100.0**	**—**	100.0	—	100.0	—
PureTech Securities II Corp.[2]	**100.0**	**—**	100.0	—	—	—
Inactive subsidiaries						
Appeering, Inc.[2]	**—**	**100.0**	—	100.0	—	100.0
Commense Inc.[2,6]	**—**	**99.1**	—	99.1	—	99.1
Enlight Biosciences, LLC[2]	**86.0**	**—**	86.0	—	86.0	—
Ensof Biosystems, Inc. (held indirectly through Enlight)[1,2]	**57.7**	**28.3**	57.7	28.3	57.7	28.3
Knode Inc. (indirectly held through Enlight)[2]	**—**	**86.0**	—	86.0	—	86.0
Libra Biosciences, Inc.[2]	**—**	**100.0**	—	100.0	—	100.0
Mandara Sciences, LLC[2]	**98.3**	**—**	98.3	—	98.3	—
Tal Medical, Inc.[1,2]	**—**	**100.0**	—	100.0	—	100.0

1 The voting percentage is impacted by preferred shares that are classified as liabilities, which results in the ownership percentage not being the same as the ownership percentage used in allocations to non-controlling interests disclosed in Note 18. The allocation of losses/profits to the noncontrolling interest is based on the holdings of subordinated stock that provide ownership rights in the subsidiaries. The ownership of liability classified preferred shares are quantified in Note 15.

2 Registered address is Corporation Trust Center, 1209 Orange St., Wilmington, DE 19801, USA.

3 Registered address is 2711 Centerville Rd., Suite 400, Wilmington, DE 19808, USA.

4 The Company's interests in its subsidiaries are predominantly in the form of preferred shares, which have a liquidation preference over the common stock, are convertible into common stock at the holder's discretion or upon certain liquidity events, are entitled to one vote per share on all matters submitted to shareholders for a vote and entitled to receive dividends when and if declared. In the case of Enlight, Mandara and PureTech Health LLC, the holdings are membership interests in an LLC. The holders of common stock are entitled to one vote per share on all matters submitted to shareholders for a vote and entitled to receive dividends when and if declared.

5 On July 19, 2019, all of the outstanding notes, plus accrued interest, issued by Follica to PureTech converted into 15,216,214 shares of Series A-3 Preferred Shares and 12,777,287 shares of common share pursuant to a Series A-3 Note Conversion Agreement between Follica and the noteholders. Please refer to Note 16.

6 Commense turned inactive during 2019.

7 On July 1, 2019 PureTech lost control of Gelesis and Gelesis was deconsolidated from the Group's financial statements, resulting in only the profits and losses generated by Gelesis through the deconsolidation date being included in the Group's Consolidated Statement of Comprehensive Income/(Loss). See Notes 5 and 6 for further details about the accounting for the investments in Gelesis subsequent to deconsolidation.

8 On March 15, 2019, PureTech lost control of Karuna, Karuna was deconsolidated from the Group's financial statements and is no longer considered a subsidiary. This results in only the profits and losses generated by Karuna through the deconsolidation date being included in the Group's Consolidated Statement of Comprehensive Income/(Loss).. See Note 5 for further details about the accounting for the investment in Karuna subsequent to deconsolidation.

9 On February 12, 2019, PureTech lost control of Vor, Vor was deconsolidated from the Group's financial statements and is no longer considered a subsidiary. This results in only the profits and losses generated by Vor through the deconsolidation date being included in the Group's Consolidated Statement of Comprehensive Income/(Loss). See Note 5 for further details about the accounting for the investment in Vor subsequent to deconsolidation.

10 See note 26 regarding Gelesis business combination with Capstar Special Purpose Acquisition Corp after balance sheet date and the Group's ownership rights in the new combined public entity.

Change in subsidiary ownership and loss of control

Changes in the Group's interest in a subsidiary that do not result in a loss of control are accounted for as equity transactions.

Where the Group loses control of a subsidiary, the assets and liabilities are derecognized along with any related non-controlling interest ("NCI"). Any interest retained in the former subsidiary is measured at fair value when control is lost. Any resulting gain or loss is recognized as profit or loss in the Consolidated Statements of Comprehensive Income/(Loss).

1. Accounting policies — continued

Associates

As used in these financial statements, the term associates are those entities in which the Group has no control but maintains significant influence over the financial and operating policies. Significant influence is presumed to exist when the Group holds between 20 and 50 percent of the voting power of an entity, unless it can be clearly demonstrated that this is not the case. The Group evaluates if it maintains significant influence over associates by assessing if the Group has lost the power to participate in the financial and operating policy decisions of the associate.

Application of the equity method to associates

Associates are accounted for using the equity method (equity accounted investees) and are initially recognized at cost, or if recognized upon deconsolidation they are initially recorded at fair value at the date of deconsolidation. The consolidated financial statements include the Group's share of the total comprehensive income and equity movements of equity accounted investees, from the date that significant influence commences until the date that significant influence ceases.

To the extent the Group holds interests in associates that are not providing access to returns underlying ownership interests, the instrument held by PureTech is accounted for in accordance with IFRS 9 as investments held at fair value.

When the Group's share of losses exceeds its equity method investment in the investee, losses are applied against Long-Term Interests, which are investments accounted for under IFRS 9. Investments are determined to be Long-Term Interests when they are long-term in nature and in substance they form part of the Group's net investment in that associate. This determination is impacted by many factors, among others, whether settlement by the investee through redemption or repayment is planned or likely in the foreseeable future, whether the investment can be converted and/or is likely to be converted to common stock or other equity instrument and other factors regarding the nature of the investment. Whilst this assessment is dependent on many specific facts and circumstances of each investment, typically conversion features whereby the investment is likely to convert to common stock or other equity instruments would point to the investment being a Long-Term Interest. Similarly, where the investment is not planned or likely to be settled through redemption or repayment in the foreseeable future, this would indicate that the investment is a Long-Term Interest. When the net investment in the associate, which includes the Group's investments in other long-term interests, is reduced to nil, recognition of further losses is discontinued except to the extent that the Group has incurred legal or constructive obligations or made payments on behalf of an investee.

The Group has also adopted the amendments to IAS 28 Investments in Associates that addresses the dual application of IAS 28 and IFRS 9 (see below) when equity method losses are applied against Long-Term Interests (LTI). The amendments provide the annual sequence in which both standards are to be applied in such a case. The Group has applied the equity method losses to the LTIs presented as part of Investments held at fair value subsequent to remeasuring such investments to their fair value at balance sheet date.

Financial Instruments

Classification

The Group classifies its financial assets in the following measurement categories:

- Those to be measured subsequently at fair value (either through other comprehensive income, or through profit or loss), and
- Those to be measured at amortized cost.

The classification depends on the Group's business model for managing the financial assets and the contractual terms of the cash flows.

For assets measured at fair value, gains and losses will are recorded in profit or loss. For investments in debt instruments, this will depend on the business model in which the investment is held. For investments in equity instruments that are not held for trading, this will depend on whether the Group has made an irrevocable election at the time of initial recognition to account for the equity investment at FVOCI. As of balance sheet dates, none of the Company's financial assets are accounted for as FVOCI.

Measurement

At initial recognition, the Group measures a financial asset at its fair value plus, in the case of a financial asset not at FVTPL, transaction costs that are directly attributable to the acquisition of the financial asset. Transaction costs of financial assets that are carried at FVTPL are expensed.

Impairment

The Group assesses on a forward-looking basis the expected credit losses associated with its debt instruments carried at amortized cost. The Group had no debt instruments carried at amortized cost as of balance sheet date. For trade receivables, the Group applies the simplified approach permitted by IFRS 9, which requires expected lifetime losses to be recognized from initial recognition of the receivables.

Financial Assets

The Group's financial assets consist of cash and cash equivalents, trade and other receivables, investments in equity securities, short-term note, other deposits and investments in associates' preferred shares. The Group's financial assets are classified into the following categories: investments held at fair value, trade and other receivables, short-term investments (if applicable) and cash and cash equivalents. The Group determines the classification of financial assets at initial recognition depending on the purpose for which the financial assets were acquired.

1. Accounting policies — continued

Investments held at fair value are investments in equity instruments that are not held for trading. Such investments consist of the Group's minority interest holdings where the Group has no significant influence or preferred share investments in the Group's associates that are not providing access to returns underlying ownership interests. These financial assets are initially measured at fair value and subsequently re-measured at fair value at each reporting date. The Company elects if the gain or loss will be recognized in Other Comprehensive Income/(Loss) or through profit and loss on an instrument by instrument basis. The Company has elected to record the changes in fair values for the financial assets falling under this category through profit and loss. Please refer to Note 5.

Changes in the fair value of financial assets at FVTPL are recognized in other income/(expense) in the Consolidated Statements of Comprehensive Income/(Loss) as applicable.

The short term note from an associate, since its contractual terms do not consist solely of cash flow payments of principal and interest on the principal amount outstanding, is initially and subsequently measured at fair value, with changes in fair value recognized through profit and loss.

Trade and other receivables are non-derivative financial assets with fixed and determinable payments that are not quoted on active markets. These financial assets are carried at the amounts expected to be received less any expected lifetime losses. Such losses are determined taking into account previous experience, credit rating and economic stability of counterparty and economic conditions. When a trade receivable is determined to be uncollectible, it is written off against the available provision. Trade and other receivables are included in current assets, unless maturities are greater than 12 months after the end of the reporting period.

Financial Liabilities

The Group's financial liabilities consist of trade and other payables, subsidiary notes payable, preferred shares, and warrant liability. Warrant liabilities are initially recognized at fair value. After initial recognition, these financial liabilities are re-measured at FVTPL using an appropriate valuation technique. Subsidiary notes payable without embedded derivatives are accounted for at amortized cost.

The majority of the Group's subsidiaries have preferred shares and notes payable with embedded derivatives, which are classified as current liabilities. When the Group has preferred shares and notes with embedded derivatives that qualify for bifurcation, the Group has elected to account for the entire instrument as FVTPL after determining under IFRS 9 that the instrument qualifies to be accounted for under such FVTPL method.

The Group derecognizes a financial liability when its contractual obligations are discharged, cancelled or expire.

Equity Instruments Issued by the Group

Financial instruments issued by the Group are treated as equity only to the extent that they meet the following two conditions, in accordance with IAS 32:

1. They include no contractual obligations upon the Group to deliver cash or other financial assets or to exchange financial assets or financial liabilities with another party under conditions that are potentially unfavorable to the Group; and
2. Where the instrument will or may be settled in the Group's own equity instruments, it is either a non-derivative that includes no obligation to deliver a variable number of the Group's own equity instruments or is a derivative that will be settled by the Group exchanging a fixed amount of cash or other financial assets for a fixed number of its own equity instruments.

To the extent that this definition is not met, the financial instrument is classified as a financial liability. Where the instrument so classified takes the legal form of the Group's own shares, the amounts presented in the Group's shareholders' equity exclude amounts in relation to those shares.

Changes in the fair value of liabilities at FVTPL are recognized in Net finance income (costs) in the Consolidated Statements of Comprehensive Income/(Loss) as applicable.

IFRS 15, Revenue from Contracts with Customers

The standard establishes a five-step principle-based approach for revenue recognition and is based on the concept of recognizing an amount that reflects the consideration for performance obligations only when they are satisfied and the control of goods or services is transferred.

The majority of the Group's contract revenue is generated from licenses and services, some of which are part of collaboration arrangements.

Management reviewed contracts where the Group received consideration in order to determine whether or not they should be accounted for in accordance with IFRS 15. To date, PureTech has entered into transactions that generate revenue and meet the scope of either IFRS 15 or IAS 20 Accounting for Government Grants. Contract revenue is recognized at either a point-in-time or over time, depending on the nature of the performance obligations.

1. Accounting policies — continued

The Group accounts for agreements that meet the definition of IFRS 15 by applying the following five step model:

- Identify the contract(s) with a customer – A contract with a customer exists when (i) the Group enters into an enforceable contract with a customer that defines each party's rights regarding the goods or services to be transferred and identifies the payment terms related to those goods or services, (ii) the contract has commercial substance and, (iii) the Group determines that collection of substantially all consideration for goods or services that are transferred is probable based on the customer's intent and ability to pay the promised consideration.
- Identify the performance obligations in the contract – Performance obligations promised in a contract are identified based on the goods or services that will be transferred to the customer that are both capable of being distinct, whereby the customer can benefit from the good or service either on its own or together with other resources that are readily available from third parties or from the Group, and are distinct in the context of the contract, whereby the transfer of the goods or services is separately identifiable from other promises in the contract.
- Determine the transaction price – The transaction price is determined based on the consideration to which the Group will be entitled in exchange for transferring goods or services to the customer. To the extent the transaction price includes variable consideration, the Group estimates the amount of variable consideration that should be included in the transaction price utilizing either the expected value method or the most likely amount method depending on the nature of the variable consideration. Variable consideration is included in the transaction price if, in the Group's judgement, it is probable that a significant future reversal of cumulative revenue under the contract will not occur.
- Allocate the transaction price to the performance obligations in the contract – If the contract contains a single performance obligation, the entire transaction price is allocated to the single performance obligation. Contracts that contain multiple performance obligations require an allocation of the transaction price to each performance obligation based on a relative standalone selling price basis.
- Recognize revenue when (or as) the Group satisfies a performance obligation – The Group satisfies performance obligations either over time or at a point in time as discussed in further detail below. Revenue is recognized at the time the related performance obligation is satisfied by transferring a promised good or service to a customer.

Revenue generated from services agreements (typically where licenses and related services were combined into one performance obligation) is determined to be recognized over time when it can be determined that the services meet one of the following: (a) the customer simultaneously receives and consumes the benefits provided by the entity's performance as the entity performs; (b) the entity's performance creates or enhances an asset that the customer controls as the asset is created or enhanced; or (c) the entity's performance does not create an asset with an alternative use to the entity and the entity has an enforceable right to payment for performance completed to date.

It was determined that the Group has contracts that meet criteria (a), since the customer simultaneously receives and consumes the benefits provided by the Company's performance as the Company performs. Therefore revenue is recognized over time using the input method based on costs incurred to date as compared to total contract costs. The Company believes that in research and development service type agreements using costs incurred to date represents the most faithful depiction of the entity's performance towards complete satisfaction of a performance obligation.

Revenue from licenses that are not part of a combined performance obligation are recognized at a point in time due to the licenses relating to intellectual property that has significant stand-alone functionality and as such represent a right to use the entity's intellectual property as it exists at the point in time at which the license is granted.

Royalty income received in respect of licensing agreements is recognized as the related third party sales in the licensee occur.

Amounts that are receivable or have been received per contractual terms but have not been recognized as revenue since performance has not yet occurred or has not yet been completed are recorded as deferred revenue. The Company classifies as non-current deferred revenue amounts received for which performance is expected to occur beyond one year or one operating cycle.

Grant Income

The Company recognizes grants from governmental agencies as grant income in the Consolidated Statement of Comprehensive Income/(Loss), gross of the expenditures that were related to obtaining the grant, when there is reasonable assurance that the Company will comply with the conditions within the grant agreement and there is reasonable assurance that payments under the grants will be received. The Company evaluates the conditions of each grant as of each reporting date to ensure that the Company has reasonable assurance of meeting the conditions of each grant arrangement and that it is expected that the grant payment will be received as a result of meeting the necessary conditions.

The Company submits qualifying expenses for reimbursement after the Company has incurred the research and development expense. The Company records an unbilled receivable upon incurring such expenses. In cases were grant income is received prior to the expenses being incurred or recognized, the amounts received are deferred until the related expense is incurred and/or recognized. Grant income is recognized in the Consolidated Statements of Comprehensive Income/(Loss) at the time in which the Company recognizes the related reimbursable expense for which the grant is intended to compensate.

1. Accounting policies — continued

Functional and Presentation Currency
These consolidated financial statements are presented in United States dollars ("US dollars"). The functional currency of virtually all members of the Group is the U.S. dollar. The assets and liabilities of a previously held subsidiary were translated to U.S. dollars at the exchange rate prevailing on the balance sheet date and revenues and expenses were translated at the average exchange rate for the period. Foreign exchange differences resulting from the translation were reported in Other Comprehensive Income/(Loss).

Foreign Currency
Transactions in foreign currencies are translated to the respective functional currencies of Group entities at the foreign exchange rate ruling at the date of the transaction. Monetary assets and liabilities denominated in foreign currencies at the balance sheet date are retranslated to the functional currency at the foreign exchange rate ruling at that date. Foreign exchange differences arising on remeasurement are recognized in the Consolidated Statement of Comprehensive Income/(Loss). Non-monetary assets and liabilities that are measured in terms of historical cost in a foreign currency are translated using the exchange rate at the date of the transaction.

Cash and Cash Equivalents
Cash and cash equivalents include all highly liquid instruments with original maturities of three months or less.

Share Capital
Ordinary shares are classified as equity. The Group is comprised of share capital, share premium, merger reserve, other reserve, translation reserve, and accumulated deficit.

Property and Equipment
Property and equipment is stated at cost less accumulated depreciation and any accumulated impairment losses. Cost includes expenditures that are directly attributable to the acquisition of the asset. Assets under construction represent leasehold improvements and machinery and equipment to be used in operations or research and development activities. When parts of an item of property and equipment have different useful lives, they are accounted for as separate items (major components) of property and equipment. Depreciation is calculated using the straight-line method over the estimated useful life of the related asset:

Laboratory and manufacturing equipment	2-8 years
Furniture and fixtures	7 years
Computer equipment and software	1-5 years
Leasehold improvements	5-10 years, or the remaining term of the lease, if shorter

Depreciation methods, useful lives and residual values are reviewed at each balance sheet date.

Intangible Assets
Intangible assets, which include purchased patents and licenses with finite useful lives, are carried at historical cost less accumulated amortization, if amortization has commenced. Intangible assets with finite lives are amortized from the time they are available for use. Amortization is calculated using the straight-line method to allocate the costs of patents and licenses over their estimated useful lives.

Research and development intangible assets, which are still under development and have accordingly not yet obtained marketing approval, are presented as In-Process Research and Development (IPR&D). IPR&D is not amortized since it is not yet available for its intended use, but it is evaluated for potential impairment on an annual basis or more frequently when facts and circumstances warrant.

Impairment
Impairment of Non-Financial Assets
The Group reviews the carrying amounts of its property and equipment and intangible assets at each reporting date to determine whether there are indicators of impairment. If any such indicators of impairment exist, then an asset's recoverable amount is estimated. The recoverable amount is the higher of an asset's fair value less cost of disposal and value in use.

The Company's IPR&D intangible assets are not yet available for their intended use. As such, they are tested for impairment at least annually.

1. Accounting policies — continued

An impairment loss is recognized when an asset's carrying amount exceeds its recoverable amount. For the purposes of impairment testing, assets are grouped at the lowest levels for which there are largely independent cash flows. If a non-financial asset instrument is impaired, an impairment loss is recognized in the Consolidated Statements of Comprehensive Income/(Loss).

The Company did not record any impairment of such assets during the reported periods.

Investments in associates are considered impaired if, and only if, objective evidence indicates that one or more events, which occurred after the initial recognition, have had an impact on the future cash flows from the net investment and that impact can be reliably estimated. If an impairment exists the Company measures an impairment by comparing the carrying value of the net investment in the associate to its recoverable amount and recording any excess as an impairment loss. See Note 6 for impairment recorded in respect of an investment in associate during the year ended December 31, 2019.

Employee Benefits

Short-Term Employee Benefits

Short-term employee benefit obligations are measured on an undiscounted basis and expensed as the related service is provided. A liability is recognized for the amount expected to be paid if the Group has a present legal or constructive obligation due to past service provided by the employee, and the obligation can be estimated reliably.

Defined Contribution Plans

A defined contribution plan is a post-employment benefit plan under which an entity pays fixed contributions into a separate entity and has no legal or constructive obligation to pay further amounts. Obligations for contributions to defined contribution plans are recognized as an employee benefit expense in the periods during which related services are rendered by employees. Prepaid contributions are recognized as an asset to the extent that a cash refund or a reduction in future payments is available.

Share-based Payments

Share-based payment arrangements, in which the Group receives goods or services as consideration for its own equity instruments, are accounted for as equity-settled share-based payment transactions (except certain restricted stock units – see below) in accordance with IFRS 2, regardless of how the equity instruments are obtained by the Group. The grant date fair value of employee share-based payment awards is recognized as an expense with a corresponding increase in equity over the requisite service period related to the awards. The amount recognized as an expense is adjusted to reflect the actual number of awards for which the related service and non-market performance conditions are expected to be met, such that the amount ultimately recognized as an expense is based on the number of awards that do meet the related service and non-market performance conditions at the vesting date. For share-based payment awards with market conditions, the grant date fair value is measured to reflect such conditions and there is no true-up for differences between expected and actual outcomes.

Certain restricted stock units are treated as liability settled awards starting in 2021. Such awards are remeasured at every reporting date until settlement date and are recognized as compensation expense over the requisite service period. Differences in remeasurement are recognized in profit and loss. The cumulative cost that will ultimately be recognized in respect of these awards will equal to the amount at settlement.

The fair value of the awards is measured using option pricing models and other appropriate models, which take into account the terms and conditions of the awards granted. See further details in Note 8.

Development Costs

Expenditures on research activities are recognized as incurred in the Consolidated Statements of Comprehensive Income/(Loss). In accordance with IAS 38 development costs are capitalized only if the expenditure can be measured reliably, the product or process is technically and commercially feasible, future economic benefits are probable, the Group can demonstrate its ability to use or sell the intangible asset, the Group intends to and has sufficient resources to complete development and to use or sell the asset, and it is able to measure reliably the expenditure attributable to the intangible asset during its development. The point at which technical feasibility is determined to have been reached is, generally, when regulatory approval has been received where applicable. Management determines that commercial viability has been reached when a clear market and pricing point have been identified, which may coincide with achieving meaningful recurring sales. Otherwise, the development expenditure is recognized as incurred in the Consolidated Statements of Comprehensive Income/(Loss). As of balance sheet date the Group has not capitalized any development costs.

1. Accounting policies — continued

Provisions
A provision is recognized in the Consolidated Statements of Financial Position when the Group has a present legal or constructive obligation due to a past event that can be reliably measured, and it is probable that an outflow of economic benefits will be required to settle the obligation. Provisions are determined by discounting the expected future cash flows at a pre-tax rate that reflects risks specific to the liability.

Leases
The Group leases real estate (and some minor equipment) for use in operations. These leases generally have lease terms of 1 to 10 years. The Group includes options that are reasonably certain to be exercised as part of the determination of the lease term. The group determines if an arrangement is a lease at inception of the contract in accordance with guidance detailed in IFRS 16. ROU assets represent the Group's right to use an underlying asset for the lease term and lease liabilities represent our obligation to make lease payments arising from the lease. Operating lease ROU assets and lease liabilities are recognized at commencement date based on the present value of the lease payments over the lease term. As most of our leases do not provide an implicit rate, we use the Group's estimated incremental borrowing rate based on information available at commencement date in determining the present value of future payments.

The Group's operating leases are virtually all leases of real estate.

The Group has elected to account for lease payments as an expense on a straight-line basis over the life of the lease for:

- Leases with a term of 12 months or less and containing no purchase options; and
- Leases where the underlying asset has a value of less than $5,000.

The right-of-use asset is depreciated on a straight-line basis and the lease liability gives rise to an interest charge.

Further information regarding the subleases, right of use asset and lease liability can be found in Note 21.

Finance Income and Finance Costs
Finance income is comprised of income on funds invested in U.S. treasuries, income on money market funds and income on a finance lease. Financing income is recognized as it is earned. Finance costs comprise mainly of loan, notes and lease liability interest expenses and the changes in the fair value of financial liabilities carried at FVTPL (such changes can consist of finance income when the fair value of such financial liabilities decreases).

Taxation
Tax on the profit or loss for the year comprises current and deferred income tax. In accordance with IAS 12, tax is recognized in the Consolidated Statements of Comprehensive Income/(Loss) except to the extent that it relates to items recognized directly in equity.

Current income tax is the expected tax payable or receivable on the taxable income or loss for the year, using tax rates enacted or substantially enacted at the reporting date, and any adjustment to tax payable in respect of previous years.

Deferred tax is recognized due to temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for taxation purposes. Deferred tax assets are recognized for unused tax losses, unused tax credits and deductible temporary differences to the extent that it is probable that future taxable profits will be available against which they can be used. Deferred tax assets with respect to investments in associates are recognized only to the extent that it is probable the temporary difference will reverse in the foreseeable future and taxable profit will be available against which the temporary difference can be utilized. Deferred tax assets are reviewed at each reporting date and are reduced to the extent that it is no longer probable that the related tax benefit will be realized.

Deferred tax is measured at the tax rates that are expected to be applied to temporary differences when they reverse, using tax rates enacted or substantively enacted at the reporting date.

Deferred income tax assets and liabilities are offset when there is a legally enforceable right to offset current tax assets against current tax liabilities and when the deferred income tax assets and liabilities relate to income taxes levied by the same taxation authority on either the same taxable entity or different taxable entities where there is an intention to settle the balances on a net basis.

1. Accounting policies — continued

Fair Value Measurements

The Group's accounting policies require that certain financial assets and certain financial liabilities be measured at their fair value.

The Group uses valuation techniques that are appropriate in the circumstances and for which sufficient data are available to measure fair value, maximizing the use of relevant observable inputs and minimizing the use of unobservable inputs. Fair values are categorized into different levels in a fair value hierarchy based on the inputs used in the valuation techniques as follows:

- Level 1: quoted prices (unadjusted) in active markets for identical assets or liabilities.
- Level 2: inputs other than quoted prices included in Level 1 that are observable for the asset or liability, either directly (i.e. as prices) or indirectly (i.e. derived from prices).
- Level 3: inputs for the asset or liability that are not based on observable market data (unobservable inputs).

The Group recognizes transfers between levels of the fair value hierarchy at the end of the reporting period during which the change has occurred.

The carrying amount of cash and cash equivalents, accounts receivable, restricted cash, deposits, accounts payable, accrued expenses and other current liabilities in the Group's Consolidated Statements of Financial Position approximates their fair value because of the short maturities of these instruments.

Operating Segments

Operating segments are reported in a manner that is consistent with the internal reporting provided to the chief operating decision maker ("CODM"). The CODM reviews discrete financial information for the operating segments in order to assess their performance and is responsible for making decisions about resources allocated to the segments. The CODM has been identified as the Group's Directors.

2. New Standards and Interpretations Not Yet Adopted

A number of new standards, interpretations, and amendments to existing standards are effective for annual periods commencing on or after January 1, 2022 and have not been applied in preparing the consolidated financial information. The Company's assessment of the impact of these new standards and interpretations is set out below.

Effective January 1, 2023, the definition of accounting estimates has been amended as an amendment to IAS 8 Accounting Policies, Changes in Accounting Estimates and Errors. The amendments clarify how companies should distinguish changes in accounting policies from changes in accounting estimates. The distinction is important because changes in accounting estimates are applied prospectively only to future transactions and future events, but changes in accounting policies are generally also applied retrospectively to past transactions and other past events. This amendment is not expected to have an impact on the Group's financial statements.

Effective January 1, 2023, IAS 1 has been amended to clarify that liabilities are classified as either current or non-current, depending on the rights that exist at the end of the reporting period. Classification is unaffected by the expectations of the entity or events after the reporting date. The Company does not expect this amendment will have a material impact on its financial statements.

Effective January 1, 2023, IAS 12 is amended to narrow the scope of the initial recognition exemption (IRE) so that it does not apply to transactions that give rise to equal and offsetting temporary differences. As a result, companies will need to recognise a deferred tax asset and a deferred tax liability for temporary differences arising on initial recognition of a lease and a decommissioning provision. The amendment is not expected to have an impact on the Group's financial statements as the Group has already recognized a deferred tax asset and deferred tax liability that arose on initial recognition of its leases (the Group does not have decommissioning provisions).

None of the other new standards, interpretations, and amendments are applicable to the Company's financial statements and therefore will not have an impact on the Company.

3. Revenue

Revenue recorded in the Consolidated Statement of Comprehensive Income/(Loss) consists of the following:

For the years ended December 31,	**2021 $000s**	2020 $000s	2019 $000s
Contract revenue	**9,979**	8,341	8,688
Grant income	**7,409**	3,427	1,119
Total revenue	**17,388**	11,768	9,807

All amounts recorded in contract revenue were generated in the United States. For the years ended December 31, 2021 and 2020 contract revenue includes royalties received from an associate in the amount of $231 thousand and $54 thousand, respectively.

Primarily all of the Company's contracts in the years ended December 31, 2021, 2020 and 2019 were determined to have a single performance obligation which consists of a combined deliverable of license to intellectual property and research and development services (not including the license acquired by Imbrium upon option exercise – see below). Therefore, for such contracts, revenue is recognized over time based on the input method which the Company believes is a faithful depiction of the transfer of goods and services. Progress is measured based on costs incurred to date as compared to total projected costs. Payments for such contracts are primarily made up front at the inception of the contract (or upon achieving a milestone event) and to a lesser extent payments are made periodically over the contract term.

During the year ended December 31, 2021, the company received a $6.5 million payment from Imbrium Therapeutics, Inc. following the exercise of the option to acquire an exclusive license for the Initial Product Candidate, as defined in the agreement. Since the license transferred was a functional license, revenue from the option exercise was recognized at a point in time upon transfer of the license, which occurred during the year ended December 31, 2021.

During the year ended December 31, 2020, the Company received a $2.0 million milestone payment from Karuna Therapeutics, Inc. following initiation of its KarXT Phase 3 clinical study pursuant to the Exclusive Patent License Agreement between PureTech and Karuna. This milestone was recognized as revenue during the year ended December 31, 2020.

Disaggregated Revenue

The Group disaggregates contract revenue in a manner that depicts how the nature, amount, timing, and uncertainty of revenue and cash flows are affected by economic factors. The Group disaggregates revenue based on contract revenue or grant revenue, and further disaggregates contract revenue based on the transfer of control of the underlying performance obligations.

Timing of contract revenue recognition For the years ended December 31,	**2021 $000s**	2020 $000s	2019 $000s
Transferred at a point in time – Licensing Income[1]	**6,809**	2,054	—
Transferred over time[2]	**3,171**	6,286	8,688
	9,979	8,341	8,688

1 2021 – Attributed to Internal segment ($6.5 million), Controlled Founded Entities segment ($74 thousand) and to Parent Company and Other ($235 thousand); 2020 – Attributed to Parent Company and Other. See note 4, Segment information.

2 2021 – Attributed to Internal segment ($1,629 thousand) and Controlled Founded Entities segment ($1,541 thousand); 2020 – Attributed to Internal segment ($5,297 thousand), and Controlled Founded Entities segment ($990 thousand), 2019 – Attributed to Internal segment ($7,077 thousand), Controlled founded entities segment ($1,474 thousand) and Parent Company and Other ($137 thousand). See Note 4, Segment Information.

3. Revenue — continued

Customers over 10% of revenue	**2021 $000s**	2020 $000s	2019 $000s
Customer A	**—**	1,518	4,973
Customer B	**1,500**	896	1,433
Customer C	**—**	2,043	1,091
Customer D	**7,250**	1,736	1,013
Customer E	**—**	2,000	—
	8,750	8,193	8,510

Accounts receivables represent rights to consideration in exchange for products or services that have been transferred by the Group, when payment is unconditional and only the passage of time is required before payment is due. Accounts receivables do not bear interest and are recorded at the invoiced amount. Accounts receivable are included within Trade and other receivables on the Consolidated Statement of Financial Position.

Contract liabilities represent the Group's obligation to transfer products or services to a customer for which consideration has been received, or for which an amount of consideration is due from the customer. Contract liabilities are included within deferred revenue on the Consolidated Statement of Financial Position.

Contract Balances	**2021 $000s**	2020 $000s
Accounts receivable	**704**	711
Deferred revenue – short term	**65**	1,472

During the year ended December 31, 2021, $1.4 million of revenue was recognized from deferred revenue outstanding at December 31, 2020.

Remaining performance obligations represent the transaction price of unsatisfied or partially satisfied performance obligations within contracts with an original expected contract term that is greater than one year and for which fulfillment of the contract has started as of the end of the reporting period. The aggregate amount of transaction consideration allocated to remaining performance obligations as of December 31, 2021, was nil.

4. Segment Information

Basis for Segmentation

The Directors are the Group's strategic decision-makers. The Group's operating segments are reported based on the financial information provided to the Directors periodically for the purposes of allocating resources and assessing performance. The Group has determined that each entity is representative of a single operating segment as the Directors monitor the financial results at this level. When identifying the reportable segments the Group has determined that it is appropriate to aggregate multiple operating segments into a single reportable segment given the high level of operational and financial similarities across the entities.

The Group has identified multiple reportable segments as presented below. There was no change to reportable segments in 2021, except the change in the composition of the segments with respect to Alivio, as explained below. Virtually all of the revenue and profit generating activities of the Group are generated within the United States and accordingly, no geographical disclosures are provided.

During the year ended December 31, 2021, the Company acquired the non-controlling interest in Alivio and since then Alivio is wholly owned by the Company and is managed within the Internal segment. The Company has revised in these financial statements the prior period financial information to conform to the presentation as of and for the period ending December 31, 2021. The change in segments reflects how the Company's Board of Directors reviews the Group's results, allocates resources and assesses performance of the Group at this time.

Internal

The Internal segment (the "Internal segment"), is advancing Wholly Owned Programs which is focused on immunological, fibrotic and lymphatic system disorders and builds upon validated biologic pathways and proven pharmacology. The Internal segment is comprised of the technologies that are wholly owned and will be advanced through either PureTech Health funding or non-dilutive sources of financing in the near-term. The operational management of the Internal segment is conducted by the PureTech Health team, which is responsible for the strategy, business development, and research and development. As of December 31, 2021, this segment included PureTech LYT (formerly Ariya Therapeutics), PureTech LYT-100 and Alivio Therapeutics, Inc.

Controlled Founded Entities

The Controlled Founded Entity segment (the "Controlled Founded Entity segment") is comprised of the Group's subsidiaries that are currently consolidated operational subsidiaries that either have, or have plans to hire, independent management teams and currently have already raised third-party dilutive capital. These subsidiaries have active research and development programs and either have entered into or plan to seek an equity or debt investment partner, who will provide additional industry knowledge and access to networks, as well as additional funding to continue the pursued growth of the company. As of December 31, 2021, this segment included Entrega Inc., Follica Incorporated, Sonde Health Inc., and Vedanta Biosciences, Inc.

Non-Controlled Founded Entities

The Non-Controlled Founded Entities segment (the "Non-Controlled Founded Entities segment") is comprised of the entities in respect of which PureTech Health (i) no longer holds majority voting control as a shareholder and no longer has the right to elect a majority of the members of the subsidiaries' Board of Directors. Upon deconsolidation of an entity the segment disclosure is restated to reflect the change on a retrospective basis, as this constitutes a change in the composition of its reportable segments. The Non-Controlled Founded Entities segment includes Vor Biopharma Inc. ("Vor"), Karuna Therapeutics, Inc. ("Karuna"), and Gelesis Inc. ("Gelesis"), which were deconsolidated during the year ended December 31, 2019.

The Non-Controlled Founded Entities segment incorporates the operational results of the aforementioned entities to the date of deconsolidation. Following the date of deconsolidation, the Company accounts for its investment in each entity at the parent level, and therefore the results associated with investment activity following the date of deconsolidation is included in the Parent Company and Other section.

Parent Company and Other

Parent Company and Other includes activities that are not directly attributable to the operating segments, such as the activities of the Parent, corporate support functions and certain research and development support functions that are not directly attributable to a strategic business segment as well as the elimination of intercompany transactions. Intercompany transactions between segments consist primarily of management fees charged from the Parent Company to the other segments. This section also captures the accounting for the Company's holdings in entities for which control has been lost, which is inclusive of the following items: gain on deconsolidation, gain or loss on investments held at fair value, gain on loss of significant influence, and the share of net income/ (loss) of associates accounted for using the equity method. As of December 31, 2021, this segment included PureTech Health plc, PureTech Health LLC, PureTech Management, Inc., PureTech Securities Corp. and PureTech Securities II Corp., as well as certain other dormant, inactive and shell entities.

4. Segment Information — continued

Information About Reportable Segments:

	2021				
	Internal $000s	Controlled Founded Entities $000s	Non-Controlled Founded Entities $000s	Parent Company & Other $000s	Consolidated $000s
Consolidated Statements of Comprehensive Income/(Loss)					
Contract revenue	8,129	1,615	—	235	9,979
Grant revenue	1,253	6,156	—	—	7,409
Total revenue	9,382	7,771	—	235	17,388
General and administrative expenses	(8,673)	(20,729)	—	(27,797)	(57,199)
Research and development expenses	(65,444)	(43,783)	—	(1,244)	(110,471)
Total operating expense	(74,118)	(64,512)	—	(29,041)	(167,671)
Other income/(expense):					
Gain/(loss) on investments held at fair value	—	—	—	179,316	179,316
Loss realized on sale of investments	—	—	—	(20,925)	(20,925)
Gain/(loss) on disposal of assets	(1)	(51)	—	—	(53)
Other income/(expense)	—	121	—	1,523	1,645
Total other income/(expense)	(1)	70	—	159,914	159,983
Net finance income/(costs)	(16)	6,744	—	(1,679)	5,050
Share of net income/(loss) of associates accounted for using the equity method	—	—	—	(73,703)	(73,703)
Income/(loss) before taxes	(64,753)	(49,927)	—	55,727	(58,953)
Income/(loss) before taxes pre IFRS 9 fair value accounting, finance costs – subsidiary preferred shares, share-based payment expense, depreciation of tangible assets and amortization of intangible assets	(60,368)	(50,583)	—	63,628	(47,323)
Finance income/(costs) – IFRS 9 fair value accounting	—	9,606	—	—	9,606
Share-based payment expense	(3,066)	(6,256)	—	(4,628)	(13,950)
Depreciation of tangible assets	(1,319)	(1,518)	—	(1,510)	(4,347)
Amortization of ROU assets	—	(1,174)	—	(1,764)	(2,938)
Amortization of intangible assets	—	(2)	—	—	(2)
Taxation	—	—	—	(3,756)	(3,756)
Income/(loss) for the year	(64,753)	(49,927)	—	51,971	(62,709)
Other comprehensive income/(loss)	—	—	—	—	—
Total comprehensive income/(loss) for the year	(64,753)	(49,927)	—	51,971	(62,709)
Total comprehensive income/(loss) attributable to:					
Owners of the Company	(64,657)	(47,857)	—	51,956	(60,558)
Non-controlling interests	(96)	(2,069)	—	15	(2,151)
	December 31, 2021 $000s				
Consolidated Statements of Financial Position:					
Total assets	125,726	66,274	—	754,007	946,006
Total liabilities[1]	228,789	228,857	—	(95,787)	361,859
Net assets/(liabilities)	(103,063)	(162,584)	—	849,794	584,147

1 Parent Company and Other Includes eliminations of intercompany liabilities between the Parent Company and the reportable segments in the amount of $233.3 million.

4. Segment Information — continued

	2020				
	Internal $000s	Controlled Founded Entities $000s	Non-Controlled Founded Entities $000s	Parent Company & Other $000s	Consolidated $000s
Consolidated Statements of Comprehensive Income/(Loss)					
Contract revenue	5,297	990	—	2,054	8,341
Grant revenue	1,563	1,864	—	—	3,427
Total revenue	6,860	2,853	—	2,054	11,768
General and administrative expenses	(3,482)	(13,691)	—	(32,267)	(49,440)
Research and development expenses	(45,346)	(36,279)	—	(234)	(81,859)
Total Operating expenses	(48,828)	(49,970)	—	(32,500)	(131,299)
Other income/(expense):					
Gain/(loss) on investments held at fair value	—	—	—	232,674	232,674
Loss realized on sale of investments	—	—	—	(54,976)	(54,976)
Gain/(loss) on disposal of assets	(15)	(15)	—	—	(30)
Other income/(expense)	—	100	—	965	1,065
Other income/(expense)	(15)	85	—	178,662	178,732
Net finance income/(costs)	19	(5,204)	—	(930)	(6,115)
Share of net income/(loss) of associate accounted for using the equity method	—	—	—	(34,117)	(34,117)
Income/(loss) before taxes	(41,964)	(52,236)	—	113,170	18,969
(Loss)/income before taxes pre IFRS 9 fair value accounting, finance costs – subsidiary preferred shares, share-based payment expense, depreciation of tangible assets and amortization of intangible assets	(38,349)	(42,602)	—	121,644	40,694
Finance income/(costs) – subsidiary preferred shares	—	—	—	—	—
Finance income/(costs) – IFRS 9 fair value accounting	—	(4,351)	—	—	(4,351)
Share-based payment expense	(2,762)	(2,552)	—	(5,405)	(10,718)
Depreciation of tangible assets	(854)	(1,544)	—	(1,547)	(3,945)
Amortization of ROU assets	—	(1,186)	—	(1,523)	(2,709)
Amortization of intangible assets	—	(1)	—	—	(1)
Taxation	—	(1)	—	(14,400)	(14,401)
Income/(loss) for the year	(41,964)	(52,237)	—	98,769	4,568
Other comprehensive income/(loss)	—	—	—	469	469
Total comprehensive income/(loss) for the year	(41,964)	(52,237)	—	99,238	5,037
Total comprehensive income/(loss) attributable to:					
Owners of the Company	(41,773)	(51,026)	—	99,253	6,454
Non-controlling interests	(191)	(1,211)	—	(15)	(1,417)
	December 31, 2020 $000s				
Consolidated Statements of Financial Position:					
Total assets	89,214	67,433	—	833,347	989,994
Total liabilities	130,049	200,457	—	5,949	336,455
Net (liabilities)/assets	(40,835)	(133,023)	—	827,397	653,539

The proportion of net assets shown above that is attributable to non-controlling interest is disclosed in Note 18.

4. Segment Information — continued

	2019				
	Internal $000s	Controlled Founded Entities $000s	Non-Controlled Founded Entities $000s	Parent Company & Other $000s	Consolidated $000s
Consolidated Statements of Comprehensive Loss					
Contract revenue	7,077	1,474	—	137	8,688
Grant revenue	928	191	—	—	1,119
Total revenue	8,006	1,664	—	137	9,807
General and administrative expenses	(3,252)	(13,569)	(10,439)	(32,098)	(59,358)
Research and development expenses	(28,874)	(39,883)	(15,555)	(1,536)	(85,848)
Total operating expense	(32,126)	(53,451)	(25,994)	(33,634)	(145,206)
Other income/(expense):					
Gain on deconsolidation	—	—	—	264,409	264,409
Gain/(loss) on investments held at fair value	—	—	—	(37,863)	(37,863)
Gain/(loss) on disposal of assets	17	(39)	—	(60)	(82)
Gain on loss of significant influence	—	—	—	445,582	445,582
Other income/(expense)	—	166	—	(45)	121
Other income/(expense)	17	127	—	672,023	672,167
Net finance income/(costs)	—	(16,947)	(30,141)	941	(46,147)
Share of net income/(loss) of associate accounted for using the equity method	—	—	—	30,791	30,791
Impairment of investment in associate	—	—	—	(42,938)	(42,938)
Income/(loss) before taxes	(24,104)	(68,608)	(56,135)	627,320	478,474
(Loss)/income before taxes pre IAS 39 fair value accounting, finance costs – subsidiary preferred shares, share-based payment expense, depreciation of tangible assets and amortization of intangible assets	(23,698)	(47,188)	(21,873)	640,298	547,540
Finance income/(costs) – subsidiary preferred shares	—	107	(1,564)	(1)	(1,458)
Finance income/(costs) – IFRS 9 fair value accounting	—	(17,294)	(28,737)	(444)	(46,475)
Share-based payment expense	(19)	(1,664)	(3,543)	(9,242)	(14,468)
Depreciation of tangible assets	(390)	(1,517)	(207)	(1,114)	(3,228)
Amortization of ROU assets	—	(1,060)	(83)	(2,177)	(3,320)
Amortization of intangible assets	4	7	(128)	—	(117)
Taxation	—	(134)	(162)	(112,113)	(112,409)
Income/(loss) for the year	(24,104)	(68,741)	(56,297)	515,207	366,065
Other comprehensive income/(loss)	—	—	(10)	—	(10)
Total comprehensive income/(loss) for the year	(24,104)	(68,741)	(56,307)	515,207	366,055
Total comprehensive income/(loss) attributable to:					
Owners of the Company	(6,461)	(55,258)	(32,353)	515,207	421,133
Non-controlling interests	(17,643)	(13,483)	(23,953)	—	(55,079)

5. Investments held at fair value

Investments held at fair value include both unlisted and listed securities held by PureTech. These investments, which include interests in Akili, Vor, Karuna, Gelesis (other than the investment in common shares which is accounted for under the equity method), and other insignificant investments, are initially measured at fair value and are subsequently re-measured at fair value at each reporting date with changes in the fair value recorded through profit and loss. Interests in these investments were accounted for as shown below:

Investments held at fair value	$000's
Balance as of January 1, 2020	714,905
Sale of Karuna shares	(347,538)
Sale of resTORbio shares	(3,048)
Loss realised on sale of investments	(54,976)
Cash purchase of Gelesis preferred shares (please refer to Note 6)	10,000
Cash purchase of Vor preferred shares	1,150
Unrealized Loss – fair value through profit and loss	232,674
Balance as of January 1, 2021 before allocation of share in associate loss to long-term interest	553,167
Sale of Karuna shares	(218,125)
Loss realised on sale of investments (see below)	(20,925)
Cash purchase of Vor preferred shares	500
Unrealized gain – fair value through profit and loss	179,271
Balance as of December 31, 2021 before allocation of share in associate loss to long-term interest	**493,888**
Share of associate loss allocated to long-term interest (see Note 6)	(96,709)
Balance as of December 31, 2021 after allocation of share in associate loss to long-term interest[1]	**397,179**

1 Fair value of investments accounted for at fair value, does not take into consideration contribution from milestones that occurred after December 31, 2021, the value of the Group's consolidated Founded Entities (Vedanta, Follica, Sonde and Entrega), the Internal segment, or cash and cash equivalents.

Vor

On February 12, 2019, Vor completed a Series A-2 Preferred Shares financing round with PureTech and several new third party investors. The financing provided for the purchase of 62,819,866 shares of Vor Series A-2 Preferred Shares at the purchase price of $0.40 per share.

As a result of the issuance of Series A-2 preferred shares to third-party investors, PureTech's ownership percentage and corresponding voting rights dropped from 79.5 percent to 47.5 percent, and PureTech simultaneously lost control on Vor's Board of Directors, both of which triggered a loss of control over the entity. As of February 12, 2019, Vor was deconsolidated from the Group's financial statements, resulting in only the profits and losses generated by Vor through the deconsolidation date being included in the Consolidated Statement of Comprehensive Income/(Loss). While the Company no longer controlled Vor, it was concluded that PureTech still had significant influence over Vor by virtue of its large, albeit minority, ownership stake and its continued representation on Vor's Board of Directors. During the year ended December 31, 2019, the Company recognized a $6.4 million gain on the deconsolidation of Vor, which was recorded to the Gain on the deconsolidation of subsidiary line item in the Consolidated Statement of Comprehensive Income/(Loss).

As PureTech did not hold common shares in Vor upon deconsolidation and the preferred shares it held did not have equity-like features, PureTech had no basis to account for its investment in Vor under IAS 28. The preferred shares held by PureTech fell under the guidance of IFRS 9 and were treated as a financial asset held at fair value with changes in fair value recorded in the Consolidated Statement of Comprehensive Income/(Loss). The fair value of the preferred shares at deconsolidation was $12.0 million.

On February 12, 2020, PureTech participated in the second closing of Vor's Series A-2 Preferred Share financing. For consideration of $0.7 million, PureTech received 1,625,000 A-2 shares. On June 30, 2020, PureTech participated in the first closing of Vor's Series B Preferred Share financing. For consideration of $0.5 million, PureTech received 961,538 shares. Upon the conclusion of such Vor financings PureTech no longer had significant influence over Vor.

On January 8, 2021, PureTech participated in the second closing of Vor's Series B Preferred Share financing. For consideration of $0.5 million, PureTech received an additional 961,538 B Preferred shares.

On February 9, 2021, Vor closed its initial public offering (IPO) of 9,828,017 shares of its common stock at a price to the public of $18.00 per share. Subsequent to the closing, PureTech held 3,207,200 shares of Vor common stock, representing 8.6 percent of Vor common stock. Following its IPO, the valuation of Vor common stock is based on level 1 inputs in the fair value hierarchy. See Note 16.

During the years ended December 31, 2021, 2020 and 2019, the Company recognized a gain of $3.9 million, a gain of $19.1 million, and a gain of $0.6 million, respectively for the changes in the fair value of the investment that were recorded in the line item Gain/(loss) on investments held at fair value within the Consolidated Statement of Comprehensive Income/(Loss). Please refer to Note 16 for information regarding the valuation of these instruments.

5. Investments held at fair value — continued

Gelesis

As of July 1, 2019, Gelesis was deconsolidated from the Group's financial statements, resulting in only the profits and losses generated by Gelesis through the deconsolidation date being included in the Group's Consolidated Statement of Income/(Loss). At the date of deconsolidation, PureTech recorded a $156.0 million gain on the deconsolidation of Gelesis, which was recorded to the Gain on the deconsolidation of subsidiary line item in the Consolidated Statement of Income/(Loss). The preferred shares and warrants held by PureTech fall under the guidance of IFRS 9 and are treated as financial assets held at fair value, where changes to the fair value of the preferred shares and warrant are recorded through the Consolidated Statement of Income/(Loss). The fair value of the preferred shares and warrants at deconsolidation was $49.2 million. Please refer to Note 6 for information regarding the Company's investment in Gelesis as an associate.

On August 12, 2019, Gelesis issued a convertible promissory note to the Company in the amount of $2.0 million. On October 7, 2019, Gelesis issued an amended and restated convertible note (the "Gelesis Note") to the Company in the principal amount of up to $6.5 million. The Gelesis Note was payable in installments, with $2.0 million of the note drawn down upon execution of the original note in August 2019 and an additional $3.3 million and $1.2 million drawn down on October 7, 2019 and November 5, 2019, respectively. The Gelesis Note was convertible upon the occurrence of Gelesis' next qualified equity financing, or at the demand of the Company at any date after December 31, 2019. The Gelesis Note fell under the guidance of IFRS 9 and was treated as a financial asset held at fair with all movements to the value of the note recorded through the Consolidated Statement of Income/(Loss).

On December 5, 2019, Gelesis closed its Series 3 Growth Preferred Stock financing, at which point all outstanding principal and interest under the Gelesis Note converted into shares of Series 3 Growth Preferred Stock. In addition to the shares issued upon conversion of the Gelesis Note, PureTech purchased $8.0 million of Series 3 Growth Preferred Stock in the December financing.

On April 1, 2020, PureTech participated in the 2nd closing of Gelesis's Series 3 Growth Preferred Share financing. For consideration of $10.0 million, PureTech received 579,038 Series 3 Growth shares.

During the years ended December 31, 2021, 2020 and 2019, the Company recognized a gain of $34.6 million, a gain of $7.1 million and a loss of $18.7 million, respectively related to the change in the fair value of the preferred shares and warrants that was recorded in the line item Gain/(loss) on investments held at fair value within the Consolidated Statement of Comprehensive Income/(Loss). The loss recorded in 2019 was primarily as a result of the Gelesis Series 3 Growth financing, which was executed with terms that resulted in a decrease in fair value across all other classes of preferred shares. Please refer to Note 16 for information regarding the valuation of these instruments. Additionally, due to the equity method based investment in Gelesis being reduced to zero, the Group allocated a portion of its share in the net loss in Gelesis in the years ended December 31, 2021 and 2020, totaling $73.7 million and $23.0 million, respectively, to its preferred share and warrant investments in Gelesis, which are considered to be long-term interests in Gelesis. As of December 31, 2021, the investment in Gelesis preferred shares and warrants was entirely reduced to nil.

See Note 26 for subsequent event regarding the investment in Gelesis.

Karuna

2019

On March 15, 2019, Karuna completed the closing of a Series B Preferred Share financing with PureTech and several new third party investors. The financing provided for the purchase of 5,285,102 shares of Karuna Series B Preferred Shares at a purchase price of $15.14 per share.

As a result of the issuance of the preferred shares to third-party investors, PureTech's ownership percentage and corresponding voting rights related to Karuna dropped from 70.9 percent to 44.3 percent, and PureTech simultaneously lost control over Karuna's Board of Directors, both of which triggered a loss of control over the entity. As of March 15, 2019, Karuna was deconsolidated from the Group's financial statements, resulting in only the profits and losses generated by Karuna through the deconsolidation date being included in the Group's Consolidated Statement of Comprehensive Income/(Loss). At the date of deconsolidation, PureTech recorded a $102.0 million gain on the deconsolidation of Karuna, which was recorded to the Gain on the deconsolidation of subsidiary line item in the Consolidated Statement of Comprehensive Income/(Loss). While the Company no longer controls Karuna, it was concluded that PureTech still had significant influence over Karuna by virtue of its large, albeit minority, ownership stake and its continued representation on Karuna's Board of Directors. As PureTech had significant influence over Karuna, the entity was accounted for as an associate under IAS 28.

Upon the date of deconsolidation, PureTech held both preferred and common shares in Karuna and a warrant issued by Karuna to PureTech. The preferred shares and warrant held by PureTech fell under the guidance of IFRS 9 and were treated as financial assets held at fair value, and all movements to the value of preferred shares held by PureTech were recorded through the Consolidated Statement of Comprehensive Income/(Loss), in accordance with IFRS 9. The fair value of the preferred shares and warrant at deconsolidation was $72.4 million. Subsequent to deconsolidation, PureTech purchased an additional $5.0 million of Karuna Series B Preferred shares.

Due to the immaterial investment in common shares and overwhelmingly large losses by Karuna, the common share investment accounted for under the equity method was remeasured to nil immediately following both the deconsolidation and the exercise of the warrant in the first half of 2019.

5. Investments held at fair value — continued

On June 28, 2019, Karuna priced its IPO. PureTech's ownership percentage and corresponding voting rights related to Karuna dropped from 44.3 percent percent to 31.6 percent; however, PureTech retained significant influence due to its continued presence on the board and its large, albeit minority, equity stake in the company. Upon completion of the IPO, the Karuna preferred shares held by PureTech converted to common shares. In light of PureTech's common share holdings in Karuna and corresponding voting rights, PureTech had re-established a basis to account for its investment in Karuna under IAS 28. The preferred shares investment held at fair value was therefore reclassified to investment in associate upon completion of the conversion. During the year ended December 31, 2019 and up to June 28, 2019, the Company recognized a gain of $40.6 million that was recorded on the line item Gain on investments held at fair value within the Consolidated Statement of Comprehensive Income/(Loss) related to the preferred shares that increased in value between the date of deconsolidation and the date of Karuna's IPO.

As of December 2, 2019 it was concluded that the Company no longer exerted significant influence over Karuna owing to the resignation of the PureTech designee from Karuna's Board of Directors, with PureTech retaining no ability to reappoint representation. Furthermore, PureTech was not involved in any manner, or had any influence, on the management of Karuna, or on any of its decision making processes and had no ability to do so. As such, PureTech lost the power to participate in the financial and operating policy decisions of Karuna. As a result, Karuna was no longer deemed an Associate and did not meet the scope of equity method accounting, resulting in the investment being accounted for as an investment held at fair value. As of December 2, 2019 the Company's interest in Karuna was 28.4 percent. For the period of June 28, 2019 through December 2, 2019, PureTech's investment in Karuna was subject to equity method accounting. In accordance with IAS 28, the Company's investment was adjusted by the share of losses generated by Karuna (weighted average of 31.4 percent based on common stock ownership interest), which resulted in a net loss of associates accounted for using the equity method of $6.3 million during the year ended December 31, 2019.

Upon PureTech's loss of significant influence, the investment in Karuna was reclassified to an investment held at fair value. This change led PureTech to recognize a gain on loss of significant influence of $445.6 million that was recorded to the Consolidated Statement of Comprehensive Income/(Loss) on the line item Gain on loss of significant influence during the year ended December 31, 2019. The investment in Karuna after the recording of the gain on loss of significant influence was $557.2 million, which was reclassified from Investments in associates to Investments held at fair value. Additionally, from December 2, 2019 PureTech recorded a $0.7 million loss on the line item Gain/(loss) on investments held at fair value within the Consolidated Statement of Comprehensive Income/(Loss) for the year ended December 31, 2019.

2020 and 2021

On January 22, 2020, PureTech sold 2,100,000 shares of Karuna common shares for aggregate proceeds of $200.9 million. On May 26, 2020, PureTech sold an additional 555,500 Karuna common shares for aggregate proceeds of $45.0 million. On August 26, 2020, PureTech sold 1,333,333 common shares of Karuna for aggregate proceeds of $101.6 million. As a result of the sales, Puretech recorded a loss of $54.8 million attributable to blockage discount included in the sales price, to the line item Loss Realized on Sale of Investment within the Consolidated Statement of Comprehensive Income/(Loss). See below for gain recorded in respect of the change in fair value of the Karuna investment.

On February 9, 2021, the Group sold 1,000,000 common shares of Karuna for $118.0 million. Following the sale the Group held 2,406,564 common shares of Karuna, which represented 8.2 percent of Karuna common stock at the time of sale. On November 9, 2021, the group sold an additional 750,000 common shares of Karuna for $100.1 million. Following the sale the group holds 1,656,564 common shares of Karuna, which represented 5.6 percent at time of sale. As a result of the aforementioned sales, the Company recorded a loss of $20.9 million, attributable to blockage discount included in the sales price, to the line item Loss Realised on Sale of Investment within the Consolidated Statement of Comprehensive Income/(Loss) for the year ended December 31, 2021. See below for gain recorded in respect of the change in fair value of the Karuna investment.

During the years ended December 31, 2021 and 2020, the Company recognized a gain of $110.0 million and a gain of $191.2 million, respectively for the changes in the fair value of the Karuna investment that were recorded in the line item Gain/(loss) on investments held at fair value within the Consolidated Statement of Comprehensive Income/(Loss). As of December 31, 2021, PureTech continued to hold Karuna common shares or 5.6 percent of total outstanding Karuna common shares. Please refer to Note 16 for information regarding the valuation of these instruments.

Akili

As PureTech does not hold common shares in Akili and the preferred shares it holds do not have equity-like features, PureTech has no basis to account for its investment in Akili under IAS 28. The preferred shares held by PureTech Health fall under the guidance of IFRS 9 and are treated as a financial asset held at fair value and all movements to the value of the preferred shares are recorded through the Consolidated Statements of Comprehensive Income/(Loss), in accordance with IFRS 9.

On May 25, 2021, Akili completed its Series D financing for gross proceeds of $110.0 million in which Akili issued 13,053,508 Series D preferred shares. The Group did not participate in this round of financing and as a result, the Group's interest in Akili was reduced from 41.9 percent to 27.5 percent.

During the years ended December 31, 2021, 2020 and 2019, the Company recognized a gain of $32.2 million, a gain of $14.4 million, and a gain of $11.5 million, respectively for the changes in the fair value of the investment in Akili that was recorded on the line item Gain/(loss) on investments held at fair value within the Consolidated Statement of Comprehensive Income/(Loss). Please refer to Note 16 for information regarding the valuation of these instruments.

5. Investments held at fair value — continued

resTORbio

On November 15, 2019, resTORbio announced that top line data from the Protector 1 Phase 3 study evaluating the safety and efficacy of RTB101 in preventing clinically symptomatic respiratory illness in adults age 65 and older, did not meet its primary endpoint and the Company has stopped the development of RTB101 in this indication. As a result of ceasing the development of RTB101, resTORbio's share price witnessed a decline in price. In November and December 2019, PureTech Health sold 7,680,700 common shares of resTORbio for aggregate proceeds of $9.3 million. Immediately following the sale of common shares, PureTech Health held 2,119,696 common shares, or 5.8 percent, of resTORbio. During the year ended December 31, 2019 PureTech recorded a loss of $71.9 million for the adjustment to fair value of its investment in resTORbio to the Consolidated Statement of Comprehensive Income/(Loss) in the line item Gain/(loss) on investments held at fair value.

On April 30, 2020, PureTech sold its remaining 2,119,696 resTORbio common shares, for aggregate proceeds of $3.0 million. As a result of the sale, the Company recorded a loss of $0.2 million attributable to blockage discount included in the sales price, to the line item Loss realized on sale of investments within the Consolidated Statement of Comprehensive Income/(Loss). Additionally, during the year ended December 31, 2020, the Company recognized a gain of $0.1 million that was recorded on the line item Gain/(loss) on investments held at fair value within the Consolidated Statement of Comprehensive Income/(Loss).

Gain on deconsolidation

The following table summarizes the gain on deconsolidation recognized by the Company:

Year ended December 31,	**2021 $000s**	2020 $000s	2019 $000s
Gain on deconsolidation of Vor	—	—	6,357
Gain on deconsolidation of Karuna	—	—	102,038
Gain on deconsolidation of Gelesis [Note 6]	—	—	156,014
Total gain on deconsolidation	—	—	264,409

6. Investments in Associates

Gelesis

Gelesis was founded by PureTech and raised funding through preferred shares financings as well as issuances of warrants and loans. As of January 1, 2019, PureTech maintained control of Gelesis and Gelesis's financial results were fully consolidated in the Group's consolidated financial statements.

On July 1, 2019, the Gelesis Board of Directors was restructured, resulting in two of the three PureTech representatives resigning from the Board with PureTech retaining no ability to reappoint Directors to these board seats. As a result of this restructuring, PureTech lost control over Gelesis' Board of Directors, which triggered a loss of control over the entity. At the deconsolidation date, PureTech held a 25.2 percent voting interest in Gelesis. As of July 1, 2019, Gelesis was deconsolidated from the Group's financial statements, resulting in only the profits and losses generated by Gelesis through the deconsolidation date being included in the Group's Consolidated Statement of Income/(Loss) and Other Comprehensive Income/(Loss). At the date of deconsolidation, PureTech recorded a $156.0 million gain on the deconsolidation of Gelesis, which was recorded to the Gain on the deconsolidation of subsidiary line item in the Consolidated Statement of Comprehensive Income/(Loss). While the Company no longer controls Gelesis, it was concluded that PureTech still has significant influence over Gelesis by virtue of its large, albeit minority, ownership stake and its continued representation on Gelesis' Board of Directors and as such Gelesis is accounted for as an associate under IAS 28, starting at the date of deconsolidation.

Upon the date of deconsolidation, PureTech held preferred shares and common shares of Gelesis and a warrant issued by Gelesis to PureTech. PureTech's investment in common shares of Gelesis is subject to equity method accounting with an initial investment of $16.4 million. In accordance with IAS 28, PureTech's investment was adjusted by the share of profits and losses generated by Gelesis subsequent to the date of deconsolidation. See table below for the Group's share in the profits and losses of Gelesis for the periods presented.

The preferred shares and warrant held by PureTech fall under the guidance of IFRS 9 and are treated as financial assets held at fair value, where changes to the fair value of the preferred shares and warrant are recorded through the Consolidated Statement of Income/(Loss) and Other Comprehensive Income/(Loss), in accordance with IFRS 9. The fair value of the preferred shares and warrant at deconsolidation was $49.2 million. See Note 5 for changes in the fair value subsequent to deconsolidation date.

6. Investments in Associates — continued

Impairment loss for the year ended December 31, 2019

Following the issuance of the Gelesis Series 3 Preferred Shares at a higher valuation than the previous round with some favorable liquidation provisions primarily to PureTech and also to the other Series 3 preferred share investors, which resulted in adjustments to the fair values of other preferred shares, warrant classes and Gelesis common stock, the Company assessed the investment in common shares held in Gelesis for impairment. Management compared the recoverable amount of the investment to its carrying amount as of December 31, 2019, which resulted in an impairment loss to the Investment in Gelesis. The recoverable amount was estimated based on the fair value of the Gelesis common shares held by PureTech, which are considered to be within Level 3 of the fair value hierarchy. The costs of disposal are immaterial for the calculation of Gelesis investment's recoverable amount. The total fair value of common shares was determined utilizing a hybrid valuation approach with significant unobservable inputs within the PureTech valuation framework. The multi-scenario hybrid valuation approach utilized the recent transaction method within an option pricing framework and an IPO scenario within a probability-weighted-expected return framework to determine the value allocation for the common share class of Gelesis. The PWERM maintained a 75.0 percent probability of occurrence while the OPM maintained a 25.0 percent probability of occurrence. The probability weighted term to exit was 1.57 years. The discount rate utilized was 20.0 percent while the risk-free rate and volatility utilized were 1.62 percent and 56.0 percent, respectively.

The impairment loss amounted to $42.9 million and was recorded to Impairment of investment in associate within the Consolidated Statement of Comprehensive Income/(Loss) for the year ended December 31, 2019. As of December 31, 2019 the investment in Gelesis was $10.6 million, which is equal to the fair value of the common shares held by PureTech.

Years ended December 31, 2020 and 2021

During the year ended December 31, 2021 and 2020, the Group recorded its share in the losses of Gelesis. In 2020 the Group's investment in associates accounted for under the equity method was reduced to zero. Since the Group has investments in Gelesis warrants and preferred shares that are deemed to be Long-term interests, the Company continued recognizing its share in Gelesis losses while applying such losses to its preferred share and warrant investment in Gelesis accounted for as an investment held at fair value. In 2021, the total investment in Gelesis, including the Long-term interests, was reduced to zero. Since the Group did not incur legal or constructive obligations or made payments on behalf of Gelesis, the Group discontinued recognizing equity method losses. As of December 31, 2021, unrecognized equity method losses amounted to $38.1 million, which included $0.7 million of unrecognized other comprehensive loss.

During 2021, due to exercise of stock options into common shares in Gelesis the Group's equity interest in Gelesis was reduced from 47.9 percent at December 31, 2020 to 42.0 percent as of December 31, 2021. The gain resulting from the issuance of shares to third parties and the resulting reduction in the Group's share in the accumulated deficit of Gelesis under the equity method was fully offset by the unrecognized equity method losses.

Karuna

For the period of June 28, 2019, through December 2, 2019, PureTech's investment in Karuna was subject to equity method accounting. In accordance with IAS 28, the Company's investment was adjusted by the share of losses generated by Karuna (weighted average of 31.4 percent based on common stock ownership interest), which resulted in a net loss of $6.3 million during the year ended December 31, 2019, recorded in the line item Share of net income/(loss) of associates. Starting December 2, 2019, due to the loss of significant influence in Karuna on such date, the Company is accounting for the investment in Karuna as an investment held at fair value. See Note 5 for further detail on the Group's investment in Karuna.

The following table summarizes the activity related to the investment in associates balance for the years ended December 31, 2021, 2020 and 2019.

Investment in Associates	$000's
As of January 1, 2019	—
Reclassification of Karuna investment at initial public offering	118,006
Investment in Gelesis upon deconsolidation	16,444
Share of net loss of Karuna accounted for using the equity method	(6,345)
Share of net profit of Gelesis accounted for using the equity method	37,136
Impairment of investment in Gelesis	(42,938)
Reclassification of investment upon loss of significant influence	(111,661)
As of December 31, 2019 and January 1, 2020	10,642
Share of net loss in Gelesis	(34,117)
Share of other comprehensive income in Gelesis	469
Share of losses recorded against long term interests	23,006
As of December 31, 2020 and January 1, 2021	—
Share of net loss in Gelesis	(73,703)
Share of losses recorded against long term interests	73,703
As of December 31, 2021	—

6. Investments in Associates — continued

Summarized financial information

The following table summarizes the financial information of Gelesis as included in its own financial statements, adjusted for fair value adjustments at deconsolidation and differences in accounting policies. The table also reconciles the summarized financial information to the carrying amount of the Company's interest in Gelesis. The information for the year ended December 31, 2019, includes the results of Gelesis only for the period July 1, 2019 to December 31, 2019, as Gelesis was consolidated prior to this period.

As of and for the year ended December 31,	**2021 $000s**	2020 $000s
Percentage ownership interest	**42.0%**	47.9%
Non-current assets	**357,508**	372,184
Current assets	**66,092**	92,875
Non-current liabilities	**(120,786)**	(133,743)
Current liabilities	**(537,432)**	(300,748)
Non controlling interests and options issued to third parties	**(14,216)**	(6,577)
Net assets attributable to shareholders of Gelesis Inc.	**(248,834)**	23,989
Group's share of net assets	**(104,527)**	11,481
Goodwill	**7,211**	8,216
Impairment provision balance	**(37,495)**	(42,702)
Equity method losses recorded against Long-term Interests	**96,709**	23,006
Unrecognized equity method losses (*)	**38,101**	—
Investment in associate	**—**	—

	2021 $000s	2020 $000s	2019 $000s
Revenue	**11,185**	21,442	—
Income/(loss) from continuing operations (100%)	**(271,430)**	(71,157)	74,573
Total comprehensive income/(loss) (100%)	**(273,005)**	(70,178)	74,573
Group's share in net income (losses) – limited to net investment amount	**(73,703)**	(34,117)	37,136
Group's share of total comprehensive income (loss) – limited to net investment amount	**(73,703)**	(33,648)	37,136

(*) Unrecognized equity method losses includes unrecognized other comprehensive loss of $0.7 million.

See Note 26, for the completion of the business combination of Gelesis with Capstar Special Purpose Acquisition Corp ("Capstar") on January 13, 2022. The publicly traded company began trading on the New York Stock exchange under the ticker symbol "GLS" on January 14, 2022.

On December 30, 2021, PureTech signed a Backstop agreement with Capstar according to which PureTech committed to acquire Capstar class A common shares immediately prior to the closing of the business combination between Gelesis and Capstar, in case subsequent to the redemptions of Capstar shares being completed, the Available Funds, as defined in the agreement, are less than$15.0 million. Puretech committed to acquire two thirds of the necessary shares at $10 per share so that the Available Funds increase to $15.0 million. According to the Backstop agreement, in case PureTech is required to acquire any shares under the agreement, PureTech will receive an additional 1,322,500 class A common shares of Capstar (immediately prior to the closing of the business combination) at no additional consideration.

The Company determined that such agreement meets the definition of a derivative under IFRS 9 and as such should be recorded at fair value with changes in fair value recorded through profit and loss. For the year ended December 31, 2021 the changes in fair value were de minimis. The derivative was initially recorded at fair value adjusted to defer the day 1 gain equal to the difference between the fair value of $11.2 million and transaction price of zero on the effective date and as such was initially recorded at zero. The deferred gain is amortized to Other income (expense) in the Consolidated Statement of Income (loss) over the period from the effective date until settlement date. As such, the Group recognized $0.8 million income in 2021 for the portion of the deferred gain amortized in 2021.

On January 13, 2022, as part of the conclusion of the aforementioned Backstop agreement, the Group acquired 496,145 class A common shares of Capstar for $5.0 million and received an additional 1,322,500 common A shares of Capstar for no additional consideration.

7. Operating Expenses

Total operating expenses were as follows:

For the years ending December 31,	2021 $000s	2020 $000s	2019 $000s
General and administrative	**57,199**	49,440	59,358
Research and development	**110,471**	81,859	85,848
Total operating expenses	**167,671**	131,299	145,206

The average number of persons employed by the Group during the year, analyzed by category, was as follows:

For the years ending December 31,	2021	2020	2019
General and administrative	**52**	43	39
Research and development	**119**	95	90
Total	**171**	138	129

The aggregate payroll costs of these persons were as follows:

For the years ending December 31,	2021 $000s	2020 $000s	2019 $000s
General and administrative	**26,438**	22,943	24,468
Research and development	**28,950**	20,674	20,682
Total	**55,388**	43,616	45,150

Detailed operating expenses were as follows:

For the years ending December 31,	2021 $000s	2020 $000s	2019 $000s
Salaries and wages	**36,792**	29,403	27,703
Healthcare benefits	**2,563**	1,866	1,511
Payroll taxes	**2,084**	1,629	1,468
Share-based payments	**13,950**	10,718	14,468
Total payroll costs	**55,388**	43,616	45,150
Other selling, general and administrative expenses	**30,761**	26,497	34,890
Other research and development expenses	**81,521**	61,186	65,166
Total other operating expenses	**112,282**	87,683	100,056
Total operating expenses	**167,671**	131,299	145,206

Auditor's remuneration:

For the years ending December 31,	2021 $000s	2020 $000s	2019 $000s
Audit of these financial statements	**1,183**	1,145	870
Audit of the financial statements of subsidiaries	**312**	291	290
Audit of the financial statements of associate**	**571**	350	—
Audit-related assurance services*	**1,868**	490	163
Non-audit related services	**—**	173	778
Total	**3,934**	2,449	2,101

* 2021 – $468.2 thousand represents prepaid expenses related to an expected initial public offering of a subsidiary.

** Audit fees of $500.0 thousand and $350.0 thousand in respect of financial statements of associates for the years ended December 31, 2021, and 2020, respectively, are not included within the consolidated financial statements. Fees related to the audit of the financial statements of associates have been disclosed in respect of both 2021 and 2020 as these fees went towards supporting the audit opinion on the Group accounts. Such amounts were not previously disclosed in the 2020 financial statements.

Please refer to Note 8 for further disclosures related to share-based payments and Note 24 for management's remuneration disclosures.

8. Share-based Payments

Share-based payments includes stock options, restricted stock units ("RSUs") and performance-based RSUs in which the expense is recognized based on the grant date fair value of these awards, except for performance based RSUs to executives that are treated as liability awards where expense is recognized based on reporting date fair value up until settlement date.

Share-based Payment Expense

The Group share-based payment expense for the years ended December 31, 2021, 2020 and 2019, were comprised of charges related to the PureTech Health plc incentive stock and stock option issuances and subsidiary stock plans.

The following table provides the classification of the Group's consolidated share-based payment expense as reflected in the Consolidated Statement of Income/(Loss):

Year ended December 31,	2021 $000s	2020 $000s	2019 $000s
General and administrative	**9,310**	7,650	10,677
Research and development	**4,640**	3,068	3,791
Total	**13,950**	10,718	14,468

8. Share-based Payments — continued

Ariya Stock Option Exchange- 2019

In conjunction with the acquisition of the remaining minority interests of PureTech LYT (previously named Ariya Therapeutics, Inc.) on October 1, 2019 (Please refer to Note 18), PureTech Health exchanged subsidiary stock options previously granted to the co-inventors, advisors and employees of PureTech LYT with stock options to purchase 2,147,965 of the Company's ordinary shares under the PureTech Health Performance Share Plan. As this was an exchange of awards within the consolidated group, whereby the Company's stock options were replacing Ariya's stock options, the exchange was accounted for as a modification of the original award and the incremental fair value on the date of the replacement was amortized over the remaining vesting period of the awards.

The Performance Share Plan

In June 2015, the Group adopted the Performance Stock Plan ("PSP"). Under the PSP and subsequent amendments, awards of ordinary shares may be made to the Directors, senior managers and employees of, and other individuals providing services to the Company and its subsidiaries up to a maximum authorized amount of 10.0 percent of the total ordinary shares outstanding. The shares have various vesting terms over a period of service between two and four years, provided the recipient remains continuously engaged as a service provider.

The share-based awards granted under the PSP are generally equity settled (see cash settlements below) and expire 10 years from the grant date. As of December 31, 2021, the Company had issued share-based awards to purchase an aggregate of 21,756,187 shares under this plan.

RSUs

RSU activity for the years ended December 31, 2021, 2020 and 2019 is detailed as follows:

	Number of Shares/Units	Wtd Avg Grant Date Fair Value (GBP) (*)
Outstanding (Non-vested) at January 1, 2019	**6,598,783**	**1.29**
RSUs Granted in Period	1,775,569	2.95
Vested	(3,738,005)	1.10
Forfeited	—	—
Outstanding (Non-vested) at December 31, 2019 and January 1, 2020	**4,636,347**	**2.08**
RSUs Granted in Period	1,759,011	1.80
Vested	(2,781,687)	1.54
Forfeited	(191,089)	2.37
Outstanding (Non-vested) at December 31, 2020 and January 1, 2021	**3,422,582**	**2.46**
RSUs Granted in Period	2,195,133	2.15
Vested	(1,176,695)	2.93
Forfeited	(808,305)	2.25
Outstanding (Non-vested) at December 31, 2021	**3,632,715**	**1.91**

(*) 2021 – for liability awards based on fair value at reporting date.

Each RSU entitles the holder to one ordinary share on vesting and the RSU awards are generally based on a cliff vesting schedule over a one to three-year requisite service period in which the Company recognizes compensation expense for the RSUs. Following vesting, each recipient will be required to make a payment of one pence per ordinary share on settlement of the RSUs. Vesting of the majority of the RSUs is subject to the satisfaction of performance and market conditions. The grant date fair value of market condition awards that are treated as equity settled awards is measured to reflect such conditions and there is no true-up for differences between expected and actual outcomes. For liability settled awards, see below.

The Company recognizes the estimated fair value of performance-based awards as share-based compensation expense over the performance period based upon its determination of whether it is probable that the performance targets will be achieved. The Company assesses the probability of achieving the performance targets at each reporting period. Cumulative adjustments, if any, are recorded to reflect subsequent changes in the estimated outcome of performance-related conditions.

The fair value of the market and performance-based awards is based on the Monte Carlo simulation analysis utilizing a Geometric Brownian Motion process with 100,000 simulations to value those shares. The model considers share price volatility, risk-free rate and other covariance of comparable public companies and other market data to predict distribution of relative share performance.

The performance and market conditions attached to the RSU awards are based on the achievement of total shareholder return ("TSR"), based on the achievement of absolute TSR targets, and to a lesser extent based on TSR as compared to the FTSE 250 Index, and the MSCI Europe Health Care Index. The remaining portion is based on the achievement of strategic targets. The RSU award performance criteria have changed over time as the criteria is continually evaluated by the Group's Remuneration Committee.

8. Share-based Payments — continued

In 2017, the Company granted certain executives RSUs that vested based on the service, market and performance conditions, as described above. The vesting of all RSUs was achieved by December 31, 2019 where all service, market and performance conditions were met. The remuneration committee of PureTech's Board of Directors approved the achievement of the vesting conditions as of December 31, 2019 and reached the decision during the year ended December 31, 2020 to cash settle the 2017 RSUs. The settlement value was determined based on the 3 day average closing price of the shares. The settlement value was $12.5 million (which after deducting tax withheld on behalf of recipients amounted to $7.2 million). The settlement value did not exceed the fair value at settlement date and as such the cash settlement was treated as an equity transaction in the financial statements as of and for the year ended December 31, 2020, whereby the full repurchase cash settlement amount was charged to equity in Other reserves.

Similarly in 2018, the Company granted certain executives RSUs that vested based on service, market and performance conditions, as described above. The vesting of all RSUs was achieved by December 31, 2020 where all service, market and performance conditions were met. In February 2021 the remuneration committee of PureTech's board of directors approved the achievement of the vesting conditions as of December 31, 2020 and on May 28, 2021 reached the decision to cash settle RSUs to certain employees while others were issued shares. The settlement value was determined based on the three day average closing price of the shares. The settlement value was $10.7 million (which after deducting tax withheld on behalf of recipients amounted to $6.4 million). The settlement value did not exceed the fair value at settlement date and as such the cash settlement was treated as an equity transaction, whereby the full repurchase cash settlement amount was charged to equity in Other reserves in the financial statements as of and for the year ended December 31, 2021.

Following the different cash settlements, the Company concluded that although the remaining RSUs are to be settled by shares according to their respective agreements, and any cash settlement is at the Company's discretion, due to past practice of cash settlement to multiple employees, some for multiple years, these RSUs to the company executives should be treated as liability awards and as such adjusted to fair value at every reporting date with changes in fair value recorded in earnings as stock based compensation expense.

Consequently, the Company reclassified $1.9 million from equity to other non-current liabilities and $4.8 million from equity to other payables equal to the fair value of the awards at the date of reclassification. The Company treated the excess of the fair value at the reclassification date over the grant date fair value of the RSUs (for the portion of the vesting period that has already elapsed) in the amount of $2.9 million as an equity transaction. Therefore the full amount of the liability at reclassification was recorded as a charge to equity. The changes in fair value of the liability from reclassification date to balance sheet date or settlement date are recorded as stock-based compensation expense in the Consolidated Statement of Comprehensive Income (loss).

The Company incurred share-based payment expenses for performance, market and service based RSUs of $1.5 million (including $0.6 million expense in respect of RSU liability awards), $5.7 million and $2.2 million for the years ended December 31, 2021, 2020 and 2019, respectively. The decrease in the share based compensation expense in respect of the RSUs for the year ended December 31, 2021, as compared to the year ended December 31, 2020 is due to reduction in the fair value of the liability awards as compared to their value at the date the awards were reclassified from equity awards to liability awards, as well as forfeitures of certain awards due to unexpected terminations of RSU holders.

As of December 31, 2021, the carrying amount of the RSU liability awards was $7.4 million ($4.7 million current; $2.7 million non current), out of which $4.6 million related to awards that have met all their performance and market conditions.

Stock Options

Stock option activity for the years ended December 31, 2021, 2020 and 2019, is detailed as follows:

	Number of Options	Wtd Average Exercise Price (GBP)	Wtd Average of remaining contractual term (in years)	Wtd Average Stock Price at Exercise (GBP)
Outstanding at January 1, 2019	**5,075,734**	**1.40**	**8.78**	
Granted	3,634,183	0.84		
Exercised	(237,090)	1.98		2.81
Forfeited	—	—		
Options Exercisable at December 31, 2019 and January 1, 2020	**4,349,921**	**0.93**	**8.34**	
Outstanding at December 31, 2019 and January 1, 2020	**8,472,827**	**1.16**	**8.55**	
Granted	4,076,982	3.14		
Exercised	(514,410)	1.52		2.88
Forfeited	(1,119,313)	1.88		
Options Exercisable at December 31, 2020 and January 1, 2021	**5,447,405**	**0.98**	**7.46**	
Outstanding at December 31, 2020 and January 1, 2021	**10,916,086**	**1.81**	**8.38**	
Granted	5,424,000	3.34		
Exercised	(2,238,187)	0.70		3.63
Forfeited	(687,781)	2.53		
Options Exercisable at December 31, 2021	**4,773,873**	**1.42**	**6.50**	
Outstanding at December 31, 2021	**13,414,118**	**2.58**	**8.29**	

8. Share-based Payments — continued

The fair value of the stock options awarded by the Company was estimated at the grant date using the Black-Scholes option valuation model, considering the terms and conditions upon which options were granted, with the following weighted-average assumptions:

At December 31,	**2021**	2020	2019
Expected volatility	**41.05%**	41.25%	35.68%
Expected terms (in years)	**6.16**	6.11	5.81
Risk-free interest rate	**1.06%**	0.53%	1.85%
Expected dividend yield	**—**	—	—
Grant date fair value	**$1.87**	$1.72	$2.23

The Company incurred share-based payment expense for the stock options of $6.2 million, $2.1 million and $9.2 million for the years ended December 31, 2021, 2020 and 2019, respectively. The increase in expense for the year ended December 31, 2021, as compared to the year ended December 31, 2020, is due to the new grants granted in 2021. The significant decrease for the year ended December 31, 2020, as compared to the year ended December 31, 2019, is largely attributable to the exchange of the Ariya awards with the Company's stock options in the year ended December 31, 2019, which resulted in an additional expense recorded in such year, as described above.

For shares outstanding as of December 31, 2021, the range of exercise prices is detailed as follow:

Range of Exercise Prices (GBP)	Options Outstanding	Wtd Average Exercise Price (GBP)	Wtd Average of remaining contractual term (in years)
0.01	842,762	—	7.76
1.00 to 2.00	3,521,839	1.42	5.81
2.00 to 3.00	1,251,017	2.47	8.35
3.00 to 4.00	7,798,500	3.39	9.46
Total	**13,414,118**	**2.58**	**8.29**

Subsidiary Plans

Certain subsidiaries of the Group have adopted stock option plans. A summary of stock option activity by number of shares in these subsidiaries is presented in the following table:

	Outstanding as of January 1, 2021	**Granted During the Year**	**Exercised During the Year**	**Expired During the Year**	**Forfeited During the Year**	**Outstanding as of December 31, 2021**
Alivio	**3,888,168**	**197,398**	**(2,373,750)**	**(506,260)**	**(1,205,556)**	**—**
Entrega	**962,000**	**—**	**(525,000)**	**(87,500)**	**—**	**349,500**
Follica	**1,309,040**	**1,383,080**	**—**	**(6,000)**	**—**	**2,686,120**
Sonde	**2,192,834**	**—**	**—**	**(51,507)**	**(92,323)**	**2,049,004**
Vedanta	**1,741,888**	**451,532**	**(52,938)**	**(76,491)**	**(72,354)**	**1,991,637**

	Outstanding as of January 1, 2020	Granted During the Year	Exercised During the Year	Expired During the Year	Forfeited During the Year	Outstanding as of December 31, 2020
Alivio	3,698,244	189,924	—	—	—	3,888,168
Entrega	972,000	—	—	—	(10,000)	962,000
Follica	1,309,040	—	—	—	—	1,309,040
Sonde	1,829,004	363,830	—	—	—	2,192,834
Vedanta	1,450,100	493,951	(813)	—	(201,350)	1,741,888

8. Share-based Payments — continued

	Outstanding as of January 1, 2019	Granted During the Year	Exercised During the Year	Expired During the Year	Forfeited During the Year	Outstanding as of December 31, 2019
Gelesis	3,681,732	—	—	(110,386)	(3,571,346)[1]	—
Alivio	2,393,750	1,329,494	(3,125)	—	(21,875)	3,698,244
PureTech LYT	2,180,000	—	—	—	(2,180,000)[2]	—
Commense	540,416	—	—	—	(540,416)	—
Entrega	914,000	58,000	—	—	—	972,000
Follica	1,229,452	79,588	—	—	—	1,309,040
Karuna	1,949,927	—	—	—	(1,949,927)[1]	—
Sonde	22,500	1,806,504	—	—	—	1,829,004
Vedanta	1,373,750	154,193	—	—	(77,843)	1,450,100

1 These shares represent the options outstanding on the date of deconsolidation of Karuna and Gelesis.
2 These shares represent the options outstanding on the date of exchange to PureTech stock options.

The weighted-average exercise prices and remaining contractual life for the options outstanding as of December 31, 2021, were as follows:

Outstanding at December 31, 2021	Number of options	Weighted-average exercise price $	Weighted-average contractual life outstanding
Alivio	—	—	**0**
Entrega	**349,500**	**1.88**	**4.62**
Follica	**2,686,120**	**1.39**	**7.28**
Sonde	**2,049,004**	**0.20**	**7.71**
Vedanta	**1,991,637**	**13.42**	**5.92**

The weighted average exercise prices for the options granted for the years ended December 31, 2021, 2020 and 2019, were as follows:

For the years ended December 31,	2021 $	2020 $	2019 $
Alivio	—	0.47	0.49
Follica	**1.86**	—	0.03
Sonde	—	0.18	0.20
Vedanta	**19.69**	19.59	19.13

The weighted average exercise prices for options forfeited during the year ended December 31, 2021, were as follows:

Forfeited during the year ended December 31, 2021	Number of options	Weighted-average exercise price $
Alivio	**1,205,556**	**0.48**
Sonde	**92,323**	**0.18**
Vedanta	**72,354**	**19.36**

The weighted average exercise prices for options exercised during the year ended December 31, 2021, were as follows:

Exercised during the year ended December 31, 2021	Number of options	Weighted-average exercise price $
Alivio	**2,373,750**	**0.03**
Entrega	**525,000**	**0.03**
Vedanta	**52,938**	**0.96**

8. Share-based Payments — continued

The weighted average exercise prices for options exercisable as of December 31, 2021, were as follows:

Exercisable at December 31, 2021	Number of Options	Weighted-average exercise price $	Exercise Price Range $
Alivio	—	—	—
Entrega	**349,500**	**1.88**	**0.03-2.36**
Follica	**2,686,120**	**1.01**	**0.03-1.86**
Sonde	**2,049,004**	**0.20**	**0.13-0.20**
Vedanta	**1,991,637**	**9.64**	**0.02-19.94**

Significant Subsidiary Plans

Vedanta 2010 Stock Incentive Plan

In 2010, the Board of Directors for Vedanta approved the 2010 Stock Incentive Plan (the "Vedanta Plan"). Through subsequent amendments, as of December 31, 2021, it allowed for the issuance of 2,797,055 share-based compensation awards through incentive share options, nonqualified share options, and restricted shares to employees, Directors, and nonemployees providing services to Vedanta. At December 31, 2021, 747,270 shares remained available for issuance under the Vedanta Plan.

The options granted under Vedanta Plan are equity settled and expire 10 years from the grant date. Typically, the awards vest in four years but vesting conditions can vary based on the discretion of Vedanta's Board of Directors.

Options granted under the Vedanta Plan are exercisable at a price per share not less than the fair market value of the underlying ordinary shares on the date of grant. The estimated fair value of options, including the effect of estimated forfeitures, is recognized over the options' vesting period.

The fair value of the stock option grants has been estimated at the date of grant using the Black-Scholes option pricing model with the following range of assumptions:

Assumption/Input	**2021**	2020	2019
Expected award life (in years)	**6.00-7.11**	6.00-10.00	5.86-6.07
Expected award price volatility	**88.05%-88.59%**	89.24%-95.46%	89.24%-95.46%
Risk free interest rate	**0.96%-1.32%**	0.32%-0.87%	1.73%-1.88%
Expected dividend yield	**—**	—	—
Grant date fair value	**$13.84-$16.23**	$13.09-$16.54	$14.12-$15.61
Share price at grant date	**$19.00-$21.35**	$19.59	$18.71-$19.94

Vedanta incurred share-based compensation expense of $5.4 million, $2.4 million and $1.7 million for the years ended December 31, 2021, 2020 and 2019, respectively.

Other Plans

The stock compensation expense under plans at other subsidiaries of the Group not including Vedanta amounted to $0.84 million, $0.42 million and $0.01 million for the years ended December 31, 2021, 2020 and 2019, respectively.

9. Finance Cost, net

The following table shows the breakdown of finance income and costs:

For the years ended December 31,	**2021 $000s**	2020 $000s	2019 $000s
Finance income			
Interest income from financial assets	**214**	1,183	4,362
Total finance income	**214**	1,183	4,362
Finance costs			
Contractual interest expense on notes payable	**(1,031)**	(96)	(149)
Interest expense on other borrowings	**(1,502)**	(496)	—
Interest expense on lease liability	**(2,181)**	(2,354)	(2,495)
Gain/(loss) on foreign currency exchange	**(56)**	—	68
Total finance cost – contractual	**(4,771)**	(2,946)	(2,576)
Gain/(loss) from change in fair value of warrant liability	**1,419**	(117)	(11,890)
Gain/(loss) from change in fair value of preferred shares	**8,362**	(4,234)	(34,585)
Gain/(loss) from change in fair value of convertible debt	**(175)**	—	—
Total finance income/(costs) – fair value accounting	**9,606**	(4,351)	(46,475)
Total finance costs – subsidiary preferred shares	**—**	—	(1,458)
Total finance income/(costs)	**9,606**	(4,351)	(47,933)
Finance income/(costs), net	**5,050**	(6,115)	(46,147)

10. Earnings/(Loss) per Share

The basic and diluted loss per share has been calculated by dividing the income/(loss) for the period attributable to ordinary shareholders by the weighted average number of ordinary shares outstanding during the years ended December 31, 2021, 2020 and 2019, respectively. During the year ended December 31, 2021 the Company incurred a net loss and therefore all outstanding potential securities were considered anti-dilutive. The amount of potential securities that were excluded from the calculation amounted to 6,553,905 shares.

Earnings/(Loss) Attributable to Owners of the Company:

	2021		2020		2019	
	Basic $000s	**Diluted $000s**	Basic $000s	Diluted $000s	Basic $000s	Diluted $000s
Income/(loss) for the year, attributable to the owners of the Company	**(60,558)**	**(60,558)**	5,985	5,985	421,144	421,144
Income/(loss) attributable to ordinary shareholders	**(60,558)**	**(60,558)**	5,985	5,985	421,144	421,144

Weighted-Average Number of Ordinary Shares:

	2021		2020		2019	
	Basic	**Diluted**	Basic	Diluted	Basic	Diluted
Issued ordinary shares at January 1,	**285,885,025**	**285,885,025**	285,370,619	285,370,619	282,493,867	282,493,867
Effect of shares issued	**705,958**	**705,958**	233,048	233,048	932,600	932,600
Effect of dilutive shares (please refer to Note 8)	**—**	**—**	—	7,252,246	—	8,355,866
Weighted average number of ordinary shareholders at December 31,	**286,590,983**	**286,590,983**	285,603,667	292,855,913	283,426,467	291,782,333

Earnings/(Loss) per Share:

	2021		2020		2019	
	Basic $	**Diluted $**	Basic $	Diluted $	Basic $	Diluted $
Basic and diluted earnings/(loss) per share	**(0.21)**	**(0.21)**	0.02	0.02	1.49	1.44

11. Property and Equipment

Cost	Laboratory and Manufacturing Equipment $000s	Furniture and Fixtures $000s	Computer Equipment and Software $000s	Leasehold Improvements $000s	Construction in process $000s	Total $000s
Balance as of January 1, 2020	7,385	1,452	1,508	17,656	646	28,647
Additions, net of transfers	1,536	—	51	399	3,347	5,332
Disposals	(642)	—	(40)	—	—	(682)
Reclassifications	141	—	—	—	(141)	—
Balance as of December 31, 2020	8,420	1,452	1,519	18,054	3,852	33,297
Additions, net of transfers	1,424	—	92	183	6,723	8,422
Disposals	(323)	—	(282)	—	—	(605)
Reclassifications	2,211	—	—	248	(2,459)	—
Balance as of December 31, 2021	**11,733**	**1,452**	**1,329**	**18,485**	**8,116**	**41,115**

Accumulated depreciation and impairment loss	Laboratory and Manufacturing Equipment $000s	Furniture and Fixtures $000s	Computer Equipment and Software $000s	Leasehold Improvements $000s	Construction in process $000s	Total $000s
Balance as of January 1, 2020	(2,968)	(239)	(1,030)	(2,955)	—	(7,192)
Depreciation	(1,572)	(215)	(297)	(1,860)	—	(3,944)
Disposals	576	—	40	—	—	616
Balance as of December 31, 2020	(3,965)	(454)	(1,287)	(4,815)	—	(10,520)
Depreciation	(1,973)	(208)	(174)	(1,991)	—	(4,346)
Disposals	251	—	271	—	—	522
Balance as of December 31, 2021	**(5,686)**	**(663)**	**(1,190)**	**(6,806)**	**—**	**(14,344)**

Property and Equipment, net	Laboratory and Manufacturing Equipment $000s	Furniture and Fixtures $000s	Computer Equipment and Software $000s	Leasehold Improvements $000s	Construction in process $000s	Total $000s
Balance as of December 31, 2020	4,456	998	232	13,239	3,852	22,777
Balance as of December 31, 2021	**6,047**	**790**	**139**	**11,679**	**8,116**	**26,771**

Depreciation of property and equipment is included in the General and administrative expenses and Research and development expenses line items in the Consolidated Statements of Comprehensive Income/(Loss). The Company recorded depreciation expense of $4.3 million, $3.9 million and $3.2 million for the years ended December 31, 2021, 2020 and 2019, respectively.

12. Intangible Assets

Intangible assets consist of licenses of intellectual property acquired by the Group through various agreements with third parties and are recorded at the value of the consideration transferred. Information regarding the cost and accumulated amortization of intangible assets is as follows:

Cost	Licenses $000s
Balance as of January 1, 2020	625
Additions	275
Balance as of December 31, 2020	900
Additions	90
Balance as of December 31, 2021	**990**

Accumulated amortization	Licenses $000s
Balance as of January 1, 2020	—
Amortization	(1)
Balance as of December 31, 2020	(1)
Amortization	(2)
Balance as of December 31, 2021	**(3)**

Intangible assets, net	Licenses $000s
Balance as of December 31, 2020	899
Balance as of December 31, 2021	**987**

Substantially all the intangible asset licenses represent in-process-research-and-development assets since they are still being developed and are not ready for their intended use. As such, these assets are not yet amortized but tested for impairment annually.

The Company tested such assets for impairment as of balance sheet date and concluded that none were impaired.

Amortization expense was included in the Research and development expenses line item in the accompanying Consolidated Statements of Comprehensive Income/(Loss). Amortization expense, recorded using the straight-line method, was approximately $0.0 million, $0.0 million and $0.1 million for the years ended December 31, 2021 2020 and 2019, respectively.

13. Other Financial Assets

Other financial assets consist of restricted cash held, which represents amounts that are reserved as collateral against letters of credit with a bank that are issued for the benefit of a landlord in lieu of a security deposit for office space leased by the Group. Information regarding restricted cash was as follows:

As of December 31,	**2021 $000s**	2020 $000s
Restricted cash	**2,124**	2,124
Total other financial assets	**2,124**	2,124

14. Equity

Total equity for PureTech as of December 31, 2021, and 2020, was as follows:

Equity	**December 31, 2021 $000s**	December 31, 2020 $000s
Share capital, £0.01 par value, issued and paid 287,796,585 and 285,885,025 as of December 31, 2021 and 2020, respectively	**5,444**	5,417
Merger Reserve	**138,506**	138,506
Share premium	**289,303**	288,978
Translation reserve	**469**	469
Other reserves	**(40,077)**	(24,050)
Retained earnings/(accumulated deficit)	**199,871**	260,429
Equity attributable to owners of the Group	**593,515**	669,748
Non-controlling interests	**(9,368)**	(16,209)
Total equity	**584,147**	653,539

Changes in share capital and share premium relate primarily to incentive options exercises during the period.

Shareholders are entitled to vote on all matters submitted to shareholders for a vote. Each ordinary share is entitled to one vote. Each ordinary share is entitled to receive dividends when and if declared by the Company's Directors. The Company has not declared any dividends in the past.

On June 18, 2015, the Company acquired the entire issued share capital of PureTech LLC in return for 159,648,387 Ordinary Shares. This was accounted for as a common control transaction at cost. It was deemed that the share capital was issued in line with movements in share capital as shown prior to the transaction taking place. In addition, the merger reserve records amounts previously recorded as share premium.

Other reserves comprise the cumulative credit to share-based payment reserves corresponding to share-based payment expenses recognized through Consolidated Statements of Comprehensive Income/(Loss), settlements of vested share based payment awards as well as other additions that flow directly through equity such as the excess or deficit from changes in ownership of subsidiaries while control is maintained by the Group.

15. Subsidiary Preferred Shares

Preferred shares issued by subsidiaries and affiliates often contain redemption and conversion features that are assessed under IFRS 9 in conjunction with the host preferred share instrument. This balance represents subsidiary preferred shares issued to third parties.

The subsidiary preferred shares are redeemable upon the occurrence of a contingent event, other than full liquidation of the Company, that is not considered to be within the control of the Company. Therefore these subsidiary preferred shares are classified as liabilities. These liabilities are measured at fair value through profit and loss. The preferred shares are convertible into ordinary shares of the subsidiaries at the option of the holder and mandatorily convertible into ordinary shares upon a subsidiary listing in a public market at a price above that specified in the subsidiary's charter or upon the vote of the holders of subsidiary preferred shares specified in the charter. Under certain scenarios the number of ordinary shares receivable on conversion will change and therefore, the number of shares that will be issued is not fixed. As such the conversion feature is considered to be an embedded derivative that normally would require bifurcation. However, since the preferred share liabilities are measured at fair value through profit and loss, as mentioned above, no bifurcation is required.

The preferred shares are entitled to vote with holders of common shares on an as converted basis.

The Group recognized the preferred share balance upon the receipt of cash financing or upon the conversion of notes into preferred shares at the amount received or carrying balance of any notes and derivatives converted into preferred shares.

The balance as of December 31, 2021 and 2020, represents the fair value of the instruments for all subsidiary preferred shares. The following summarizes the subsidiary preferred share balance:

As of December 31,	**2021 $000s**	2020 $000s
Entrega	**669**	1,291
Follica	**11,191**	12,792
Sonde	**13,362**	12,821
Vedanta Biosciences	**148,796**	92,068
Total subsidiary preferred share balance	**174,017**	118,972

15. Subsidiary Preferred Shares — continued

As is customary, in the event of any voluntary or involuntary liquidation, dissolution or winding up of a subsidiary, the holders of subsidiary preferred shares which are outstanding shall be entitled to be paid out of the assets of the subsidiary available for distribution to shareholders and before any payment shall be made to holders of ordinary shares. A merger, acquisition, sale of voting control or other transaction of a subsidiary in which the shareholders of the subsidiary immediately before the transaction do not own a majority of the outstanding shares of the surviving company shall be deemed to be a liquidation event. Additionally, a sale, lease, transfer or other disposition of all or substantially all of the assets of the subsidiary shall also be deemed a liquidation event.

As of December 31, 2021 and 2020, the minimum liquidation preference reflects the amounts that would be payable to the subsidiary preferred holders upon a liquidation event of the subsidiaries, which is as follows:

As of December 31,	**2021 $000s**	2020 $000s
Entrega	**2,216**	2,216
Follica	**6,405**	6,405
Sonde	**12,000**	12,000
Vedanta Biosciences	**149,568**	86,161
Total minimum liquidation preference	**170,189**	106,782

For the years ended December 31, 2021 and 2020, the Group recognized the following changes in the value of subsidiary preferred shares:

	$000s
Balance as of January 1, 2020	100,989
Issuance of new preferred shares	13,750
Increase in value of preferred shares measured at fair value	4,234
Balance as of January 1, 2021	118,972
Issuance of new preferred shares - financing cash flow	37,610
Conversion of convertible notes into preferred shares - non cash financing activity	25,797
decrease in value of preferred shares measured at fair value - finance costs (income)	(8,362)
Balance as December 31, 2021	**174,017**

2021

On July 21, 2021 Vedanta closed a Series D financing in which Vedanta issued 2,387,675 Preferred D shares for consideration of $68.4 million. From such consideration of $68.4 million, $25.8 million was received from Pfizer through conversion of its convertible note (see Note 17) and $5.0 million was received from PureTech in exchange for 174,520 Preferred D shares. The amount received from PureTech was eliminated in the consolidated financial statements.

2020

In January 2020 and April 2020, Sonde Health issued and sold shares of Series A-2 preferred shares for aggregate proceeds of $4.8 million, of which none was contributed by PureTech.

In April 2020 and July 2020, Vedanta issued and sold shares of Series C-2 preferred shares for aggregate proceeds of $9.0 million, of which none was contributed by PureTech.

16. Financial Instruments

The Group's financial instruments consist of financial liabilities, including preferred shares, convertible notes, warrants and loans payable, as well as financial assets classified as assets held at fair value.

Fair Value Process

For financial instruments measured at fair value under IFRS 9 the change in the fair value is reflected through profit and loss. Using the guidance in IFRS 13, the total business enterprise value and allocable equity of each entity being valued was determined using a discounted cash flow income approach, replacement cost/asset approach, market/asset – PWERM approach, or market backsolve approach through a recent arm's length financing round. The approaches, in order of strongest fair value evidence, are detailed as follows:

Valuation Method	Description
Market – Backsolve	The market backsolve approach benchmarks the original issue price (OIP) of the company's latest funding transaction as current value.
Market/Asset – PWERM	Under a PWERM, the company value is based upon the probability-weighted present value of expected future investment returns, considering each of the possible future outcomes available to the enterprise. An Asset approach may be included as an expected future outcome within the PWERM method. Possible future outcomes can include IPO scenarios, potential SPAC transactions, merger and acquisition transactions as well as other similar exit transactions of the investee.
Income Based – DCF	The income approach is used to estimate fair value based on the income streams, such as cash flows or earnings, that an asset or business can be expected to generate.
Asset/Cost	The asset/cost approach considers reproduction or replacement cost as an indicator of value.

As of December 31, 2021 and 2020, at each measurement date, the total fair value of preferred shares and warrants, including embedded conversion rights that are not bifurcated, was determined using the following allocation methods: option pricing model ("OPM"), Probability-Weighted Expected Return Method ("PWERM"), or Hybrid allocation framework. The methods are detailed as follows:

Allocation Method	Description
OPM	The OPM model treats preferred stock as call options on the enterprise's equity value, with exercise prices based on the liquidation preferences of the preferred stock.
PWERM	Under a PWERM, share value is based upon the probability-weighted present value of expected future investment returns, considering each of the possible future outcomes available to the enterprise, as well as the rights of each share class.
Hybrid	The hybrid method ("HM") is a combination of the PWERM and OPM. Under the hybrid method, multiple liquidity scenarios are weighted based on the probability of the scenarios occurrence, similar to the PWERM, while also utilizing the OPM to estimate the allocation of value in one or more of the scenarios.

Valuation policies and procedures are regularly monitored by the Company's finance group. Fair value measurements, including those categorized within Level 3, are prepared and reviewed on their issuance date and then on an annual basis for reasonableness and compliance with the fair value measurements guidance under IFRS. The Group measures fair values using the following fair value hierarchy that reflects the significance of the inputs used in making the measurements:

Fair Value Hierarchy Level	Description
Level 1	Inputs that are quoted market prices (unadjusted) in active markets for identical instruments.
Level 2	Inputs other than quoted prices included within Level 1 that are observable either directly (i.e. as prices) or indirectly (i.e. derived from prices).
Level 3	Inputs that are unobservable. This category includes all instruments for which the valuation technique includes inputs not based on observable data and the unobservable inputs have a significant effect on the instrument's valuation.

Whilst the Group considers the methodologies and assumptions adopted in fair value measurements as supportable, reasonable and robust, because of the inherent uncertainty of valuation, those estimated values may differ significantly from the values that would have been used had a ready market for the investment existed.

COVID-19 Consideration

At December 31, 2021, the Group assessed certain key assumptions within the valuation of its unquoted instruments and considered the impact of the COVID-19 pandemic on all unobservable inputs (Level 3). The assumptions considered with respect to COVID-19 included but were not limited to the following: exit scenarios and timing, discount rates, revenue assumptions as well as volatilities. The Group views any impact of the COVID-19 pandemic on its unquoted instruments as immaterial as of December 31, 2021.

16. **Financial Instruments** — continued

Subsidiary Preferred Shares Liability and Subsidiary Convertible Notes

The following table summarizes the changes in the Group's subsidiary preferred shares and convertible note liabilities measured at fair value, which were categorized as Level 3 in the fair value hierarchy:

	Subsidiary Preferred Shares $000s	Subsidiary Convertible Notes $000s
Balance at January 1, 2019	217,519	9,333
Value at issuance	51,048	1,607
Conversion to preferred	4,894	(4,894)
Conversion to common	—	(2,418)
Deconsolidation	(207,346)	(5,017)
Change in fair value	33,636	1,389
Finance Costs	1,458	—
Other	(112)	—
Cash distribution	(108)	—
Balance at December 31, 2019 and January 1, 2020	100,989	—
Value at issuance	13,750	25,000
Change in fair value	4,234	—
Balance at December 31, 2020 and January 1, 2021	118,972	25,000
Value at issuance	37,610	2,215
Conversion to subsidiary preferred shares	25,797	(25,797)
Accrued interest – contractual	—	867
Change in fair value	(8,362)	175
Balance at December 31, 2021	**174,017**	**2,461**

The change in fair value of preferred shares and convertible notes are recorded in Finance income/(costs) – fair value accounting in the Consolidated Statements of Comprehensive Income/(Loss).

The table below sets out information about the significant unobservable inputs used at December 31, 2021, in the fair value measurement of the Group's material subsidiary preferred shares liabilities categorized as Level 3 in the fair value hierarchy:

Fair Value at December 31, 2021	Valuation Technique	Unobservable Inputs	Weighted Average	Sensitivity to Decrease in Input
148,796	Market/Asset – PWERM & Hybrid allocation	Estimated time to exit	0.93	Fair value increase
		Discount rate	30.0%	
		Volatility	95.0%	
11,860	Income – DCF & OPM allocation	Estimated time to exit	2.94	Fair value decrease
		Probability of Success	76.5%	
		Discount rate	21.9%	Fair value increase
		Terminal value growth rate	(1.3)%	Fair value decrease
		Volatility	57.1%	
13,362	Market – Backsolve & OPM allocation	Estimated time to exit	2.00	Fair value increase
		Volatility	40.0%	

Subsidiary Preferred Shares Sensitivity

The following summarizes the sensitivity from the assumptions made by the Company with respect to the significant unobservable inputs which are categorized as Level 3 in the fair value hierarchy and used in the fair value measurement of the Group's subsidiary preferred shares liabilities (Please refer to Note 15):

Input	Subsidiary Preferred Share Liability	
As of December 31, 2021	Sensitivity Range	Financial Liability Increase/(Decrease) $000s
Subsidiary Enterprise Value	-2%	(3,041)
	+2%	3,140
Time to Liquidity	-6 Months	5,934
	+6 Months	(6,838)
Volatility	-10%	737
	+10%	(682)
Discount Rate	-5%	10,575
	+5%	(6,068)

16. Financial Instruments — continued

Subsidiary Convertible Notes

Vedanta issued convertible promissory notes in December 2020 and Sonde issued convertible notes in April 2021 and November 2021 (collectively the "Notes"). See Note 17 Subsidiary Notes payable for further details. The Notes contain one or more embedded derivatives. The Company elected to account for these Notes as FVTPL liabilities, whereby the embedded derivatives are not bifurcated but rather the Notes are recorded at fair value with changes in fair value recorded in the Finance Income (Cost) line item in the Consolidated statement of comprehensive income (loss).

In July 2021 the entire convertible note issued by Vedanta was converted into Vedanta Series D preferred shares – see Note 15 for further details.

The aggregate fair value of the Sonde Notes was determined to be approximately $2.5 million at December 31, 2021. The valuations of the Notes were each categorized as Level 3 in the fair value hierarchy. In estimating the fair value of these Notes, a probability-weighted methodology was utilized, whereby the Notes' expected returns under various Note-specific liquidity scenarios were analyzed and weighted to arrive at a probability-adjusted fair value at December 31, 2021. The significant unobservable input used at December 31, 2021, in the fair value measurement of Sonde's convertible notes constituted the estimated time to exit, which was 0.59 years.

Financial Assets Held at Fair Value

Karuna and Vor Valuation

Karuna (Nasdaq: KRTX) and Vor (Nasdaq: VOR) and additional immaterial investments are listed entities on an active exchange and as such the fair value for the year ended December 31, 2021, was calculated utilizing the quoted common share price. Please refer to Note 5 for further details.

Akili and Gelesis

In accordance with IFRS 9, the Company accounts for its preferred share investments in Akili and Gelesis as financial assets held at fair value through the profit and loss. During the year ended December 31, 2021, the Company recorded its investment in such preferred shares at fair value and recognized the change in fair value of such investments as a gain of $66.7 million that was recorded to the Consolidated Statements of Comprehensive Income/(Loss) in the line item Gain/(loss) on investments held at fair value.

The following table summarizes the changes in the Group's investments held at fair value, which were categorized as Level 3 in the fair value hierarchy:

	$'000s
Balance at January 1, 2019	85,163
Deconsolidation of Vor	12,028
Deconsolidation of Karuna	77,373
Deconsolidation of Gelesis	49,170
Reclass of Karuna to Associate	(118,006)
Gain/(Loss) on changes in fair value	48,867
Issuance of note receivable	6,480
Conversion of note receivable	(6,630)
Balance at December 31, 2019 and January 1, 2020	154,445
Cash purchase of Gelesis preferred shares (please refer to Note 6)	10,000
Cash purchase of Vor preferred shares	1,150
Gain/(Loss) on changes in fair value	41,297
Balance at January 1, 2021 before allocation of associate loss to long-term interest	206,892
Cash purchase of Vor preferred shares	500
Reclassification of Vor from level 3 to level 1	(33,365)
Gain/(Loss) on changes in fair value	65,505
Balance as of December 31, 2021 before allocation of associate loss to long-term interest	**239,533**
Share of associate loss allocated to long-term interest (please refer to Note 5)	(96,709)
Balance as of December 31, 2021 after allocation of associate loss to long-term interest	**142,824**

The change in fair value of investments held at fair value are recorded in Gain/(loss) on investments held at fair value in the Consolidated Statements of Comprehensive Income/(Loss).

The table below sets out information about the significant unobservable inputs used at December 31, 2021, in the fair value measurement of the Group's material investments held at fair value categorized as Level 3 in the fair value hierarchy:

Fair Value at December 31, 2021	Valuation Technique	Unobservable Inputs	Weighted Average	Sensitivity to Decrease in Input
238,231	Market – PWERM & Hybrid allocation	Estimated time to exit (*)	0.76	
		Discount rate	20.0%	Fair value increase
		Volatility	62.0%	

16. Financial Instruments — continued

The following summarizes the sensitivity from the assumptions made by the Company with respect to the significant unobservable inputs which are categorized as Level 3 in the fair value hierarchy and used in the fair value measurement of the Group's investments held at fair value (Please refer to Note 5):

Input	Investments Held at Fair Value	
As of December 31, 2021	Sensitivity Range	Financial Asset Increase/ (Decrease) $000s
Investee Enterprise Value	-2%	(4,559)
	+2%	4,652
Time to Liquidity (*)	-6 Months	11,828
	+6 Months	(14,691)
Discount Rate	-5%	3,842
	+5%	(3,408)

(*) Gelesis investment in preferred shares was excluded from the sensitivity calculation with regard to the time to liquidity as changing the time to liquidity in the Gelesis valuation would result in an unreasonable assumption leading to an unreasonable alternative value considering the circumstances on the financial reporting date.

Warrants

Warrants issued by subsidiaries within the Group are classified as liabilities, as they will be settled in a variable number of preferred shares. The following table summarizes the changes in the Group's subsidiary warrant liabilities, which were categorized as Level 3 in the fair value hierarchy:

	Subsidiary Warrant Liability $000s
Balance at January 1, 2019	13,012
Warrant Issuance	4,706
Gelesis Deconsolidation	(21,611)
Change in fair value	11,890
Balance at December 31, 2019 and January 1, 2020	7,997
Warrant Issuance	92
Change in fair value	117
Balance at December 31, 2020 and January 1, 2021	8,206
Change in fair value - finance costs (income)	(1,419)
Balance at December 31, 2021	**6,787**

The change in fair value of warrants are recorded in Finance income/(costs) – fair value accounting in the Consolidated Statements of Comprehensive Income/(Loss).

In connection with various amendments to its 2010 Loan and Security Agreement, Follica issued Series A-1 preferred share warrants at various dates in 2013 and 2014. Each of the warrants has an exercise price of $0.14 and a contractual term of ten years from the date of issuance. In 2017, in conjunction with the issuance of convertible notes, the exercise price of the warrants was adjusted to $0.07 per share.

In connection with the September 2, 2020 Oxford Finance LLC loan issuance, Vedanta also issued Oxford Finance LLC 12,886 Series C-2 preferred share warrants with an exercise price of $23.28 per share, expiring September 2030.

The $6.8 million warrant liability at December 31, 2021, was largely attributable to the outstanding Follica preferred share warrants.

The table below sets out the weighted average of significant unobservable inputs used at December 31, 2021, with respect to determining the fair value of the Group's warrants categorized as Level 3 in the fair value hierarchy:

Assumption/Input	Warrants
Expected term	1.66
Expected volatility	49.1%
Risk free interest rate	0.7%
Expected dividend yield	—%
Estimated fair value of the preferred share	$2.72

16. Financial Instruments — continued

The following summarizes the sensitivity from the assumptions made by the Company with respect to the significant unobservable inputs which are categorized as Level 3 in the fair value hierarchy and used in the fair value measurement of the Group's warrant liabilities:

Input	Warrant Liability	
As at December 31, 2021	Sensitivity Range	Financial Liability Increase/(Decrease) $000s
Discount Rate used in the calculation of estimated fair value of the preferred share	-5%	8,390
	+5%	(4,222)

Short-term Note from Associate

On December 7, 2021, Gelesis issued PureTech a $15.0 million note to be repaid the earlier of three business days after the closing of the business combination of Gelesis with Capstar Special Acquisition Corp ("Capstar"), or 30 days following the termination of such business combination. In the event of the business combination termination, the Company, who represented the majority of the note holders, could have elected to convert the note at the next equity financing at a discount of 25% from the financing price. The note bears interest at a rate of 10% per annum.

The note was repaid by Gelesis in January 2022 due to the closing of the business combination between Gelesis and Capstar on January 13, 2022.

The Note is measured at fair value in accordance with IFRS 9 with changes in fair value recorded as profit or loss in the Consolidated Statement of Comprehensive Income/(Loss). The fair value as of December 31, 2021, of $15.1 million approximated the note's contractual amount and the change in fair value from issuance date to December 31, 2021, was not material.

Fair Value Measurement and Classification

The fair value of financial instruments by category at December 31, 2021 and 2020:

	2021					
	Carrying Amount		Fair Value			
	Financial Assets $000s	Financial Liabilities $000s	Level 1 $000s	Level 2 $000s	Level 3 $000s	Total $000s
Financial assets:						
Money Markets[1]	**432,649**	**—**	**432,649**	**—**	**—**	**432,649**
Short-term note from associate	**15,120**	**—**	**—**	**—**	**15,120**	**15,120**
Investments held at fair value[2]	**493,888**	**—**	**254,355**	**—**	**239,533**	**493,888**
Trade and other receivables[3]	**3,174**	**—**	**—**	**3,174**	**—**	**3,174**
Total financial assets	**944,832**	**—**	**687,005**	**3,174**	**254,653**	**944,832**
Financial liabilities:						
Subsidiary warrant liability	**—**	**6,787**	**—**	**—**	**6,787**	**6,787**
Subsidiary preferred shares	**—**	**174,017**	**—**	**—**	**174,017**	**174,017**
Subsidiary notes payable	**—**	**3,916**	**—**	**1,330**	**2,586**	**3,916**
Share based liability awards	**—**	**7,362**	**6,081**	**—**	**1,281**	**7,362**
Total financial liabilities	**—**	**192,082**	**6,081**	**1,330**	**184,671**	**192,082**

1 Issued by a diverse group of corporations, largely consisting of financial institutions, virtually all of which are investment grade.
2 Balance prior to share of associate loss allocated to long-term interest (please refer to Note 5).
3 Outstanding receivables are owed primarily by government agencies, virtually all of which are investment grade.

	2020					
	Carrying Amount		Fair Value			
	Financial Assets $000s	Financial Liabilities $000s	Level 1 $000s	Level 2 $000s	Level 3 $000s	Total $000s
Financial assets:						
Money Markets[1]	394,143	—	394,143	—	—	394,143
Investments held at fair value[2]	553,167	—	346,275	—	206,892	553,167
Loans and receivables:						
Trade and other receivables[3]	2,558	—	—	2,558	—	2,558
Total financial assets	949,867	—	740,417	2,558	206,892	949,867
Financial liabilities:						
Subsidiary warrant liability	—	8,206	—	—	8,206	8,206
Subsidiary preferred shares	—	118,972	—	—	118,972	118,972
Subsidiary notes payable	—	26,455	—	1,330	25,125	26,455
Total financial liabilities	—	153,633	—	1,330	152,303	153,633

1 Issued by a diverse group of corporations, largely consisting of financial institutions, virtually all of which are investment grade.
2 Balance prior to share of associate loss allocated to long-term interest (please refer to Note 5).
3 Outstanding receivables are owed primarily by corporations and government agencies, virtually all of which are investment grade.

17. Subsidiary Notes Payable

The subsidiary notes payable are comprised of loans and convertible notes. As of December 31, 2021 and 2020, the loan in Follica and the financial instruments for Knode and Appeering did not contain embedded derivatives and therefore these instruments continue to be held at amortized cost. The notes payable consist of the following:

As of December 31,	**2021 $000s**	2020 $000s
Loans	**1,330**	1,330
Convertible notes	**2,586**	25,125
Total subsidiary notes payable	**3,916**	26,455

Loans

In October 2010, Follica entered into a loan and security agreement with Lighthouse Capital Partners VI, L.P. The loan is secured by Follica's assets, including Follica's intellectual property and bears interest at a rate of 12.0 percent. The outstanding loan balance totaled approximately $1.3 million and $1.3 million as of December 31, 2021 and December 31, 2020. The accrued interest on such loan balance is presented as Other current liabilities and totaled approximately $0.6 million and $0.5 million as of December 31, 2021 and December 31, 2020, respectively. The increase in 2021 is attributed to interest expense for the year ended December 31, 2021.

Convertible Notes

Convertible Notes outstanding were as follows:

	Vedanta $000s	Knode $000s	Appeering $000s	Sonde $000s	Total $000s
January 1, 2020	—	50	75	—	125
Gross principal – issuance of notes	25,000	—	—	—	25,000
Change in fair value	—	—	—	—	—
December 31, 2020 and January 1, 2021	25,000	50	75	—	25,125
Gross principal – issuance of notes – financing activity	—	—	—	2,215	2,215
Accrued interest on convertible notes – finance costs	797	—	—	70	867
Conversion to subsidiary preferred shares	(25,797)	—	—	—	(25,797)
Change in fair value – finance costs	—	—	—	175	175
December 31, 2021	**—**	**50**	**75**	**2,461**	**2,586**

On December 30, 2020, Vedanta issued a $25.0 million convertible promissory note to an investor. The note bore interest at an annual rate of 6.0 percent and its maturity date was the first anniversary of the note. Prepayment of the note was not allowed and there was no conversion discount feature on the note. The note was mandatorily convertible in a Qualified equity financing and a Qualified Public Offering at the current price of the financing or offering, all as defined in the note purchase agreement. In addition, the note allowed for optional conversion immediately prior to a Non Qualified public offering, Non Qualified Equity financing, or a Corporate transaction and for a pay-out in the case of a change of control transaction. On July 19, 2021, upon the occurrence of Vedanta's Series D preferred share issuance that was considered to be a Qualified Equity Financing, the entire outstanding amount of the note, principal and interest, was converted into Series D preferred shares of Vedanta at the current price of the financing. For further details, please see Note 15.

On April 6, 2021, and on November 24, 2021, Sonde issued unsecured convertible promissory notes to its existing shareholders for a combined total of $4.3 million, of which $2.2 million were issued to third party shareholders (and $2.1 million were issued to the Company and eliminated in consolidation). The notes bear interest at an annual rate of 6.0 percent and mature on the second anniversary of the issuance. The notes mandatorily convert in a Qualified Financing, as defined in the note purchase agreement, at a discount of 20.0 percent from the price per share in the Qualified Financing. In addition, the notes allow for optional conversion concurrently with the closing of a Non-Qualified Equity Financing to the Non-Qualified Equity Securities then issued and sold at a discount of 20.0 percent from the price per share in the Non Qualified Equity Financing. In the event of no conversion or repayment of the notes prior to a Change in Control, the notes shall become immediately due and payable prior to the closing of such Change in Control at three times the outstanding principal plus accrued interest.

For the Vedanta and Sonde convertible notes, since these Notes contain embedded derivatives, the Notes were assessed under IFRS 9 and the entire financial instruments were elected to be accounted for as FVTPL. The Vedanta convertible note was settled through its conversion in July 2021. See above. See Note 16 for further details on the fair value of the Sonde notes.

18. Non-Controlling Interest

During the year ended December 31, 2021, the Company acquired the non-controlling interest in Alivio which resulted in Alivio being transferred to the Internal segment. The Company has revised in the 2021 financial statements the prior period financial information related to the segmentation of NCI, to conform to the presentation as of and for the year ending December 31, 2021. Please refer to Note 4 "Segment Information" for further details regarding reportable segments.

The following table summarizes the changes in the equity classified non-controlling ownership interest in subsidiaries by reportable segment:

	Internal $000s	Controlled Founded Entities $000s	Non-Controlled Founded Entities $000s	Parent Company & Other $000s	Total $000s
Balance at January 1, 2019 *	(15,102)	(20,800)	(73,225)	592	(108,535)
Share of comprehensive loss	(17,643)	(13,483)	(23,953)	—	(55,079)
Deconsolidation of subsidiary	—	—	97,178	—	97,178
Subsidiary note conversion and changes in NCI ownership interest	—	23,049	—	—	23,049
Equity settled share-based payments	—	1,683	—	—	1,683
Acquisition of a subsidiary non controlling interest	24,039	—	—	—	24,039
Other	24	—	—	1	25
Balance at December 31, 2019 and January 1, 2020	(8,682)	(9,551)	—	593	(17,639)
Share of comprehensive loss	(191)	(1,211)	—	(15)	(1,417)
Equity settled share-based payments	305	2,517	—	—	2,822
Other	—	30	—	(6)	24
Balance at December 31, 2020 and January 1, 2021	(8,567)	(8,215)	—	574	(16,209)
Share of comprehensive income (loss)	(96)	(2,069)	—	15	(2,151)
NCI exercise of share-based awards in subsidiaries – change in NCI interest	—	(5,922)	—	—	(5,922)
Equity settled share-based payments	(4)	6,256	—	—	6,252
Acquisition of a subsidiary non controlling interest	8,668	—	—	—	8,668
Other	—	—	—	(6)	(6)
Balance as of December 31, 2021	**—**	**(9,950)**	**—**	**583**	**(9,368)**

(*) Revised to reclassify Alivio into the Internal segment to comply with current period classification. See Note 4.

The following tables summarize the financial information related to the Group's subsidiaries with material non-controlling interests, aggregated for interests in similar entities, and before and after intra group eliminations.

	2021				
For the year ended December 31	Internal $000s	Controlled Founded Entities $000s	Non-Controlled Founded Entities $000s	Intra-group eliminations $000s	Total $000s
Statement of Comprehensive Loss					
Total revenue	**—**	**7,771**	**—**	**—**	**7,771**
Income/(loss) for the year	**—**	**(50,436)**	**—**	**792**	**(49,644)**
Other comprehensive income/(loss)	**—**	**—**	**—**	**—**	**—**
Total comprehensive income/(loss) for the year	**—**	**(50,436)**	**—**	**792**	**(49,644)**
Statement of Financial Position					
Total assets	**—**	**66,279**	**—**	**(161)**	**66,118**
Total liabilities	**—**	**228,856**	**—**	**(10,755)**	**218,101**
Net assets/(liabilities)	**—**	**(162,576)**	**—**	**10,594**	**(151,982)**

As of December 31, 2021, Controlled Founded Entities with non-controlling interests primarily include Follica Incorporated, Sonde Health Inc., Entrega Inc. and Vedanta Biosciences, Inc. Ownership interests of the non-controlling interests in Follica Incorporated, Entrega Inc., Sonde Health Inc., and Vedanta Biosciences, Inc are 19.9 percent, 11.7 percent, 6.2 percent and 3.7 percent, respectively. In addition, Non-controlling interests include the amounts recorded for subsidiary stock options, with the vast majority comprising of Vedanta stock options.

18. Non-Controlling Interest — continued

For the year ended December 31	Internal $000s	Controlled Founded Entities $000s	Non-Controlled Founded Entities $000s	Intra-group eliminations $000s	Total $000s
			2020		
Statement of Comprehensive Loss					
Total revenue	3,267	1,957	—	—	5,224
Income/(loss) for the year	(2,407)	(53,535)	—	1,073	(54,869)
Total comprehensive income/(loss) for the year	(2,407)	(53,535)	—	1,073	(54,869)
Statement of Financial Position					
Total assets	1,297	67,048	—	(7)	68,339
Total liabilities	12,086	188,345	—	(14,621)	185,809
Net assets/(liabilities)	(10,788)	(121,296)	—	14,615	(117,470)

As of December 31, 2020, Internal segment with non-controlling interests include Alivio, Controlled Founded Entities with non-controlling interests primarily include, Follica Incorporated, Sonde Health Inc., and Vedanta Biosciences, Inc. Ownership interests of the non-controlling interests in Alivio Therapeutics, Inc., Follica Incorporated, Sonde Health Inc., and Vedanta Biosciences, Inc are 8.1 percent, 19.9 percent, 4.5 percent and 0.4 percent, respectively. In addition, Non-controlling interests include the amounts recorded for subsidiary stock options, with the vast majority comprising of Vedanta stock options.

For the year ended December 31	Internal $000s	Controlled Founded Entities $000s	Non-Controlled Founded Entities $000s
		2019	
Statement of Comprehensive Loss			
Total revenue	8,006	41	—
Income/(loss) for the year	(26,668)	(23,871)	(47,905)
Other comprehensive income/(loss)	—	—	(10)
Total comprehensive income/(loss) for the year	(26,668)	(23,871)	(47,915)

On July 19, 2019 PureTech and a third party investor converted their convertible debt in Follica to Follica Preferred shares (presented as liabilities) and Follica common shares. The amount of convertible debt converted by the third party investor into Follica common shares amounted to $2.4 million (see also Note 16). As a result of the conversion Follica NCI share (in Follica common stock) was reduced from 68 percent to 19.9 percent, which resulted in a reduction in the NCI share in Follica's shareholders' deficit of $19.9 million. The excess of the change in the book value of NCI ($19.9 million noted above) over the contribution made by NCI ($2.4 million) amounted to $17.5 million and was recorded as a loss directly in shareholders' equity.

During 2019 a subsidiary of the Company fully funded by the Company ceased its operations and became inactive. This resulted in a change in the NCI share in the subsidiary deficit. As a result the Company recorded a loss directly in equity of $3.1 million.

On October 1, 2019, PureTech acquired the remaining 10.0 percent of minority non-controlling interests of PureTech LYT, Inc. (previously named Ariya Therapeutics, Inc.), increasing its ownership from 90.0 percent to 100.0 percent. In consideration for the acquisition of minority interests, PureTech issued 2,126,338 shares of common shares. The fair value of the shares issued in consideration for the minority non-controlling interest amounted to $9.1 million. The carrying amount of the non-controlling interest at the acquisition was a $24.0 million deficit and the excess of the consideration paid over the book value of the non-controlling interest of approximately $33.1 million was recorded directly in shareholders' equity.

On June 11, 2021, PureTech acquired the remaining 17.1 percent of the minority non-controlling interests of Alivio (after exercise of all in the money stock options) increasing its ownership to 100.0 percent of Alivio. The consideration for such non controlling interests amounted to $1.2 million, to be paid in three equal installments, with the first installment of $0.4 million paid at the effective date of the transaction and two additional installment to be paid upon the occurrence of certain contingent events. The Group recorded a contingent consideration liability of $0.6 million at fair value for the two additional installments, resulting in a total acquisition cost of $1.0 million. The excess of the consideration paid over the book value of the non-controlling interest of approximately $9.6 million was recorded directly as a charge to shareholders' equity. The second installment of $0.4 million was paid in July 2021, upon the occurrence of the contingent event specified in the agreement. The contingent consideration liability is adjusted to fair value at the end of each reporting period with changes in fair value recorded in earnings. Changes in fair value of the aforementioned contingent consideration liability were not material.

On December 1, 2021, options holders in Entrega exercised options into shares of common stock, increasing the NCI interest held from 0.2 percent to 11.7 percent. During 2021 option holders in Vedanta exercised options and increased the NCI interest to 3.7 percent. The exercise of the options resulted in an increase in the NCI share in Entrega's and Vedanta's shareholder's deficit of $5.9 million. The consideration paid by NCI ($0.1 million) together with the increase in NCI share in Entrega's and Vedanta's shareholder deficit ($5.9 million) amounted to $6.0 million and was recorded as a gain directly in shareholders' equity.

19. Trade and Other Payables

Information regarding Trade and other payables was as follows:

As of December 31,	**2021 $000s**	2020 $000s
Trade payables	**11,346**	8,871
Accrued expenses	**17,309**	9,090
Income tax payable	**57**	1,260
Liability settled share based awards	**4,703**	—
Other	**2,403**	2,606
Total trade and other payables	**35,817**	21,826

20. Long-term loan

In September 2020, Vedanta entered into a $15.0 million loan and security agreement with Oxford Finance LLC. The loan is secured by Vedanta's assets, including equipment, inventory and intellectual property. The loan bears a floating interest rate of 7.7 percent plus the greater of (i) 30 day U.S. Dollar LIBOR reported in the Wall Street Journal or (ii) 0.17 percent. The loan matures September 2025 and requires interest only payments for the initial 24 months. The loan also carries a final fee upon full repayment of 7.0 percent of the original principal, or $1.1 million. For loan consideration, Vedanta also issued Oxford Finance LLC 12,886 Series C-2 preferred share warrants with an exercise price of $23.28 per share, expiring September 2030. The outstanding loan balance totaled approximately $15.1 million as of December 31, 2021.

The following table summarizes long-term loan activity for the years ended December 31, 2021 and 2020:

	Long-term loan	
	2021 $000s	2020 $000s
Balance at January 1,	**14,818**	—
Net loan proceeds	**—**	14,720
Accrued interest	**1,502**	496
Interest paid	**(1,201)**	(296)
Other	**—**	(102)
Balance at December 31,	**15,118**	14,818

The following table summarizes Vedanta's future principal payments for the long-term loan as of December 31, 2021:

Balance Type	2022	2023	2024	2025	Total
Principal	857	5,143	5,143	3,857	15,000
Balance of accreted premium net of unamortized issuance costs					118
Total					**15,118**

The long-term loan is presented as follows in the Statement of Financial Position as of December 31, 2021 and 2020:

	Long-term loan	
	2021 $000s	2020 $000s
Current portion of Long-term loan	**857**	—
Long-term loan	**14,261**	14,818
Total Long-term loan	**15,118**	14,818

21. Leases

The activity related to the Group's right of use asset and lease liability for the years ended December 31, 2021 and 2020 is as follows:

	Right of use asset, net	
	2021 $000s	2020 $000s
Balance at January 1,	**20,098**	22,383
Additions	**739**	—
Tenant improvement - lease incentive	**(733)**	—
Depreciation	**(2,938)**	(2,699)
Adjustments	**—**	414
Balance at December 31,	**17,166**	20,098

	Total lease liability	
	2021 $000s	2020 $000s
Balance at January 1,	**35,348**	37,843
Additions	**1,016**	—
Cash paid for rent - principal - financing cash flow	**(3,375)**	(2,908)
Cash paid for rent - interest	**(2,181)**	(2,354)
Interest expense	**2,181**	2,354
Adjustments	**—**	414
Balance at December 31,	**32,990**	35,348

Depreciation of the right-of-use assets, which virtually all consist of leased real estate, is included in the General and administrative expenses and Research and development expenses line items in the Consolidated Statements of Comprehensive Income/(Loss). The Company recorded depreciation expense of $2.9 million, $2.7 million and $3.2 million for the years ended December 31, 2021, 2020 and 2019, respectively.

The following details the short-term and long-term portion of the lease liability as at December 31, 2021 and 2020:

	Total lease liability	
	2021 $000s	2020 $000s
Short-term Portion of Lease Liability	**3,950**	3,261
Long-term Portion of Lease Liability	**29,040**	32,088
Total Lease Liability	**32,990**	35,348

The following table details the future maturities of the lease liability, showing the undiscounted lease payments to be paid after the reporting date:

	2021 $000s
Less than one year	**5,927**
One to two years	**6,591**
Two to three years	**6,754**
Three to four years	**5,168**
Four to five years	**4,419**
More than five years	**12,033**
Total undiscounted lease maturities	**40,893**
Interest	**7,903**
Total lease liability	**32,990**

During the year ended December 31, 2019, PureTech entered into a lease agreement for certain premises consisting of approximately 50,858 rentable square feet of space located at 6 Tide Street. The lease commenced on April 26, 2019 ("Commencement Date") for an initial term consisting of ten years and three months and there is an option to extend for two consecutive periods of five years each. The Company assessed at lease commencement date whether it is reasonably certain to exercise the extension options and deemed such options not reasonably certain to be exercised. The Company will reassess whether it is reasonably certain to exercise the options only if there is a significant event or significant changes in circumstances within its control.

21. Leases — continued

On June 26, 2019, PureTech executed a sublease agreement with Gelesis. The lease is for the approximately 9,446 rentable square feet located on the sixth floor of the Company's former offices at the 501 Boylston Street building. The sublessee obtained possession of the premises on June 1, 2019 and the rent period term began on June 1, 2019 and expires on August 31, 2025. The sublease was determined to be a finance lease. As of December 31, 2021, the balances related to the sublease were as follows:

	Total lease receivable $000s
Short-term Portion of Lease Receivable	415
Long-term Portion of Lease Receivable	1,285
Total Lease Receivable	**1,700**

The following table details the future maturities of the lease receivable, showing the undiscounted lease payments to be received after the reporting date:

	2021 $000s
Less than one year	**504**
One to two years	**513**
Two to three years	**523**
Three to four years	**353**
Total undiscounted lease receivable	**1,892**
Unearned Finance income	**192**
Net investment in the lease	**1,700**

On August 6, 2019, PureTech executed a sublease agreement with Dewpoint Therapeutics, Inc. ("Dewpoint"). The sublease was for approximately 11,852 rentable square feet located on the third floor of the 6 Tide Street building, where the Company's offices are currently located. Dewpoint obtained possession of the premises on September 1, 2019 with a rent period term that began on September 1, 2019, and expired on August 31, 2021. The sublease was determined to be an operating lease.

Rental income recognized by the Company during the years ended December 31, 2021, 2020 and 2019, was $0.65 million, $1.08 million and $0.4 million, respectively and is included in the Other income/(expense) line item in the Consolidated Statements of Comprehensive Income/(Loss).

22. Capital and Financial Risk Management

Capital Risk Management

The Group's capital and financial risk management policy is to maintain a strong capital base so as to support its strategic priorities, maintain investor, creditor and market confidence as well as sustain the future development of the business. The Group's objectives when managing capital are to safeguard its ability to continue as a going concern in order to provide returns for shareholders and benefits for other stakeholders and to maintain an optimal capital structure to reduce the cost of capital. To maintain or adjust the capital structure, the Group may issue new shares or incur new debt. The Group has some external debt and no material externally imposed capital requirements. The Group's share capital is clearly set out in Note 14.

Management continuously monitors the level of capital deployed and available for deployment in the Internal and Parent segments as well as at Controlled Founded Entities. The Directors seek to maintain a balance between the higher returns that might be possible with higher levels of deployed capital and the advantages and security afforded by a sound capital position.

The Group's Directors have overall responsibility for establishment and oversight of the Group's capital and risk management framework. The Group is exposed to certain risks through its normal course of operations. The Group's main objective in using financial instruments is to promote the development and commercialization of intellectual property through the raising and investing of funds for this purpose. The Group's policies in calculating the nature, amount and timing of investments are determined by planned future investment activity. Due to the nature of activities and with the aim to maintain the investors' funds as secure and protected, the Group's policy is to hold any excess funds in highly liquid and readily available financial instruments and maintain insignificant exposure to other financial risks.

COVID-19

In March 2020, the World Health Organization declared the COVID-19 outbreak a pandemic. The pandemic has since caused widespread and significant disruption to daily life and the global economy as governments have taken actions, including the issuance of stay-at-home orders and social distancing guidelines, and businesses have adjusted their activities. While our business, operations and financial condition and results have not been significantly impacted in 2020 or 2021, as a result of the COVID-19 pandemic, we have taken swift action to ensure the safety of our employees and other stakeholders. The Group continues to monitor the latest developments regarding the COVID-19 pandemic on business, operations, and financial condition and results, and has made certain assumptions regarding the pandemic for purposes of the Group's operational planning and financial projections, including assumptions regarding the duration and severity of the pandemic and the global macroeconomic impact of the pandemic. Despite careful tracking and planning, however, the Group is unable to accurately predict the extent of the impact of the pandemic on the business, operations, and financial condition and results in future periods due to the uncertainty of future developments. The Group is focused on all aspects of the business and is implementing measures aimed at mitigating issues where possible.

22. Capital and Financial Risk Management — continued

Credit Risk

The Group has exposure to the following risks arising from financial instruments:

Credit risk is the risk of financial loss to the Group if a customer or counterparty to a financial instrument fails to meet its contractual obligations. Financial instruments that potentially subject the Group to concentrations of credit risk consist principally of cash and cash equivalents and trade and other receivables. The Group held the following balances (not including the income tax receivable resulting from overpayment of income taxes, see Note 25):

As of December 31	**2021 $000s**	2020 $000s
Cash and cash equivalents	**465,708**	403,881
Trade and other receivables	**3,174**	2,558
Total	**468,882**	406,438

The Group invests its excess cash in U.S. Treasury Bills, U.S. debt obligations and money market accounts, which the Group believes are of high credit quality. Further the Group's cash and cash equivalents and short-term investment are held at diverse, investment-grade financial institutions.

The Group assesses the credit quality of customers on an ongoing basis. The credit quality of financial assets is assessed by historical and recent payment history, counterparty financial position, reference to credit ratings (if available) or to historical information about counterparty default rates. The Group does not have expected credit losses owing largely to a small number of counterparties and the high credit quality of such counterparties (primarily the US government and large funds in respect of grant income).

The aging of trade and other receivables that were not impaired at December 31 is as follows:

As of December 31	**2021 $000s**	2020 $000s
Not impaired	**3,174**	2,558
Total	**3,174**	2,558

Liquidity Risk

Liquidity risk is the risk that the Group will encounter difficulty in meeting the obligations associated with its financial liabilities that are settled by delivering cash or another financial asset. The Group actively manages its risk of a funds shortage by closely monitoring the maturity of its financial assets and liabilities and projected cash flows from operations, under both normal and stressed conditions, without incurring unacceptable losses or risking damage to the Group's reputation. Due to the nature of these financial liabilities, the funds are available on demand to provide optimal financial flexibility.

The table below summarizes the maturity profile of the Group's financial liabilities, including subsidiary preferred shares that have customary liquidation preferences, as of December 31, 2021 and 2020, based on contractual undiscounted payments:

	2021				
As of December 31	**Carrying Amount $000s**	**Within Three Months $000s**	**Three to Twelve Months $000s**	**One to Five Years $000s**	**Total $000s (*)**
Long-term loan (non-current + current)	**15,118**	**296**	**2,182**	**16,274**	**18,752**
Subsidiary notes payable	**3,916**	**3,916**	**—**	**—**	**3,916**
Trade and other payables	**35,817**	**35,817**	**—**	**—**	**35,817**
Warrants[2]	**6,787**	**6,787**	**—**	**—**	**6,787**
Subsidiary preferred shares (Note 15)[1]	**174,017**	**174,017**	**—**	**—**	**174,017**
Total	**235,656**	**220,833**	**2,182**	**16,274**	**239,290**

	2020				
As of December 31	Carrying Amount $000s	Within Three Months $000s	Three to Twelve Months $000s	One to Five Years $000s	Total $000s (*)
Long-term loan	14,818	296	905	18,780	19,981
Subsidiary notes payable	26,455	1,455	25,000	—	26,455
Trade and other payables	21,826	21,826	—	—	21,826
Warrants[2]	8,206	8,206	—	—	8,206
Subsidiary preferred shares (Note 15)[1]	118,972	118,972	—	—	118,972
Total	190,278	150,756	25,905	18,780	195,441

1 Redeemable only upon a liquidation or Deemed liquidation event, as defined in the applicable shareholder documents.
2 Warrants issued by subsidiaries to third parties to purchase preferred shares.
(*) Does not include payments in respect of lease obligations. For the contractual future payments related to lease obligations, see Note 21.

22. Capital and Financial Risk Management — continued

Interest Rate Sensitivity

As of December 31, 2021, the Group had cash and cash equivalents of $465.7 million. The Group's exposure to interest rate sensitivity is impacted by changes in the underlying U.K. and U.S. bank interest rates. The Group has not entered into investments for trading or speculative purposes. Due to the conservative nature of the Group's investment portfolio, which is predicated on capital preservation and investments in short duration, high-quality U.S. Treasury Bills and U.S. debt obligations and related money market accounts, a change in interest rates would not have a material effect on the fair market value of the Group's portfolio, and therefore the Group does not expect operating results or cash flows to be significantly affected by changes in market interest rates.

Controlled Founded Entity Investments

The Group maintains investments in certain Controlled Founded Entities. The Group's investments in Controlled Founded Entities are eliminated as intercompany transactions upon financial consolidation. The Group is however exposed to a preferred share liability owing to the terms of existing preferred shares and the ownership of Controlled Founded Entities preferred shares by third parties. As discussed in Note 15, certain of the Group's subsidiaries have issued preferred shares that include the right to receive a payment in the event of any voluntary or involuntary liquidation, dissolution or winding up of a subsidiary, including in the event of "deemed liquidation" as defined in the incorporation documents of the entities, which shall be paid out of the assets of the subsidiary available for distribution to shareholders and before any payment shall be made to holders of ordinary shares. The liability of preferred shares is maintained at fair value through the profit and loss. The Group's strong cash position, budgeting and forecasting processes, as well as decision making and risk mitigation framework enable the Group to robustly monitor and support the business activities of the Controlled Founded Entities to ensure no exposure to dissolution or liquidation. Accordingly, the Group views exposure to 3rd party preferred share liability as low.

Non-Controlled Founded Entity Investments

The Group maintains certain investments in Non-Controlled Founded Entities which are deemed either as investments and accounted for as investments held at fair value or associates and accounted for under the equity method (please refer to Note 1). The Group's exposure to investments held at fair value is $397.2 million as of December 31, 2021, and the Group may or may not be able to realize the value in the future. Accordingly, the Group views the risk as high. The Group's exposure to investments in associates is limited to the carrying amount of the investment in an Associate. The Group is not exposed to further contractual obligations or contingent liabilities beyond the value of initial investment. As of December 31, 2021, Gelesis was the only associate. The carrying amount of the investment in Gelesis as an associate was zero. Accordingly, the Group does not view this as a risk. Please refer to Notes 5,6 and 16 for further information regarding the Group's exposure to Non-Controlled Founded Entity Investments.

Equity Price Risk

As of December 31, 2021, the Group held 1,656,564 common shares of Karuna and 3,207,200 common shares of Vor. The fair value of the Group's investment in the common stock of Karuna and Vor was $217.0 million and $37.3 million respectively.

The investments in Karuna and Vor are exposed to fluctuations in the market price of these common shares. The effect of a 10.0 percent adverse change in the market price of Karuna and Vor common shares as of December 31, 2021, would have been a loss of approximately $21.7 million and $3.7 million respectively, recognized as a component of Other income (expense) in the Consolidated Statements of Comprehensive Income/(Loss).

Foreign Exchange Risk

The Group maintains consolidated financial statements in the Group's functional currency, which is the U.S. dollar. Monetary assets and liabilities denominated in currencies other than the functional currency are translated into the functional currency at rates of exchange prevailing at the balance sheet dates. Non-monetary assets and liabilities denominated in foreign currencies are translated into the functional currency at the exchange rates prevailing at the date of the transaction. Exchange gains or losses arising from foreign currency transactions are included in the determination of net income (loss) for the respective periods. Such foreign currency gains or losses were not material for all reported periods. See Note 9.

The Group does not currently engage in currency hedging activities since its foreign currency risk is limited, but the Group may begin to do so in the future if and when its foreign currency risk exposure changes. Instruments that may be used to hedge future risks include foreign currency forward and swap contracts. These instruments may be used to selectively manage risks, but there can be no assurance that the Group will be fully protected against material foreign currency fluctuations.

23. Commitments and Contingencies

The Group is party to certain licensing agreements where the Group is licensing IP from third parties. In consideration for such licenses the Group has made upfront payments and may be required to make additional contingent payments based on developmental and sales milestones and/or royalty on future sales. As of December 31, 2021, these milestone events have not yet occurred and therefore the Group does not have a present obligation to make the related payments in respect of the licenses. Such milestones are dependent on events that are outside of the control of the Group and many of these milestone events are remote of occurring. As of December 31, 2021, payments in respect of developmental milestones that are dependent on events that are outside the control of the Group but are reasonably possible to occur amounted to approximately $10.3 million. These milestone amounts represent an aggregate of multiple milestone payments depending on different milestone events in multiple agreements. The probability that all such milestone events will occur in the aggregate is remote. Payments made to license IP represent the acquisition cost of intangible assets. See Note 12.

The Group is party to certain sponsored research arrangements as well as arrangements with contract manufacturing and contract research organizations, whereby the counterparty provides the Company with research and/or manufacturing services. As of December 31, 2021, the noncancellable commitments in respect of such contracts amounted to approximately $6.7 million.

24. Related Parties Transactions

Related Party Subleases and royalties

During 2019, PureTech executed sublease agreements with a related party, Gelesis. Please refer to Note 21 for further details regarding the sublease.

The Group receives royalties from Gelesis on its product sales. Such royalties amounted to $231 thousand and $54 thousand for the years ended December 31, 2021 and 2020, respectively and are presented in Contract revenue in the Consolidated Statements of Comprehensive Income/(Loss).

Key Management Personnel Compensation

Key management includes executive directors and members of the executive management team of the Group (not including compensation provided to independent directors). Full details for Directors' remuneration can be found in the Directors' Remuneration Report. The key management personnel compensation of the Group was as follows for the years ended December 31:

As of December 31	**2021 $000s**	2020 $000s	2019 $000s
Short-term employee benefits	**4,666**	4,833	5,543
Share-based payments	**4,045**	5,822	2,774
Total	**8,711**	10,656	8,317

Short-term employee benefits include salaries, health care and other non-cash benefits. Share-based payments are generally subject to vesting terms over future periods.

For cash settlements of share based awards – see Note 8.

During the year ended December 31, 2021, the company incurred $782 thousand of general administrative expenses that was paid to a related party.

Convertible Notes Issued to Directors

Certain members of the Group have invested in convertible notes issued by the Group's subsidiaries. As of December 31, 2021, 2020 and 2019, the outstanding related party notes payable totaled $94 thousand, $89 thousand and $84 thousand respectively, including principal and interest.

The notes issued to related parties bear interest rates, maturity dates, discounts and other contractual terms that are the same as those issued to outside investors during the same issuances, as described in Note 17.

24. Related Parties Transactions — continued

Directors' and Senior Managers' Shareholdings and Share Incentive Awards

The Directors and senior managers hold beneficial interests in shares in the following businesses and sourcing companies as at December 31, 2021:

	Business Name (Share Class)	Number of shares held as of December 31, 2021	Number of options held as of December 31, 2021	Ownership Interest[1]
Directors:				
Ms. Daphne Zohar[2]	Gelesis (Common)	**179,443**	**1,207,006**	**5.03%**
Dr. Robert Langer	Entrega (Common)	**250,000**	**82,500**	**4.09%**
Dr. Raju Kucherlapati	Enlight (Class B Common)	**—**	**30,000**	**3.00%**
Dr. John LaMattina[3]	Akili (Series A-2 Preferred)	**37,372**	**—**	**0.80%**
	Akili (Series C Preferred)	**11,755**	**—**	**0.20%**
	Gelesis (Common)[3]	**50,540**	**—**	**0.18%**
	Gelesis (Common)[4]	**33,051**	**33,578**	**0.24%**
	Gelesis (Series A-1 Preferred)[3]	**49,523**	**—**	**0.18%**
	Vedanta Biosciences (Common)	**25,000**	**—**	**0.17%**
Senior Managers:				
Dr. Bharatt Chowrira	Karuna (Common)[4]	**5,000**	**—**	**0.02%**
Dr. Joseph Bolen	Vor (Common)	**—**	**9,191**	**0.02%**

1 Ownership interests as of December 31, 2021 are calculated on a diluted basis, including issued and outstanding shares, warrants and options (and written commitments to issue options) but excluding unallocated shares authorized to be issued pursuant to equity incentive plans and any shares issuable upon conversion of outstanding convertible promissory notes.

2 Common shares and options held by Yishai Zohar, who is the husband of Ms. Zohar. Ms. Zohar does not have any direct interest in the share capital of Gelesis. Ms. Zohar recuses herself from any and all material decisions with regard to Gelesis.

3 Dr. John and Ms. Mary LaMattina hold 50,540 shares of common shares and 49,523 shares of Series A-1 preferred shares in Gelesis. Individually, Dr. LaMattina holds 33,051 shares of Gelesis and convertible notes issued by Appeering in the aggregate principal amount of $50,000.

4 Options to purchase the listed shares were granted in connection with the service on such founded entity's Board of Directors and any value realized therefrom shall be assigned to PureTech Health, LLC.

Directors and senior managers hold 24,676,165 ordinary shares and 8.6 percent voting rights of the Company as of December 31, 2021. This amount excludes options to purchase 4,750,000 ordinary shares. This amount also excludes 4,666,514 shares, which are issuable based on the terms of performance based RSU awards granted to certain senior managers covering the financial years 2021, 2020 and 2019, and 67,140 shares, which are issuable to directors immediately prior to the Company's 2022 Annual General Meeting of Stockholders based on the terms of the RSU awards granted to non-executive directors in 2021. Such shares will be issued to such senior managers and non executive directors in future periods provided that performance and/or service conditions are met and certain of the shares will be withheld for payment of customary withholding taxes.

Short term Note from Associate

See Note 16 for details on the $15.0 million note issued by Gelesis to the Company. The Company recognized income of $0.1 million with respect to interest and changes in fair value related to the short term note.

25. Taxation

Tax on the profit or loss for the year comprises current and deferred income tax. Tax is recognized in the Consolidated Statements of Comprehensive Income/(Loss) except to the extent that it relates to items recognized directly in equity.

For the years ended December 31, 2021, 2020 and 2019, the Group filed a consolidated U.S. federal income tax return which included all subsidiaries in which the Company owned greater than 80 percent of the vote and value. For the years ended December 31, 2021, 2020 and 2019, the Group filed certain consolidated state income tax returns which included all subsidiaries in which the Company owned greater than 50 percent of the vote and value. The remaining subsidiaries file separate U.S. tax returns.

Amounts recognized in Consolidated Statements of Comprehensive Income/(Loss):

As of December 31	**2021 $000s**	2020 $000s	2019 $000s
Income/(loss) for the year	**(62,709)**	4,568	366,065
Income tax expense/(benefit)	**3,756**	14,401	112,409
Income/(loss) before taxes	**(58,953)**	18,969	478,474

Recognized income tax expense/(benefit):

As of December 31	**2021 $000s**	2020 $000s	2019 $000s
Federal	**22,138**	21,796	—
Foreign	**—**	—	—
State	**109**	—	—
Total current income tax expense/(benefit)	**22,247**	21,796	—
Federal	**(15,416)**	(7,349)	83,776
Foreign	**—**	—	—
State	**(3,075)**	(46)	28,633
Total deferred income tax expense/(benefit)	**(18,491)**	(7,395)	112,409
Total income tax expense/(benefit), recognized	**3,756**	14,401	112,409

The tax expense was $3.8 million, $14.4 million and $112.4 million in 2021, 2020 and 2019 respectively. The decrease in tax expense is primarily the result of the decrease in profit before tax in entities in the U.S. Federal and Massachusetts consolidated return groups of the Company.

Reconciliation of Effective Tax Rate

The Group is primarily subject to taxation in the U.S. A reconciliation of the U.S. federal statutory tax rate to the effective tax rate is as follows:

	2021		2020		2019	
As of December 31	**$000s**	**%**	$000s	%	$000s	%
US federal statutory rate	**(12,380)**	**21.00**	3,984	21.00	97,183	21.00
Effects of state tax rate in U.S.	**(4,484)**	**7.61**	1,844	9.72	22,111	4.78
R&D and orphan drug tax credits	**(5,056)**	**8.58**	(5,642)	(29.74)	(6,321)	(1.37)
Non deductible share based payment expenses	**555**	**(0.94)**	327	1.73	433	0.09
Finance income/(costs) – fair value accounting	**(2,017)**	**3.42**	919	4.84	3,725	0.80
Loss with respect to associate for which no deferred tax asset is recognized	**11,542**	**(19.58)**	—	—	—	—
Transaction Costs	**309**	**(0.52)**	361	1.91	—	—
Interest Expense	**217**	**(0.37)**	(2,258)	(11.91)	1,030	0.22
Executive Compensation	**746**	**(1.27)**	827	4.36	—	—
Deconsolidation adjustments	**—**	**0.00**	—	—	(13,658)	(2.95)
Recognition of deferred tax assets and tax benefits not previously recognized	**(414)**	**0.70**	—	—	(6,251)	(1.35)
Current year losses for which no deferred tax asset is recognized	**14,375**	**(24.38)**	13,948	73.53	14,514	3.14
Other	**363**	**(0.62)**	91	0.48	(356)	(0.06)
	3,756	**(6.37)**	14,401	75.92	112,409	24.29

The Company is also subject to taxation in the UK but to date no taxable income has been generated in the UK. Changes in corporate tax rates can change both the current tax expense (benefit) as well as the deferred tax expense (benefit).

25. Taxation — continued

Deferred Tax Assets and Liabilities

Deferred tax assets have been recognized in the U.S. jurisdiction in respect of the following items:

As of December 31	2021 $000s	2020 $000s
Operating tax losses	**46,982**	39,901
Tax credits	**10,673**	10,805
Share-based payments	**7,265**	5,429
Deferred revenue	**—**	358
Investment in Associates	**11,542**	—
Lease Liability	**8,969**	9,657
Other temporary differences	**2,665**	2,078
Deferred tax assets	**88,096**	68,228
Investments held at fair value	**(96,804)**	(120,676)
ROU asset	**(4,667)**	(5,491)
Fixed assets	**(3,547)**	(3,588)
Other temporary differences	**—**	(27)
Deferred tax liabilities	**(105,018)**	(129,782)
Deferred tax assets (liabilities), net	**(16,922)**	(61,554)
Deferred tax liabilities, net, recognized	**(89,765)**	(108,626)
Deferred tax assets, net, recognized	**—**	—
Deferred tax assets (liabilities), net, not recognized	**72,843**	47,072

We have recognized deferred tax assets related to entities in the U.S. Federal and Massachusetts consolidated return groups due to future reversals of existing taxable temporary differences that will be sufficient to recover the net deferred tax assets. Our unrecognized deferred tax assets of $72.8 million are primarily related to tax credit, loss carryforwards and deductible temporary differences in subsidiaries outside the U.S. Federal and Massachusetts consolidated return groups. Such deferred tax assets have not been recognized because it is not probable that future taxable profits will be available to support their realizability. The unrecognized deferred tax assets, to a lesser extent, also relate to unrecognized deferred tax assets with respect to an investment in an associate since the Group does not believe it is probable that such tax benefits will be realized in the foreseeable future.

There was movement in deferred tax recognized, which impacted income tax expense by approximately $18.5 million benefit, primarily related to changes in the value of investments. The Company sold a portion of its stock in Karuna during 2021 and was able to partially offset its gains by using various attributes (i.e. net operating losses, research and development credits, etc.) resulting in current tax expense of $22.2 million.

Unrecognized Deferred Tax Assets

Deferred tax assets have not been recognized in respect of the following carryforward losses, credits and temporary differences, because it is not probable that future taxable profit will be available against which the Group can use the benefits therefrom.

	2021 $000s		2020 $000s	
As of December 31	**Gross Amount**	**Tax Effected**	Gross Amount	Tax Effected
Deductible Temporary Difference	**59,925**	**16,224**	7,997	1,679
Tax Losses	**215,425**	**46,982**	169,731	36,273
Tax Credits	**9,636**	**9,636**	9,120	9,120
Total	**284,986**	**72,843**	186,848	47,072

Tax Losses and tax credits carryforwards

Tax losses and tax credits for which no deferred tax asset was recognized

	2021 $000s		2020 $000s	
As of December 31	**Gross Amount**	**Tax Effected**	Gross Amount	Tax Effected
Tax losses expiring:				
Within 10 years	**19,735**	**4,343**	12,530	2,760
More than 10 years	**47,937**	**11,611**	55,312	12,117
Available Indefinitely	**147,753**	**31,028**	101,889	21,397
Total	**215,425**	**46,982**	169,731	36,273
Tax credits expiring:				
Within 10 years	**4**	**4**	13	13
More than 10 years	**9,632**	**9,632**	9,107	9,107
Available indefinitely	**—**	**—**	—	—
Total	**9,636**	**9,636**	9,120	9,120

25. Taxation — continued

The Group had U.S. federal net operating losses carry forwards ("NOLs") of approximately $215.4 million, $169.7 million and $243.0 million as of December 31, 2021, 2020 and 2019, respectively, which are available to offset future taxable income. These NOLs expire through 2037 with the exception of $147.8 million which is not subject to expiration. The Group had U.S. Federal research and development tax credits of approximately $3.9 million, $3.9 million and $7.4 million as of December 31, 2021, 2020 and 2019, respectively, which are available to offset future taxes that expire at various dates through 2041. The Group also had Federal Orphan Drug credits of approximately $5.7 million and $5.2 million as of December 31, 2021, and 2020, which are available to offset future taxes that expire at various dates through 2041. A portion of these Federal NOLs and credits can only be used to offset the profits from the Company's subsidiaries who file separate Federal tax returns. These NOLs and credits are subject to review and possible adjustment by the Internal Revenue Service.

The Group had Massachusetts net operating losses carry forwards ("NOLs") of approximately $27.9 million, $67.4 million and $273.0 million for the years ended December 31, 2021, 2020 and 2019, respectively, which are available to offset future taxable income. These NOLs expire at various dates beginning in 2030. The Group had Massachusetts research and development tax credits of approximately $1.3 million, $2.1 million and $1.6 million for the years ended December 31, 2021, 2020 and 2019, respectively, which are available to offset future taxes and expire at various dates through 2036. These NOLs and credits are subject to review and possible adjustment by the Massachusetts Department of Revenue.

Utilization of the NOLs and research and development credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986 due to ownership change limitations that have occurred previously or that could occur in the future. These ownership changes may limit the amount of NOL and research and development credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. The Company notes that a 382 analysis was performed through December 31, 2021. The results of this analysis concluded that certain net operating losses were subject to limitation under Section 382 of the Internal Revenue Code. None of the Company's tax attributes which are subject to a restrictive Section 382 limitation have been recognized in the financial statements.

Tax Balances

The current tax related balances are presented in the Statement of Financial Position as follows:

As of December 31	**2021 $000s**	2020 $000s
Income tax receivable - current	**4,514**	—
Trade and Other Payables	**(57)**	(1,260)

Uncertain Tax Positions

The Company has no uncertain tax positions as of December 31, 2021. U.S. corporations are routinely subject to audit by federal and state tax authorities in the normal course of business.

26. Subsequent Events

The Company has evaluated subsequent events after December 31, 2021, the date of issuance of the Consolidated Financial Statements, and has not identified any recordable or disclosable events not otherwise reported in these Consolidated Financial Statements or notes thereto, except for the following:

On January 13, 2022 Gelesis completed its business combination with Capstar Special Purpose Acquisition Corp ("Capstar"). As part of the business combination all shares held in Gelesis, common and preferred, were exchanged for common shares of the merged entity. In addition, the Group invested $15.0 million in the class A common shares of Capstar as part of the PIPE transaction that took place immediately prior to the closing of the business combination and an additional approximately $5.0 million, as part of the Backstop agreement signed with Capstar on December 30, 2021 (see Note 6). Pursuant to the business combination, Gelesis became a wholly-owned subsidiary of Capstar and Capstar changed its name to Gelesis Holdings, Inc., which began trading on the New York Stock exchange under the ticker symbol "GLS" on January 14, 2022. Following the closing of the business combination, the PIPE transaction and the settlement of the aforementioned Backstop agreement with Capstar, PureTech holds 16,727,582 common shares of Gelesis Holdings Inc., which is equal to approximately 23.2% of Gelesis Holdings Inc's outstanding common shares.

On January 26, 2022, Akili Interactive and Social Capital Suvretta Holdings Corp a special purpose acquisition company announced they had entered into a definitive business combination agreement. Upon completion of the transaction, the combined company's securities are expected to be traded on the Nasdaq Stock Market under the ticker symbol "AKLI". The transaction is expected to close in mid-2022. As part of this transaction the Akili Interactive shares held by the Company will be exchanged for the combined company's securities and the Company's interest in the combined public entity is expected to decrease from its current voting interest in Akili of 26.7%.

PureTech Health plc Statement of Financial Position

For the years ended December 31

	Note	2021 $000s	2020 $000s
Assets			
Non-current assets			
Investment in subsidiary	2	**148,086**	161,082
Intercompany long-term receivable	3	**297,909**	297,556
Total non-current assets		**445,995**	458,638
Total current assets		**—**	—
Total assets		**445,995**	458,638
Equity and liabilities			
Equity			
Share capital	4	**5,444**	5,417
Share premium	4	**289,304**	288,978
Merger reserve	4	**138,506**	138,506
Other reserve	4	**7,730**	20,725
Accumulated deficit (Income/(loss) for the year $(3,401))	4	**(14,022)**	(10,621)
Total equity		**426,961**	443,005
Current liabilities			
Trade and other payables		**1,856**	621
Intercompany payables	5	**17,179**	15,012
Total current liabilities		**19,034**	15,633
Total equity and liabilities		**445,995**	458,638

Please refer to the accompanying Notes to the PureTech Health plc financial information. Registered number: 09582467.

The PureTech Health plc financial statements were approved by the Board of Directors and authorized for issuance on April 25, 2022 and signed on its behalf by:

Daphne Zohar
Chief Executive Officer

April 25, 2022

The accompanying Notes are an integral part of these financial statements.

PureTech Health plc Statements of Cash Flows

For the years ended December 31

	2021 $000s	2020 $000s
Cash flows from operating activities		
Net loss	**(3,401)**	(2,739)
Adjustments to reconcile net operating loss to net cash used in operating activities:		
Non-cash items:		
Changes in operating assets and liabilities:		
Intercompany payable	**2,167**	3,354
Accounts payable and accrued expenses	**465**	(614)
Net cash (used in) operating activities	**(770)**	—
Cash flows from investing activities:		
Net cash provided by (used in) investing activities	**—**	—
Cash flows from financing activities:		
Net cash provided by (used in) financing activities	**—**	—
Net decrease in cash and cash equivalents	**(770)**	—
Cash and cash equivalents at beginning of year	**—**	—
Cash and cash equivalents at end of year	**(770)**	—
Supplemental disclosure of non-cash investment and financing activities:		
Increase (Decrease) in investment against share-based awards	**(12,995)**	19,734
Exercise of share-based awards against intercompany receivable	**352**	1,025

The accompanying Notes are an integral part of these financial statements.

PureTech Health plc Statements of Changes in Equity

For the years ended December 31

	Shares	Amount $000s	Share Premium $000s	Merger Reserve $000s	Other Reserve $000s	Accumulated deficit $000s	Total equity $000s
Balance January 1, 2020	**285,370,619**	**5,408**	**287,962**	**138,506**	**991**	**(7,881)**	**424,986**
Total comprehensive loss for the period							—
Exercise of share-based awards	514,406	9	1,016	—	—	—	1,025
Settlement of restricted stock units	—	—	—	—	(12,888)	—	(12,888)
Equity settled share-based payments	—	—	—	—	33,902	—	33,902
Vesting of restricted stock units	—	—	—	—	(1,280)	—	(1,280)
Net loss	—	—	—	—	—	(2,739)	(2,739)
Balance December 31, 2020	**285,885,025**	**5,417**	**288,978**	**138,506**	**20,725**	**(10,620)**	**443,005**
Total comprehensive loss for the period							
Exercise of share-based awards	1,911,560	27	326	—	—	—	352
Equity settled share-based awards	—	—	—	—	7,109	—	7,109
Settlement of restricted stock units	—	—	—	—	(10,749)	—	(10,749)
Vesting of share-based awards and net share exercise	—	—	—	—	(2,582)	—	(2,582)
Reclassification of equity settled awards to liability awards in subsidiary	—	—	—	—	(6,773)	—	(6,773)
Net loss	—	—	—	—	—	(3,401)	(3,401)
Balance December 31, 2021	**287,796,585**	**5,444**	**289,303**	**138,506**	**7,730**	**(14,022)**	**426,961**

The accompanying Notes are an integral part of these financial statements.

Notes to the Financial Statements

1. Accounting policies

Basis of Preparation and Measurement

The financial statements of PureTech Health plc (the "Parent") are presented as of December 31, 2021 and 2020, and for the years ended December 31, 2021 and 2020, and have been prepared under the historical cost convention in accordance with international accounting standards in conformity with the requirements of UK-adopted International Financial Reporting Standards (IFRSs). The financial statements of PureTech Health plc also comply fully with IFRSs as issued by the International Accounting Standards Board (IASB). A summary of the significant accounting policies that have been applied consistently throughout the year are set out below.

Functional and Presentation Currency

The functional currency of the Parent is United States ("U.S.") Dollars and the financial statements are presented in U.S. Dollars.

Investments

Investments are stated at historic cost less any provision for impairment in value and are held for long-term investment purposes. Provisions are based upon an assessment of events or changes in circumstances that indicate that an impairment has occurred such as the performance and/or prospects (including the financial prospects) of the investee company being significantly below the expectations on which the investment was based, a significant adverse change in the markets in which the investee company operates or a deterioration in general market conditions.

Impairment

If there is an indication that an asset might be impaired, the Parent would perform an impairment review. An asset is impaired if the recoverable amount, being the higher of net realizable value and value in use, is less than its carrying amount. Value in use is measured based on future discounted cash flows attributable to the asset. In such cases, the carrying value of the asset is reduced to recoverable amount with a corresponding charge recognized in the profit and loss account.

Financial Instruments

Currently the Parent does not enter into derivative financial instruments. Financial assets and financial liabilities are recognized and cease to be recognized on the basis of when the related titles pass to or from the Parent Company.

Equity Settled Share Based Payments

Share based payment awards granted in subsidiaries to employees and consultants to be settled in Parent's equity instruments are accounted for as equity-settled share-based payment transactions in accordance with IFRS 2. The grant date fair value of employee share-based payment awards granted in subsidiaries is recognized as an increase to the investment with a corresponding increase in equity over the requisite service period related to the awards. The fair value is measured using an option pricing model, which takes into account the terms and conditions of the options granted. When the subsidiary settles the equity awards other than by the Parent's equity the settlement is recorded as a decrease in equity against a corresponding decrease to the investment account.

2. Investment in subsidiary

	$000s
Balance at May 8, 2015	—
Investment in PureTech LLC as a result of the reverse acquisition	**141,348**
Increase due to equity settled share based payments granted to employees and service providers in subsidiaries	**19,734**
Balance at December 31, 2020	**161,082**
Decrease due to equity settled share based payments granted to employees and service providers in subsidiaries	**(12,996)**
Balance at December 31, 2021	**148,086**

PureTech consists of the Parent and its subsidiaries (together, the "Group"). Investment in subsidiary represents the Parent's investment in PureTech LLC as a result of the reverse acquisition of the Group's financial statements immediately prior to the Parent's initial public offering ("IPO") on the London Stock Exchange in June 2015. PureTech LLC operates in the U.S. as a US-focused scientifically driven research and development company that conceptualizes, sources, validates and commercializes unexpected and potentially disruptive approaches to advance the needs of human health. For a summary of the Parent's indirect subsidiaries please refer to Note 1 of the Consolidated Financial Statements of PureTech Health plc.

In 2020, the Parent recognized a $19.7 million increase in its investment in its operating subsidiary PureTech LLC due to equity settled share based payments granted to employees and service providers in subsidiaries. $24.8 million out of such amount related to amounts which should have been recognized at December 31, 2019. The prior year balance sheet has not been adjusted since the Directors do not believe this item is qualitatively material to users of the financial statements, it has no impact on distributable reserves of the Parent and no impact on the Group consolidated financial statements. The disclosure relating to such share based payment awards is detailed in Note 8 of the accompanying Consolidated Financial Statements. The decrease in 2021 due to such equity settled share based payments results from settlements and payments of these equity awards by the subsidiaries, net of the expense related to the grant of such equity settled share based awards.

3. Intercompany receivables

The Parent has an accounts receivable balance from its operating subsidiary PureTech LLC of $297.9 million as of December 31, 2021 due to cash received from the IPO and other share issuances.

As of December 31, 2021and 2020, the intercompany receivable balance was classified as a long-term receivable since the Parent does not expect to realize the receivable within the next 12 months.

4. Share capital and reserves

PureTech plc was incorporated with the Companies House under the Companies Act 2006 as a public company on May 8, 2015.

On March 12, 2018, the Company raised approximately $100.0 million, before issuance costs and other expenses, by way of a Placing of 45,000,000 placing shares.

On June 24, 2015, the Company authorized 227,248,008 of ordinary share capital at one pence apiece. These ordinary shares were admitted to the premium listing segment of the United Kingdom's Listing Authority and traded on the Main Market of the London Stock Exchange for listed securities. In conjunction with the authorization of the ordinary shares, the Parent completed an IPO on the London Stock Exchange, in which it issued 67,599,621 ordinary shares at a public offering price of 160 pence per ordinary share, in consideration for$159.3 million, net of issuance costs of $11.8 million.

Additionally, the IPO included an over-allotment option equivalent to 15 percent of the total number of new ordinary shares. The stabilization manager provided notice to exercise in full its over-allotment option on July 2, 2015. As a result, the Parent issued 10,139,943 ordinary shares at the offer price of 160 pence per ordinary share, which resulted in net proceeds of $24.2 million, net of issuance costs of $0.8 million.

During the years ended December 31, 2020 and 2021, Other reserves increased (decreased) by $19.7 million and $(13.0) million respectively due to equity settled share based payments granted to employees and service providers in subsidiaries. See Note 2 above.

5. Intercompany payables

The Parent has a balance due to its operating subsidiary PureTech LLC of $17.2 million as of December 31, 2021, which is related to IPO costs and operating expenses. These intercompany payables do not bear any interest and are repayable upon demand.

6. Profit and loss account

As permitted by Section 408 of the Companies Act 2006, the Parent's profit and loss account has not been included in these financial statements. The Parent's loss for the year was $3.4 million.

7. Directors' remuneration, employee information and share-based payments

The remuneration of the executive Directors of the Parent Company is disclosed in Note 24, Related Parties Transactions, of the accompanying Consolidated Financial Statements. Full details for Directors' remuneration can be found in the Directors' Remuneration Report. Full detail of the share-based payment charge and the related disclosures can be found in Note 8, Share-based Payments, of the accompanying Consolidated Financial Statements.

The Parent had no employees during 2021 or 2020.

History and Development of the Company

We were incorporated and registered under the laws of England and Wales with the Registrar of Companies of England and Wales, United Kingdom in May 2015 as "PureTech Health plc." Our predecessor entity, PureTech Health LLC, or our Predecessor Entity, commenced formal operations and began engaging in initial sourcing activities in 2004, raising its first financing round greater than $5 million in the same year. The Predecessor Entity was acquired by PureTech Health plc on June 18, 2015 in a reorganization completed in connection with our initial public offering on the London Stock Exchange. The Predecessor Entity is now a wholly-owned subsidiary of PureTech Health plc. Our registered office is situated at 8th Floor, 20 Farringdon Street, London EC4A 4AB, United Kingdom, and our telephone number is +(1) 617 482 2333. Our U.S. operations are conducted by our wholly-owned subsidiary PureTech Health LLC, a Delaware limited liability company. Our ordinary shares have traded on the main market of the London Stock Exchange since June 2015 and our ADSs have traded on the Nasdaq Global Market since November 2020. Our agent for service of process in the United States is PureTech Health LLC located at 6 Tide Street, Suite 400, Boston, Massachusetts 02210 where our corporate headquarters and laboratories are located. Our website address is http://puretechhealth.com. The reference to our website is an inactive textual reference only and information contained in, or that can be accessed through, our website or any other website cited in this annual report is not part of hereof.

Risk Factor Annex

Our business faces significant risks. You should carefully consider all of the information set forth in this Annual Report and Accounts, including the following risk factors which we face and which are faced by our industry. These risks are not listed in any particular order of priority and are intended to supplement the risks identified elsewhere. Our business, financial condition or results of operations could be materially and adversely affected if any of these risks occurs.

This Annual Report and Accounts and our associated Annual Report on Form 20-F also contain forward-looking statements that involve risks and uncertainties. Our actual results could differ materially and adversely from those anticipated in these forward-looking statements as a result of certain factors including the risks described below and elsewhere. All statements contained in this Annual Report and Accounts and our associated Annual Report on Form 20-F, other than statements of historical fact, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "would," "could," "should," "continue" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. The forward-looking statements in this Annual Report and Accounts and associated Annual Report on Form 20-F include, among other things, statements about:

- our ability to realize value from our Founded Entities, which may be impacted if we reduce our ownership to a minority interest or otherwise cede control to other investors through contractual agreements or otherwise;
- the success, cost and timing of our clinical development of our Wholly Owned Programs, including the progress of, and results from, our preclinical and clinical trials of LYT-100, LYT-200, LYT-210, LYT-300, LYT-500, LYT-503 /IMB-150, LYT-510, or our therapeutics candidates, and our discovery programs (Alivio, Glyph, Orasome and other technologies, and our meningeal lymphatics discovery research program) and other potential therapeutic candidates within our Wholly Owned Pipeline;
- our ability to obtain and maintain regulatory clearance, authorization, or approval of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities, and any related restrictions, limitations or warnings in the label of any of the therapeutic candidates, if cleared, authorized, or approved;
- our ability to compete with companies currently marketing or engaged in the development of treatments for indications within our Wholly Owned Pipeline or those of our Founded Entities are designed to target;
- our plans to pursue research and development of other future therapeutic candidates;
- the potential advantages of the therapeutic candidates within our Wholly Owned Pipeline and the therapeutic candidates being developed by our Founded Entities;
- the rate and degree of market acceptance and clinical utility of our therapeutic candidates;
- the success of our collaborations and partnerships with third parties;
- our estimates regarding the potential market opportunity for the therapeutic candidates within our Wholly Owned Pipeline and the therapeutic candidates being developed by our Founded Entities;
- our sales, marketing and distribution capabilities and strategy;
- our ability to establish and maintain arrangements for manufacture of the therapeutic candidates within our Wholly Owned Pipeline and therapeutic candidates being developed by our Founded Entities;
- our intellectual property position;
- our expectations related to the use of capital;
- the effect of the COVID-19 pandemic, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations;
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- the impact of government laws and regulations; and
- our competitive position.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. You should refer to the below for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this Annual Report and Accounts, our associated Annual Report on Form 20-F and the documents that we have filed as exhibits to the Annual Report on 20-F completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

This Annual Report and Accounts and our associated Annual Report on Form 20-F include statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information

Risks Related to our Financial Position and Need for Additional Capital

We are a clinical-stage biopharmaceutical company and have incurred significant operating losses since our inception. We may continue to incur significant operating losses for the foreseeable future.

Investment in biotechnology therapeutic development, as well as medical device development, is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential therapeutic candidate will be unable to demonstrate effectiveness or an acceptable safety profile, gain regulatory approval and become commercially viable. To date, only two of our Founded Entities' therapeutics, Gelesis, Inc.'s Plenity and Akili Interactive Labs, Inc.'s EndeavorRx, have received marketing authorization from the U.S. Food and Drug Administration, or the FDA, and marketing authorization granted in the European Economic Area, or EEA, and in other countries that recognize the CE Mark, or CE Mark market authorizations. All of the therapeutic candidates in our Wholly Owned Pipeline and the majority of our Founded Entities' therapeutic candidates may require substantial additional development time, including extensive clinical research, and resources before we would be able to apply for or receive regulatory clearances or approvals and begin generating revenue from therapeutic sales.

Since our inception, we have invested most of our resources in developing our technology and therapeutic candidates, building our intellectual property portfolio, developing our supply chain, conducting business planning, raising capital and providing general and administrative support for these operations, including with respect to our Founded Entities. We are not operationally profitable and have incurred operating losses in each year since our inception. Our operating losses for the years ended December 31, 2019, 2020 and 2021 were $135.4 million, $119.6 million, and $149.2 million, respectively. We have no therapeutics developed in our Wholly Owned Pipeline approved for commercial sale and have not generated any revenues from therapeutic sales, and we and our Founded Entities have financed operations solely through the sale of equity securities, revenue from strategic alliances and government funding and, with respect to certain of our Founded Entities, debt financings. We continue to incur significant research and development, or R&D, and other expenses related to ongoing operations and expect to incur losses for the foreseeable future. We anticipate continued losses for the foreseeable future.

Due to risks and uncertainties associated with the development of drugs, biologics and medical devices, we are unable to predict the timing or amount of our expenses, or when we will be able to generate any meaningful revenue or achieve or maintain profitability, if ever. In addition, our expenses could increase beyond our current expectations if we are required by the FDA, the European Medicines Agency, or the EMA, or other comparable foreign regulatory authorities to perform preclinical studies or clinical trials in addition to those that we currently anticipate, or if there are any delays in any of our or our future collaborators' clinical trials or the development of our existing therapeutic candidates and any other therapeutic candidates that we may identify. Even if our existing therapeutic candidates or any future therapeutic candidates that we may identify are approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved therapeutic and ongoing compliance efforts.

As of December 31, 2021, we had never generated revenue from the therapeutic candidates within our Wholly Owned Pipeline, and we may never be operationally profitable.

While Gelesis, Inc., or Gelesis, and Akili Interactive Labs, Inc., or Akili, have received marketing authorization for Plenity and EndeavorRx, respectively, from the FDA and CE Mark market authorizations, we may never be able to develop or commercialize marketable therapeutics or achieve operational profitability. Revenue from the sale of any therapeutic candidate for which regulatory clearance, authorization or approval is obtained will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory clearance, authorization or approval, the accepted price for the therapeutic, the ability to obtain reimbursement at any price and whether we own the commercial rights for that territory. Our growth strategy depends on our ability to generate revenue. In addition, if the

number of addressable patients is not as anticipated, the indication or intended use cleared, authorized or approved by regulatory authorities is narrower than expected, or the reasonably accepted population for treatment is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such therapeutics, even if cleared, authorized or approved. Even if we are able to generate revenue from the sale of any cleared, authorized or approved therapeutics, we may not become operationally profitable and may need to obtain additional funding to continue operations. Even if we achieve operational profitability in the future, we may not be able to sustain profitability in subsequent periods.

If we are unable to achieve sustained profitability, it would depress the value of our company and could impair our ability to raise capital, expand our business, diversify our R&D pipeline, market the therapeutic candidates within our Wholly Owned Pipeline, if cleared or approved, and pursue or continue our operations. Our prior losses, combined with expected future losses, have had and may continue to have an adverse effect on our shareholders' equity and working capital.

We may require substantial additional funding to achieve our business goals. If we are unable to obtain this funding when needed and on acceptable terms, we could be forced to delay, limit or terminate certain of our therapeutic development efforts. Certain of our Founded Entities will similarly require substantial additional funding to achieve their business goals.

Across the entire portfolio, we established the underlying programs and platforms that have resulted in 27 therapeutics and therapeutic candidates that are being advanced within our Wholly Owned Programs or by our Founded Entities. Of these therapeutics and therapeutic candidates, 16 are clinical-stage and two have been authorized for marketing by the FDA and granted CE Mark marketing authorizations. Developing biopharmaceutical therapeutics is expensive and time-consuming, and with respect to the therapeutic candidates within our Wholly Owned Pipeline, we expect to require substantial additional capital to conduct research, preclinical studies and clinical trials for our current and future programs, establish pilot scale and commercial scale manufacturing processes and facilities, seek regulatory approvals for the therapeutic candidates within our Wholly Owned Pipeline and launch and commercialize any therapeutics for which we receive regulatory approval, including building our own commercial sales, marketing and distribution organization. With respect to our Founded Entities' programs, we anticipate that we will continue to fund a small portion of development costs by strategically participating in such companies' financings when doing so would be in the interests of our shareholders. The form of any such participation may include investment in public or private financings, collaboration and partnership arrangements and licensing arrangements, among others. Our management and strategic decision makers have not made decisions regarding the future allocation of certain of our resources among our Founded Entities, but evaluate the needs and opportunities with respect to each of these Founded Entities routinely and on a case-by-case basis. In connection with any collaboration agreements relating to our Wholly Owned Programs, we are also responsible for the payments to third parties of expenses that may include milestone payments, license maintenance fees and royalties, including in the case of certain of our agreements with academic institutions or other companies from whom intellectual property rights underlying their respective programs have been in-licensed or acquired. Because the outcome of any preclinical or clinical development and regulatory approval process is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development, regulatory approval process and potential commercialization of our Wholly Owned Programs and any future therapeutic candidates we may identify.

As of December 31, 2021, we had cash and cash equivalents of $465.7 million at the PureTech Health plc level. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, sales of assets or programs, other sources, such as strategic collaborations or license and development agreements, or a combination of these approaches. Even if we believe we have sufficient funds for our current or future operating plans, we may opportunistically seek additional capital if market conditions are favorable or if we have specific strategic considerations. Our spending will vary based on new and ongoing therapeutic development and corporate activities. Any such additional fundraising efforts for us may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize therapeutic candidates that we may identify and pursue. Moreover, such financing may result in dilution to shareholders, imposition of debt covenants and repayment obligations, or other restrictions that may affect our business.

Our future funding requirements, both short-term and long-term, will depend on many factors, including, but not limited to:

- the time and cost necessary to complete ongoing, planned and future unplanned clinical trials, including our ongoing clinical trials for certain of our therapeutic candidates, and potential future clinical trials for certain of our therapeutic candidates;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA, the EMA and other comparable foreign regulatory authorities;
- the progress, timing, scope and costs of our preclinical studies, clinical trials and other related activities for our ongoing and planned clinical trials, and potential future clinical trials;
- the costs of obtaining clinical and commercial supplies of raw materials and drug products for the therapeutic candidates within our Wholly Owned Pipeline, as applicable, and any other therapeutic candidates we may identify and develop;
- our ability to successfully identify and negotiate acceptable terms for third-party supply and contract manufacturing agreements with contract manufacturing organizations, or CMOs;
- the costs of commercialization activities for any of the therapeutic candidates within our Wholly Owned Pipeline that receive marketing approval, including the costs and timing of establishing therapeutic sales, marketing, distribution and manufacturing capabilities, or entering into strategic collaborations with third parties to leverage or access these capabilities;
- the amount and timing of sales and other revenues from the therapeutic candidates within our Wholly Owned Pipeline, if approved, including the sales price and the availability of coverage and adequate third-party reimbursement;
- the cash requirements of our Founded Entities and our ability and willingness to provide them with financing;
- the cash requirements of any future acquisitions or discovery of therapeutic candidates;
- the time and cost necessary to respond to technological and market developments, including other therapeutics that may compete with one or more of our Wholly Owned Programs;
- the costs of acquiring, licensing or investing in intellectual property rights, therapeutics, therapeutic candidates and businesses;
- our ability to attract, hire and retain qualified personnel as we expand R&D and establish a commercial infrastructure;
- the costs of maintaining, expanding and protecting our intellectual property portfolio; and
- the costs of operating as a public company in the United Kingdom and the United States and maintaining listings on both the London Stock Exchange, or the LSE, and The Nasdaq Global Market, or Nasdaq.

We cannot be certain that additional funding will be available on acceptable terms, or at all. If adequate funds are not available to us on a timely basis, we may be required to delay, limit or terminate one or more research or development programs or the potential commercialization of any approved therapeutics or be unable to expand operations or otherwise capitalize on business opportunities, as desired, which could materially affect our business, prospects, financial condition and results of operations.

Raising additional capital may cause dilution to our existing shareholders, restrict our operations or require us to relinquish rights to current therapeutic candidates or to any future therapeutic candidates on unfavorable terms.

We expect our expenses to increase in connection with our planned operations. Unless and until we can generate a substantial amount of revenue from the therapeutic candidates within our Wholly Owned Pipeline or royalties and other monetization events related to our Founded Entities, we expect to finance our future cash needs through a combination of public and private equity offerings, debt financings, strategic partnerships, sales of assets and alliances and licensing arrangements. We, and indirectly, our shareholders, may bear the cost of issuing and servicing any such securities and of entering into and maintaining any such strategic partnerships or other arrangements. Because any decision by us to issue debt or equity securities in the future will depend on market conditions and other factors beyond our control, we cannot predict or estimate the amount, timing or nature of any future financing transactions. To the extent that we or our Founded Entities raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a shareholder. The incurrence of additional indebtedness would result in increased fixed payment obligations and could involve additional restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Additionally, any future collaborations we enter into with third parties may provide capital in the near term, but limit our potential cash flow and revenue in the future.

If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or therapeutic candidates, or grant licenses or other rights on unfavorable terms.

In addition, if any of our Founded Entities raises funds through the issuance of equity securities, our shareholders' indirect equity interest in such Founded Entity could be substantially diminished. If any of our Founded Entities raises additional funds through collaboration and licensing arrangements, it may be necessary to relinquish some rights to our technologies or these therapeutic candidates or grant licenses on terms that are not favorable to us.

If we engage in acquisitions or strategic partnerships, this may increase our capital requirements, dilute our shareholders, cause us to incur debt or assume contingent liabilities and subject us to other risks.

We may engage in various acquisitions and strategic partnerships in the future, including licensing or acquiring complementary therapeutics, intellectual property rights, technologies or businesses. Any acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of indebtedness or contingent liabilities;
- the issuance of our equity securities which would result in dilution to our shareholders;
- assimilation of operations, intellectual property, therapeutics and therapeutic candidates of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing therapeutic programs and initiatives in pursuing such an acquisition or strategic partnership;
- retention of key employees, the loss of key personnel and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing therapeutics or therapeutic candidates and regulatory approvals; and
- our inability to generate revenue from acquired intellectual property, technology and/or therapeutics sufficient to meet our objectives or even to offset the associated transaction and maintenance costs.

In addition, if we undertake such a transaction, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense.

Risks Related to Our Founded Entities

Our ability to realize value from our Founded Entities may be impacted if we reduce our ownership or otherwise cede control to other investors through contractual agreements or otherwise.

We do not have a majority interest in our Non-Controlled Founded Entities. Our interests may be further reduced as such companies raise capital from third-party investors. In addition, we may agree to contractual arrangements for the funding of further developments by one or more of our Founded Entities. As a result, with respect to our Non-Controlled Founded Entities, we may not be able to exercise control over the affairs of such Founded Entity, including that Founded Entity's governance arrangements and access to management and financial information. We are also party to agreements with certain of our Founded Entities that contain provisions which could force us to exit from that Founded Entity at a time and/or price determined by other investor(s) (for example, by the exercise of drag-along rights). If we were forced to exit out of a Founded Entity, this could have a material adverse effect on our business, financial condition or results of operations and prospects. In addition, if the affairs of one or more Founded Entities in which we hold a minority stake were to be conducted in a manner detrimental to our interests or intentions, our business, reputation and prospects may be adversely affected.

As certain of our Founded Entities have completed equity financings, they have entered into certain agreements with the investors participating in such financings, including us. We are party to voting agreements with Entrega, Inc., or Entrega, Sonde Health, Inc., or Sonde, Vedanta Biosciences, Inc., or Vedanta, and Follica, Incorporated, or Follica; investors' rights agreements with Akili, Follica, Vedanta, Entrega, Sonde and Vor Biopharma Inc., or Vor, and stockholders' agreements with Gelesis, Akili, Follica, Vedanta, Entrega, and Sonde, pursuant to which we are subject to certain restrictions on the transfer or sale of shares (e.g., pre-emptive rights or drag-along, tag-along rights or lock up agreements), and we may not be able freely to transfer our interest in such Founded Entities or procure the sale of the entire issued share capital of such Founded Entities, similar to other investors who are party to these agreements. In addition, many of our Founded Entities have employee share plans which further dilute our interest in such business. If the affairs of one or more of our Founded Entities were to be conducted in a manner detrimental to our interests or intentions or if we were unable to realize our interest in a Founded Entity or suffer dilution of our shareholding, this could have a material adverse effect on our business, financial condition or results of operation and prospects.

Our overall value may be dominated by a single or limited number of our Founded Entities.

A large proportion of our overall value may at any time reside in a small proportion of our Founded Entities. Accordingly, there is a risk that if one or more of the intellectual property or commercial rights relevant to a valuable business were impaired, this would have a material adverse impact on our overall value. Furthermore, a large proportion of our overall revenue may at any time be the subject of one, or a small number of, licensed technologies. Should the relevant licenses be terminated or expire this would be likely to have a material adverse effect on the revenue received by us. Any material adverse impact on the value of the business of a Founded Entity could, in the situations described above, or otherwise, have a material adverse effect on our business, financial condition, trading performance and/or prospects.

We have limited information about and limited control or influence over our Non-Controlled Founded Entities.

While we maintain ownership of equity interests in our Non-Controlled Founded Entities, we do not maintain voting control or direct management and development efforts for these entities. Each of these entities are independently managed, and we do not control the clinical and regulatory development of these Non-Controlled Founded Entities' therapeutic candidates. Any failure by our Non-Controlled Founded Entities to adhere to regulatory requirements, initiate preclinical studies and clinical trials on schedule or to obtain clearances or approvals for their therapeutic candidates could have an adverse effect on our business, financial condition, results of operation and prospects. The information included in this report about our Non-Controlled Founded Entities is based on (i) our knowledge, which may in some cases be limited, (ii) information that is publicly available, including the public filings of SEC reporting companies, such as Karuna, Vor and Gelesis, and (iii) information provided to us by our Non-Controlled Founded Entities. Where a date is provided, the information included in this report about our Non-Controlled Founded Entities is as of that date and you should not assume that it is accurate as of any other date. As such, there may be developments at our Non-Controlled Founded Entities of which we are unaware that could have an adverse effect on our business, financial condition, results of operation and prospects.

Our Founded Entities are difficult to value given that many of their therapeutic candidates are in the development stage.

Investments in early-stage companies, particularly privately held entities, are inherently difficult to value since sales, cash flow and tangible asset values are very limited, which makes the valuation highly dependent on expectations of future development, and any future significant revenues would only arise in the medium to longer terms and are uncertain. Equally, investments in companies just commencing the commercial stage are also difficult to value since sales, cash flow and tangible assets are limited, they have only commenced initial receipts of revenues and valuations are still dependent on expectations of future development. There can be no guarantee that our valuation of our Founded Entities will be considered to be correct in light of the early stage of development for many of these entities and their future performance. As a result, we may not realize the full value of our ownership in such Founded Entities which could adversely affect our business and results of operations. For example, on November 15, 2019, resTORbio, Inc., or resTORbio, announced that its lead therapeutic candidate, RTB101, did not meet its primary endpoint in its Phase 3 study and ceased further development leading to a decline in resTORbio's stock price from $9.27 to $1.09 and our sale of 7,680,700 common shares of resTORbio. As a result of the foregoing, we recognized a total cash loss of approximately $10 million from our initial investment through sale of shares.

Certain of our and our Founded Entities' therapeutics and therapeutic candidates represent novel therapeutic approaches and negative perception of any therapeutic or therapeutic candidate that we or they develop could adversely affect our ability to conduct our business, obtain and maintain regulatory clearance, authorization or approvals or identify alternate regulatory pathways to market for such therapeutic candidate.

Certain of our and our Founded Entities' therapeutic candidates are considered relatively new and novel therapeutic approaches. Our and their success will depend upon physicians who specialize in the treatment of diseases targeted by our and their therapeutic candidates, prescribing potential treatments that involve the use of our and their therapeutic candidates, if approved, in lieu of, or in addition to, existing treatments with which they are more familiar and for which greater clinical data may be available. Access will also depend on consumer acceptance and adoption of therapeutics that are commercialized. In addition, responses by the U.S., state or foreign governments to negative public perception or ethical concerns may result in new legislation or regulations that could limit our or our Founded Entities' ability to develop or commercialize any

therapeutic candidates, obtain or maintain regulatory approval, identify alternate regulatory pathways to market or otherwise achieve profitability. More restrictive statutory regimes, government regulations or negative public opinion would have an adverse effect on our business, financial condition, results of operations and prospects and may delay or impair the development and commercialization of our or our Founded Entities' therapeutic candidates or demand for any therapeutics we or they may develop.

For example, in the United States and the European Union, no therapeutics to date have been approved specifically demonstrating an impact on the microbiome as part of their therapeutic effect. Vedanta is developing a pipeline of microbiome-derived modulators for immune and infectious disease. Microbiome therapies may not be successfully developed or commercialized or gain the acceptance of the public or the medical community. Additionally, adverse events, or AEs, in non-investigational new drug application, or IND, human clinical studies and clinical trials of Vedanta's therapeutic candidates or in clinical trials of other companies developing similar therapeutics and the resulting publicity, similarly to the AEs publicized with respect to Seres Therapeutics, Inc.'s SER-287 Phase 2 clinical trial, as well as any other AEs in the field of the microbiome, could result in a decrease in demand for any therapeutic that Vedanta may develop. Finally, the FDA, the EMA or other comparable foreign regulatory authorities may lack experience in evaluating the safety and efficacy of therapeutic candidates based on microbiome therapeutics, which could result in a longer than expected regulatory review process, increase expected development costs and delay or prevent potential commercialization of therapeutic candidates.

Risks Related to the Clinical Development, Regulatory Review and Approval of our and our Founded Entities' Therapeutic Candidates

Risks Related to Clinical Development

The therapeutic candidates within our Wholly Owned Pipeline and most of our Founded Entities' therapeutic candidates are in preclinical or clinical development, which is a lengthy and expensive process with uncertain outcomes and the potential for substantial delays. We cannot give any assurance that any of our and our Founded Entities' therapeutic candidates will receive regulatory clearance, authorization or approval, which is necessary before they can be commercialized.

Before obtaining marketing clearance, authorization or approval from regulatory authorities for the sale of our or our Founded Entities' therapeutic candidates, we or our Founded Entities must conduct extensive clinical trials to demonstrate the safety and efficacy, or with respect to biologics, safety, purity and potency, of the therapeutic candidates in humans. To date, we have focused substantially all of our efforts and financial resources on identifying, acquiring, and developing therapeutic candidates, including conducting lead optimization, preclinical studies and clinical trials, and providing general and administrative support for these operations. To date, only two of our Founded Entities' therapeutic candidates, Gelesis' Plenity and Akili's EndeavorRx, have received marketing authorization from the FDA, and we cannot be certain that any of our internal or our Founded Entities' other therapeutic candidates will receive regulatory clearance, authorization or approval, the timing of such clearance, authorization or approval, if received, or that clinical trials will progress as planned. Our or our Founded Entities' inability to successfully complete preclinical and clinical development could result in additional costs to us and negatively impact our ability to generate revenue. Our future success is dependent on our and our Founded Entities' ability to successfully develop, obtain regulatory clearance, authorization or approval for, and then successfully commercialize therapeutic candidates. We and our Founded Entities, with the exceptions of Gelesis and Akili, currently have no drugs or biologics approved or devices cleared, authorized or approved for sale and have not generated any revenue from sales of drugs, biologics or devices. We cannot guarantee that we or our Founded Entities will be able in the future to develop or successfully commercialize any of our or their therapeutic candidates. Additionally, there is currently no FDA approved live biological therapeutic using a defined cocktail of microbes, which could result in regulatory complexity in Vedanta's pipeline. There is also no approved drug therapy for lymphedema, which will require us to engage In further discussions with the FDA on requirements for potential approval.

Other than Gelesis' Plenity and Akili's EndeavorRx, all of our Wholly Owned Programs and our Founded Entities' therapeutic candidates require additional development; management of preclinical, clinical, and manufacturing activities; and/or regulatory clearances, authorization or approvals. In addition, we or our Founded Entities may need to obtain adequate manufacturing supply; build a commercial organization; commence marketing efforts; and obtain coverage and reimbursement before we generate any significant revenue from commercial therapeutic sales, if ever. Many of the therapeutic candidates in our Wholly Owned Pipeline and our Founded Entities' therapeutic candidates are in early-stage research or translational phases of development, and the risk of failure for these programs is high. We cannot be certain that any of the therapeutic candidates in our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates will be successful in clinical trials or receive regulatory approval, authorization or clearance. Further, our Wholly Owned Programs or our Founded Entities' therapeutic candidates may not receive regulatory clearance, authorization or approval even if we believe they are successful in clinical trials. If we or our Founded Entities do not receive regulatory clearance, authorization or approval for our or their therapeutic candidates, we may not be able to continue operations, which may result in dissolution, out-licensing the technology or pursuing an alternative strategy.

Preclinical development is uncertain. Our preclinical programs may experience delays or may never advance to clinical trials, which would adversely affect our ability to obtain regulatory clearance, authorization or approvals or commercialize these programs on a timely basis or at all, which would have an adverse effect on our business.

Certain of our Wholly Owned Programs are in the preclinical stage, and their risk of failure is high. Before we can commence clinical trials for a therapeutic candidate, we must complete extensive preclinical testing and studies that support our planned INDs, in the United States, or similar applications in other jurisdictions. We cannot be certain of the timely completion or outcome of our preclinical testing and studies and cannot predict if the FDA or other regulatory authorities will accept our proposed clinical programs or if the outcome of our preclinical testing and studies will ultimately support the further development of our programs. As a result, we cannot be sure that we will be able to submit INDs or similar applications for our preclinical programs on the timelines we expect, if at all, and we cannot be sure that submission of INDs or similar applications will result in the FDA, the EMA or other regulatory authorities allowing clinical trials to begin.

Clinical trials of our or our Founded Entities' therapeutic candidates may be delayed, and certain programs may never advance in the clinic or may be more costly to conduct than we anticipate, any of which can affect our ability to fund our company and would have a material adverse impact on our platform or our business.

Clinical testing is expensive, time-consuming, and subject to uncertainty. We cannot guarantee that any of our ongoing and planned clinical trials will be conducted as planned or completed on schedule, if at all. Moreover, even if these trials are initiated or conducted on a timely basis, issues may arise that could result in the suspension or termination of such clinical trials. A failure of one or more clinical trials can occur at any stage of testing, and our clinical trials may not be successful. Events that may prevent successful or timely initiation or completion of clinical trials include:

- inability to generate sufficient preclinical, toxicology, or other in vivo or in vitro data to support the initiation or continuation of clinical trials;
- delays in confirming target engagement, patient selection or other relevant biomarkers to be utilized in preclinical and clinical therapeutic candidate development;
- delays in reaching a consensus with regulatory agencies as to the design or implementation of our clinical studies;
- delays in reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- delays in identifying, recruiting and training suitable clinical investigators;
- delays in obtaining required Institutional Review Board, or IRB, approval at each clinical trial site;
- imposition of a temporary or permanent clinical hold by regulatory agencies for a number of reasons, including after review of an IND or amendment, clinical trial application, or CTA, or amendment, investigational device exemption, or IDE, or supplement, or equivalent application or amendment; as a result of a new safety finding that presents unreasonable risk to clinical trial participants; or a negative finding from an inspection of our clinical trial operations or study sites;
- developments in trials for other therapeutic candidates with the same targets or related modalities as our or our Founded Entities' therapeutic candidates conducted by competitors that raise regulatory or safety concerns about risk to patients of the treatment, or if the FDA finds that the investigational protocol or plan is clearly deficient to meet its stated objectives;
- difficulties in securing access to materials for the comparator arm of certain of our clinical trials;
- delays in identifying, recruiting and enrolling suitable patients to participate in clinical trials, and delays caused by patients withdrawing from clinical trials or failing to return for post-treatment follow-up;
- difficulties in finding a sufficient number of trial sites, or trial sites deviating from trial protocol or dropping out of a trial;
- difficulty collaborating with patient groups and investigators;

- failure by CROs, other third parties, or us to adhere to clinical trial requirements;
- failure by CROs, other third parties, or us to perform in accordance with the FDA's or any other regulatory authority's current good clinical practices, or GCP, requirements, or regulatory guidelines in other countries;
- occurrence of AEs or undesirable side effects or other unexpected characteristics associated with the therapeutic candidate that are viewed to outweigh its potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- the cost of clinical trials of any therapeutic candidates that we may identify and pursue being greater than we anticipate;
- clinical trials of any therapeutic candidates that we may identify and pursue producing negative or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct additional clinical trials or abandon therapeutic development programs;
- transfer of manufacturing processes to larger-scale facilities operated by a CMO, or by us, and delays or failures by our CMOs or us to make any necessary changes to such manufacturing process;
- delays in manufacturing, testing, releasing, validating, or importing/exporting sufficient stable quantities of therapeutic candidates that we may identify for use in clinical trials or the inability to do any of the foregoing; and
- factors we may not be able to control, such as current or potential pandemics or other events that may limit patients, principal investigators or staff or clinical site availability, result in clinical trial protocol deviations, or impact supply of our or our Founded Entities' therapeutic candidates (e.g., the COVID-19 pandemic or the developing conflict between Russia and Ukraine).

Any inability to successfully initiate or complete clinical trials could result in additional costs to us or impair our ability to generate revenue. In addition, if we make manufacturing or formulation changes to our Wholly Owned Programs, we may be required to or we may elect to conduct additional preclinical studies or clinical trials to bridge data obtained from our modified therapeutic candidates to data obtained from preclinical and clinical research conducted using earlier versions. Clinical trial delays could also shorten any periods during which our therapeutics have patent protection and may allow our competitors to bring therapeutics to market before we do, which could impair our ability to successfully commercialize therapeutic candidates and may harm our business and results of operations.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the data safety monitoring board, or DSMB, or by the FDA, the EMA or other comparable foreign regulatory authorities, or if the IRBs of the institutions in which such trials are being conducted suspend or terminate the participation of their clinical investigators and sites subject to their review. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA, the EMA or other comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a therapeutic candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA, the EMA or comparable foreign regulatory authorities. The FDA, the EMA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA, the EMA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA, the EMA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our Wholly Owned Programs or our Founded Entities' therapeutic candidates.

Delays in the initiation, conduct or completion of any clinical trial of the therapeutic candidates within our Wholly Owned Pipeline will increase our costs, slow down the therapeutic candidate development and approval process and delay or potentially jeopardize our ability to commence therapeutic sales and generate revenue. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates. In the event we identify any additional therapeutic candidates to pursue, we cannot be sure that submission of an IDE, IND, CTA, or equivalent application, as applicable, will result in the FDA, the EMA or comparable foreign regulatory authority allowing clinical trials to begin in a timely manner, if at all. Any of these events could have a material adverse effect on our business, prospects, financial condition and results of operations.

The results of early-stage clinical trials and preclinical studies may not be predictive of future results. Initial data in clinical trials may not be indicative of results obtained when these trials are completed or in later stage trials.

The results of preclinical studies may not be predictive of the results of clinical trials, and the results of any early-stage clinical trials we commence may not be predictive of the results of the later-stage clinical trials. The results of preclinical studies and clinical trials in one set of patients or disease indications, or from preclinical studies or clinical trials that we did not lead, may not be predictive of those obtained in another. In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same therapeutic candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. In addition, preclinical and clinical data are often susceptible to various interpretations and analyses, and many companies that have believed their therapeutic candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval. A number of companies in the pharmaceutical, biopharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies, and any such setbacks in our clinical development could have a material adverse effect on our business and operating results. Even if early-stage clinical trials are successful, we may need to conduct additional clinical trials of our Wholly Owned Programs in additional patient populations or under different treatment conditions before we are able to seek approvals or clearances from the FDA, the EMA or other comparable foreign regulatory authorities to market and sell these therapeutic candidates. Our failure to obtain marketing authorization for the therapeutic candidates within our Wholly Owned Pipeline would substantially harm our business, prospects, financial condition and results of operations.

If we encounter difficulties enrolling patients in clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

Identifying and qualifying trial participants to participate in clinical studies is critical to our success. The timing of our clinical studies depends on the speed at which we can recruit trial participants to participate in testing the therapeutic candidates within our Wholly Owned Pipeline. Delays in enrollment may result in increased costs or may affect the timing or outcome of the planned clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of the therapeutic candidates within our Wholly Owned Pipeline. If trial participants are unwilling to participate in our studies because of negative publicity from AEs in our trials or other trials of similar therapeutics, or those related to specific therapeutic area, or for other reasons, including competitive clinical studies for similar patient populations, the timeline for recruiting trial participants, conducting studies, and obtaining regulatory approval of potential therapeutics may be delayed. We also may face delays as a result of unforeseen global circumstances, for example we have experienced temporary delays in certain of our clinical development activities, including enrolling participants in certain of our clinical trials, as a result of the COVID-19 pandemic or the developing conflict between Russia and Ukraine. Any delays could result in increased costs, delays in advancing our therapeutic candidate development, delays in testing the effectiveness of the therapeutic candidates within our Wholly Owned Pipeline, or termination of the clinical studies altogether.

We may not be able to identify, recruit and enroll a sufficient number of trial participants, or those with required or desired characteristics to achieve diversity in a study, to complete our clinical studies in a timely manner. Patient and subject enrollment is affected by factors including:

- the size and nature of a patient population;
- the patient eligibility criteria defined in the applicable clinical trial protocols, which may limit the patient populations eligible for clinical trials to a greater extent than competing clinical trials for the same indication;
- the size of the study population required for analysis of the trial's primary endpoints;
- the severity of the disease under investigation;
- the proximity of patients to a trial site;
- the inclusion and exclusion criteria for the trial in question;

- the design of the trial protocol;
- the ability to recruit clinical trial investigators with the appropriate competencies and experience;
- the availability and efficacy of approved medications or therapies for the disease or condition under investigation;
- clinicians' and patients' perceptions as to the potential advantages and side effects of the therapeutic candidate being studied in relation to other available therapies and therapeutic candidates;
- the ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will not complete such trials, for any reason.

Furthermore, our or our collaborators' ability to successfully initiate, enroll and conduct a clinical trial outside the United States is subject to numerous additional risks, including:

- difficulty in establishing or managing relationships with CROs and physicians;
- differing standards for the conduct of clinical trials;
- differing standards of care for patients with a particular disease;
- an inability to locate qualified local consultants, physicians and partners; and
- the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology therapeutics and treatments.

If we have difficulty enrolling sufficient numbers of patients to conduct clinical trials as planned, we may need to delay or terminate clinical trials, either of which would have an adverse effect on our business.

Use of the therapeutic candidates within our Wholly Owned Pipeline or the therapeutic candidates being developed by our Founded Entities could be associated with side effects, AEs or other properties or safety risks, which could delay or halt their clinical development, prevent their regulatory clearance, authorization or approval, cause us to suspend or discontinue clinical trials, abandon a therapeutic candidate, limit their commercial potential, if cleared, authorized or approved, or result in other significant negative consequences that could severely harm our business, prospects, operating results and financial condition.

As is the case with pharmaceuticals generally, it is likely that there may be side effects and AEs associated with our and our Founded Entities' drug or biologic therapeutic candidates' use. Similarly, investigational devices may also be subject to side effects and AEs. Results of our clinical trials or those being conducted by Founded Entities could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by these therapeutic candidates could cause us, our Founded Entities or regulatory authorities to interrupt, delay or halt clinical trials and could result in more restrictive labeling or the delay or denial of regulatory clearance, authorization or approval by the FDA, the EMA or other comparable foreign regulatory authorities. The side effects related to the therapeutic candidate could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Moreover, if therapeutic candidates within our Wholly Owned Pipeline are associated with undesirable side effects in preclinical studies or clinical trials or have characteristics that are unexpected, we may elect to abandon their development or limit their development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective, which may limit the commercial expectations for the therapeutic candidate if approved. We may also be required to modify or terminate our study plans based on findings in our preclinical studies or clinical trials. Many therapeutic candidates that initially show promise in early-stage testing may later be found to cause side effects that prevent further development. As we work to advance existing therapeutic candidates and to identify new therapeutic candidates, we cannot be certain that later testing or trials of therapeutic candidates that initially showed promise in early testing will not be found to cause similar or different unacceptable side effects that prevent their further development.

It is possible that as we test the therapeutic candidates within our Wholly Owned Pipeline in larger, longer and more extensive clinical trials, or as the use of these therapeutic candidates becomes more widespread if they receive regulatory clearance or approval, illnesses, injuries, discomforts and other AEs that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by subjects. If such side effects become known later in development or upon approval, if any, such findings may harm our business, financial condition and prospects significantly. Additionally, adverse developments in clinical trials of pharmaceutical, biopharmaceutical or biotechnology therapeutics conducted by others may cause the FDA or other regulatory oversight bodies to suspend or terminate our clinical trials or to change the requirements for approval of any of our Wholly Owned Programs.

In addition to side effects caused by the therapeutic candidate, the administration process or related procedures also can cause adverse side effects. If any such AEs occur, our clinical trials could be suspended or terminated. If we are unable to demonstrate that any AEs were not caused by therapeutic candidate, the FDA, the European Commission, the EMA, or other regulatory authorities could order us to cease further development of, or deny clearance or approval of, a therapeutic candidate for any or all targeted indications. Even if we can demonstrate that all future serious adverse events, or SAEs, are not therapeutic-related, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the trial. Moreover, if we elect, or are required, to not initiate, delay, suspend or terminate any future clinical trial of any of our Wholly Owned Programs, the commercial prospects of such therapeutic candidates may be harmed and our ability to generate therapeutic revenues from any of these therapeutic candidates may be delayed or eliminated. Any of these occurrences may harm our ability to develop other therapeutic candidates, and may harm our business, financial condition and prospects significantly.

Additionally, if any of the therapeutic candidates within our Wholly Owned Pipeline receives marketing authorization, the FDA could impose contraindications or a boxed warning in the labeling of our therapeutic. For any of our drug or biologic therapeutic candidates receiving marketing authorization, the FDA could require us to adopt a risk evaluation and mitigation strategy, or REMS, and could apply elements to assure safe use to ensure that the benefits of the therapeutic outweigh its risks, which may include, among other things, a Medication Guide outlining the risks of the therapeutic for distribution to patients, a requirement that clinicians or health care settings to become certified prior to prescribing and to participate in additional REMS activities, such as training, patient counseling, and monitoring, and a communication plan to health care practitioners. Furthermore, if we or others later identify undesirable side effects caused by the therapeutic candidates within our Wholly Owned Pipeline once approved, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such therapeutic candidate, or seek an injunction against its manufacture or distribution;
- regulatory authorities may require additional warnings in the labeling, including boxed warnings, or issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the therapeutic;
- we may be required by the FDA to implement a REMS for a marketed drug or biologic;
- we may be required to change the way a therapeutic candidate is administered or conduct additional clinical trials;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these occurrences could prevent us from achieving or maintaining market acceptance of the particular therapeutic candidate, if approved, and may harm our business, financial condition and prospects significantly.

Risks Related to Regulatory Review and Approval

Our clinical trials may fail to demonstrate substantial evidence of the safety and effectiveness of therapeutic candidates that we may identify and pursue for their intended uses, which would prevent, delay or limit the scope of regulatory clearance, authorization or approval and potential commercialization.

Before obtaining regulatory approvals for the commercial sale of any of our drug or biological therapeutic candidates, we must demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that the applicable therapeutic candidate is both safe and effective for use in each target indication, and in the case of our Wholly Owned Programs and Founded Entities' therapeutic candidates regulated as biological therapeutics, that the therapeutic candidate is safe, pure and potent for use in its targeted indication. Each therapeutic candidate must demonstrate an adequate risk versus benefit profile in its intended patient population and for its intended use. Similarly, before obtaining regulatory clearances, authorization or approvals for the commercial sale of any of the device therapeutic candidates of our Founded Entities, our Founded Entities may be required to demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that the applicable therapeutic candidate meets the regulatory standard of clearance, authorization or approval—for example, substantial equivalence or a reasonable assurance of safety or effectiveness, as applicable—for its intended use.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical development process. Most therapeutic candidates that

begin clinical trials are never approved by regulatory authorities for commercialization. We may be unable to design and execute a clinical trial to support marketing authorization.

We cannot be certain that our clinical trials will be successful. Additionally, any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory clearances, authorization or approval of our therapeutic candidates in those and other indications, which could have a material adverse effect on our business, financial condition and results of operations. In addition, even if such clinical trials are successfully completed, we cannot guarantee that the FDA, the EMA or comparable foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our therapeutic candidates for clearance or approval. For example, the definition of clinical meaningfulness for outcome measures in lymphedema has not been firmly established by the FDA, introducing risk in evaluating and demonstrating the efficacy required to obtain FDA approval of LYT-100. As another example, while there is guidance regarding clinical meaningfulness for outcome measures in the context of acute COVID-19 treatments and potential vaccines, there is no such guidance for treatment of complications that persist following the resolution of COVID-19. Even if we believe that our and our Founded Entities' clinical trials and preclinical studies demonstrate the safety and efficacy of our and their therapeutic candidates, only the FDA and other comparable regulatory agencies may ultimately make such determination. No regulatory agency has made any such determination that any of our Wholly Owned Programs or those of our Founded Entities are safe or effective for use for any indication.

Additionally, we may utilize an "open-label" trial design for some of our future clinical trials. An open-label trial is one where both the patient and investigator know whether the patient is receiving the test article or either an existing approved drug or placebo. Open-label trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label studies are aware that they are receiving treatment. Open-label trials may be subject to a "patient bias" where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. Patients selected for early clinical studies often include the most severe sufferers and their symptoms may have been bound to improve notwithstanding the new treatment. In addition, open-label trials may be subject to an "investigator bias" where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The opportunity for bias in clinical trials as a result of open-label design may not be adequately handled and may cause any of our trials that utilize such design to fail or to be considered inadequate and additional trials may be necessary to support future marketing applications. Moreover, results acceptable to support approval in one jurisdiction may be deemed inadequate by another regulatory authority to support regulatory approval in that other jurisdiction. To the extent that the results of the trials are not satisfactory to the FDA, the EMA or comparable foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional trials in support of potential approval of our Wholly Owned Programs. Even if regulatory approval is secured for a therapeutic candidate, the terms of such approval may limit the scope and use of the specific therapeutic candidate, which may also limit its commercial potential.

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining clearance, authorization or approvals for the potential commercialization of therapeutic candidates.

Any therapeutic candidate we may develop and the activities associated with their development and potential commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA, the EMA and other comparable foreign regulatory authorities. Failure to obtain marketing authorization for a therapeutic candidate will prevent us from commercializing the therapeutic candidate in a given jurisdiction. For example, although Gelesis and Akili have received marketing authorization for Plenity and EndeavorRx, respectively, from the FDA, we and our Founded Entities have not received clearance, authorization or approval to market any of our or their other therapeutic candidates from regulatory authorities in any jurisdiction and it is possible that none of the other therapeutic candidates we and our Founded Entities may seek to develop in the future will ever obtain regulatory clearance, authorization or approval. We have no experience in filing and supporting the applications necessary to gain marketing clearance, authorization or approval and expect to rely on third-party CROs or regulatory consultants to assist us in this process. Securing regulatory clearance, authorization or approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the therapeutic candidate's safety, purity, efficacy and potency. Securing regulatory clearance, authorization or approval also requires the submission of information about the therapeutic manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Any therapeutic candidates we or our Founded Entities develop may not be effective, may be only moderately effective, or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing clearance, authorization or approval or prevent or limit commercial use, if cleared, authorized or approved.

The process of obtaining marketing clearance, authorization or approval, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if clearance, authorization or approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the therapeutic candidates involved. Changes in marketing authorization policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted therapeutic application, may cause delays in the clearance, authorization, approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for clearance, authorization or approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit, or prevent marketing approval of a therapeutic candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-market commitments that render the cleared, authorized or approved therapeutic not commercially viable.

If we experience delays in obtaining clearance, authorization or approval or if we fail to obtain clearance, authorization or approval of any therapeutic candidates we may develop, the commercial prospects for those therapeutic candidates may be harmed, and our ability to generate revenues will be materially impaired.

We have conducted, and may continue to conduct in the future, clinical trials for therapeutic candidates outside the United States, and the FDA, the EMA and comparable foreign regulatory authorities may not accept data from such trials.

We have conducted clinical trials outside of the United States in the past, and may in the future choose to conduct one or more clinical trials outside the United States, including in Europe. For example, we have conducted clinical trials in Australia and are conducting or may conduct clinical trials in additional locations outside the United States, including without limitation the U.K., Australia, Romania, Korea, Argentina, Poland and the Philippines. The acceptance of study data from clinical trials conducted outside the United States or another jurisdiction by the FDA, the EMA or any comparable foreign regulatory authority may be subject to certain conditions or may not be accepted at all. For example, in cases where data from foreign clinical trials are intended to serve as the basis for approval of a drug or biologic in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; and (iii) if necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. In addition, even where the foreign study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and well-conducted in accordance with GCP requirements and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA, the EMA or any comparable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA, the EMA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in therapeutic candidates that we may develop not receiving approval, authorization or clearance for commercialization in the applicable jurisdiction.

If we are unable to obtain regulatory clearance, authorization or approval in one or more jurisdictions for any therapeutic candidates that we may identify and develop, our business could be substantially harmed.

We cannot commercialize a therapeutic until the appropriate regulatory authorities have reviewed and cleared, authorized or approved the therapeutic candidate. Clearance, authorization or approval by the FDA, the EMA and comparable foreign regulatory authorities is lengthy and unpredictable, and depends upon numerous factors, including substantial discretion of the regulatory authorities. Clearance, authorization or approval

policies, regulations, or the type and amount of preclinical or clinical data necessary to gain clearance, authorization or approval may change during the course of a therapeutic candidate's development and may vary among jurisdictions, which may cause delays in the clearance, authorization or approval or the decision not to clear, authorize or approve an application. Gelesis and Akili have obtained marketing authorization from the FDA for Plenity and EndeavorRx, respectively, but we and our Founded Entities have not obtained regulatory clearance, authorization or approval for any other therapeutic candidates, and it is possible that our current therapeutic candidates and any other therapeutic candidates which we and our Founded Entities may seek to develop in the future will not ever obtain regulatory clearance, authorization or approval. We cannot be certain that any of our Wholly Owned Programs or our Founded Entities' therapeutic candidates will receive regulatory clearance, authorization or approval or be successfully commercialized even if we or our Founded Entities receive regulatory clearance, authorization or approval.

Obtaining marketing clearance, authorization or approval is an extensive, lengthy, expensive and inherently uncertain process, and regulatory authorities may delay, limit or deny clearance or clearance, authorization or approval of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates for many reasons, including but not limited to:

- the inability to demonstrate to the satisfaction of the FDA, the EMA or comparable foreign regulatory authorities that the applicable therapeutic candidate is safe and effective as a treatment for our targeted indications or otherwise meets the applicable regulatory standards for clearance, authorization or approval;
- the FDA, the EMA or comparable foreign regulatory authorities may disagree with the design, endpoints or implementation of our or our Founded Entities' clinical trials;
- the population studied in the clinical program may not be sufficiently broad or representative to assure safety or efficacy in the full population for which we or our Founded Entities seek clearance, authorization or approval;
- the FDA, the EMA or comparable foreign regulatory authorities may require additional preclinical studies or clinical trials beyond those that we or our Founded Entities currently anticipate;
- the FDA, the EMA or comparable foreign regulatory authorities may disagree with our or our Founded Entities' interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of therapeutic candidates that we may identify and pursue may not be sufficient to support the submission of an NDA, biologics license application, or BLA, or other submission for regulatory clearance, authorization or approval in the United States or elsewhere;
- as applicable, we or our Founded Entities may be unable to demonstrate to the FDA, the EMA or comparable foreign regulatory authorities that a therapeutic candidate's risk-benefit ratio for its proposed indication is acceptable;
- the FDA, the EMA or comparable foreign regulatory authorities may identify deficiencies in the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers with which we or our Founded Entities contract for clinical and commercial supplies; and
- the clearance, authorization or approval policies or regulations of the FDA, the EMA or comparable foreign regulatory authorities may change in a manner that renders the clinical trial design or data insufficient for clearance or approval.

The lengthy approval process, as well as the unpredictability of the results of clinical trials and evolving regulatory requirements, may result in our or our Founded Entities' failure to obtain regulatory clearance, authorization or approval to market therapeutic candidates that we or our Founded Entities may pursue in the United States or elsewhere, which would significantly harm our or our Founded Entities' business, prospects, financial condition and results of operations.

Furthermore, clearance, authorization or approval by the FDA in the United States, if obtained, does not ensure approval by regulatory authorities in other countries or jurisdictions. In order to market any therapeutics outside of the United States, we or our Founded Entities must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and effectiveness. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval processes vary among countries and can involve additional therapeutic testing and validation and additional or different administrative review periods from those in the United States, including additional preclinical studies or clinical trials, as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a therapeutic candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our therapeutics is also subject to approval. Seeking foreign regulatory approval could result in difficulties and costs for us or our Founded Entities and require additional preclinical studies or clinical trials which could be costly and time-consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our or our Founded Entities' therapeutics in those countries. The foreign regulatory approval process involves all of the risks associated with FDA approval. We do not have any therapeutic candidates approved for sale in international markets, though two of our Founded Entities, Akili and Gelesis, do. If we or our Founded Entities fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of our therapeutics will be harmed.

Interim, "top-line," and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available or as additional analyses are conducted, and as the data are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim, "top-line," or preliminary data from our clinical studies. Data from interim analyses of clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or "top-line" data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim, "top-line.," and preliminary data should be viewed with caution until the final data are available. Material adverse changes between preliminary, "top-line," or interim data and final data could significantly harm our business prospects.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular therapeutic candidate or therapeutic and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure. Any information we determine not to disclose may ultimately be deemed significant by you or others with respect to future decisions, conclusions, views, activities or otherwise regarding a particular therapeutic candidate or our business.

The complexity of a combination therapeutic that includes a drug or biologic and a medical device presents additional, unique development and regulatory challenges, which may adversely impact our or our Founded Entities' development plans and our or our Founded Entities' ability to obtain regulatory clearance, authorization or approval of our Wholly Owned Programs or our Founded Entities' therapeutic candidates.

We or our Founded Entities, such as Follica, may decide to pursue marketing authorization of a combination therapeutic. A combination therapeutic may include, amongst other possibilities, any investigational drug, device, or biologic packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biologic where both are required to achieve the intended use, indication, or effect.

Developing and obtaining regulatory clearance, authorization or approval for combination therapeutics pose unique challenges because they involve components that are regulated by the FDA under different types of regulatory requirements, and by different FDA centers. As a result, such therapeutics raise regulatory, policy and review management challenges. For example, because divisions from both FDA's Center for Drug Evaluation and Research or Center for Biologics Evaluation and Research and FDA's Center for Devices and Radiological Health must review submissions concerning therapeutic candidates that are combination therapeutics comprised of drug or biologics and devices, respectively, the regulatory review and clearance, authorization or approval process for these therapeutics may be lengthened. In addition, differences in regulatory pathways for each component of a combination therapeutic can impact the regulatory processes for all aspects of therapeutic development and management, including clinical investigation, marketing applications, manufacturing and quality control, adverse event reporting, promotion and advertising, user fees and post-clearance, authorization or approval modifications. Similarly, if applicable, the device components of a combination therapeutic candidate will require any necessary clearances or approvals or other marketing authorizations in other jurisdictions, which may prove challenging to obtain.

Certain modifications to our Founded Entities' device therapeutics may require new 510(k) clearance or other marketing authorizations and may require our Founded Entities to recall or cease marketing their therapeutics.

Akili and Gelesis received de novo classification for EndeavorRx and Plenity, respectively, from the FDA. Once a medical device is permitted to be legally marketed in the United States pursuant to a 510(k) clearance, de novo classification, or a premarket approval, or PMA, a manufacturer may be required to notify the FDA of certain modifications to the device. Manufacturers determine in the first instance whether a change to a medical device requires a new premarket submission, but the FDA may review any manufacturer's decision. The FDA may not agree with our Founded Entities' decisions regarding whether new clearances, authorizations or approvals are necessary. They may make modifications or add additional features in the future that they believe do not require a new 510(k) clearance, de novo marketing authorization, or approval of a PMA or PMA amendments or supplements. If the FDA disagrees with their determinations and requires them to submit new 510(k) notifications, requests for de novo classification, or PMAs (or PMA supplements or amendments) for modifications to their previously cleared or authorized therapeutics for which they have concluded that new clearances, authorization or approvals are unnecessary, they may be required to cease marketing or to recall the modified therapeutic until they obtain clearance, authorization or approval, and they may be subject to significant regulatory fines or penalties.

The regulatory landscape that will apply to development of therapeutic candidates by us or our Founded Entities or collaborators is rigorous, complex, uncertain and subject to change, which could result in delays or termination of development of such therapeutic candidates or unexpected costs in obtaining regulatory approvals.

We or our Founded Entities or collaborators may develop therapeutic candidates that use genome or cell editing technologies. Regulatory requirements governing therapeutics created with genome editing technology or involving gene therapy treatment have changed frequently and will likely continue to change in the future. Approvals by one regulatory agency may not be indicative of what any other regulatory agency may require for approval, and there is substantial, and sometimes uncoordinated, overlap in those responsible for regulation of gene therapy therapeutics, cell therapy therapeutics and other therapeutics created with genome editing technology. For example, the FDA established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related therapeutics, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. These and other regulatory review agencies, committees and advisory groups and the requirements and guidelines they promulgate may lengthen the regulatory review process, require us or our Founded Entities to perform additional preclinical studies or clinical trials, increase our or our Founded Entities' development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates or lead to significant post-approval limitations or restrictions.

Additionally, under the National Institutes of Health, or NIH, Guidelines for Research Involving Recombinant Synthetic Nucleic Acid Molecules, or NIH Guidelines, supervision of human gene transfer trials includes evaluation and assessment by an institutional biosafety committee, or IBC, a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment, and such review may result in some delay before initiation of a clinical trial. While the NIH Guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them.

In the EEA, the EMA has a Committee for Advanced Therapies, or CAT, that is responsible for assessing the quality, safety and efficacy of advanced therapy medicinal therapeutics. Advanced-therapy medicinal therapeutics include gene therapy medicines, somatic-cell therapy medicines and tissue-engineered medicines. The role of the CAT is to prepare a draft opinion on an application for marketing authorization for an advanced therapy medicinal candidate that is submitted to the EMA. In the EEA, the development and evaluation of a gene therapy medicinal therapeutic must be considered in the context of the relevant EMA guidelines. The EMA may issue new guidelines concerning the development and marketing authorization for gene therapy medicinal therapeutics and require that we or our Founded Entities comply with these new guidelines. Similarly complex regulatory environments exist in other jurisdictions in which we or our Founded Entities might consider seeking regulatory approvals for our Wholly Owned Programs or our Founded Entities' therapeutic candidates, further complicating the regulatory landscape. As a result, the procedures and standards applied to gene therapy therapeutics and cell therapy therapeutics may be applied to any of our or our Founded Entities' gene therapy or genome editing therapeutic candidates, but that remains uncertain at this point.

Changes in applicable regulatory guidelines may lengthen the regulatory review process for the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates, require additional studies or trials, increase development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of such therapeutic candidates, or lead to significant post-approval limitations or restrictions. Additionally, adverse developments in clinical trials conducted by others of gene therapy therapeutics or therapeutics created using genome editing technology, or adverse public perception of the field of genome editing, may cause the FDA, the EMA and other regulatory bodies to revise the requirements for approval of any therapeutic candidates we or our Founded Entities may develop or limit the use of therapeutics utilizing genome editing technologies, either of which could materially harm our or our Founded Entities' business. Furthermore, regulatory action or private litigation could result in expenses, delays or other impediments to our research programs or the development or commercialization of current or future therapeutic candidates.

As we advance therapeutic candidates alone or with collaborators, we will be required to consult with these regulatory and advisory groups and comply with all applicable guidelines, rules and regulations. If we fail to do so, we or our collaborators may be required to delay or terminate development of such therapeutic candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a therapeutic candidate to market could decrease our ability to generate sufficient therapeutic revenue to maintain our business.

We may not elect or be able to take advantage of any expedited development or regulatory review and approval processes available to drug therapeutic candidates granted breakthrough therapy or fast track designation by the FDA.

We intend to evaluate and continue ongoing discussions with the FDA on regulatory strategies that could enable us or our Founded Entities to take advantage of expedited development pathways for certain of our Wholly Owned Programs or our Founded Entities' therapeutic candidates in the future, although we cannot be certain that our Wholly Owned Programs or our Founded Entities' therapeutic candidates will qualify for any expedited development pathways or that regulatory authorities will grant, or allow us or our Founded Entities to maintain, the relevant qualifying designations. Potential expedited development pathways that we could pursue include breakthrough therapy and fast track designation.

Breakthrough therapy designation is intended to expedite the development and review of drug and biologic therapeutic candidates that are designed to treat serious or life-threatening diseases when preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation of a therapeutic candidate as a breakthrough therapy provides potential benefits that include more frequent meetings with FDA to discuss the development plan for the therapeutic candidate and ensure collection of appropriate data needed to support approval; more frequent written correspondence from FDA about such things as the design of the proposed clinical trials and use of biomarkers; intensive guidance on an efficient drug development program, beginning as early as Phase 1; organizational commitment involving senior managers; and eligibility for rolling review and priority review of an NDA or BLA. Fast track designation is designed for therapeutic candidates intended for the treatment of a serious or life-threatening disease or condition, where preclinical or clinical data demonstrate the potential to address an unmet medical need for this disease or condition. The sponsor of a fast track therapeutic candidate has opportunities for more frequent interactions with the FDA review team during product development and, once an NDA or BLA is submitted, the application may be eligible for rolling review.

Even if we believe a particular therapeutic candidate is eligible for breakthrough therapy or fast track designation, we cannot assure you that the FDA would decide to grant it. Breakthrough therapy designation and fast track designation do not change the standards for approval, and there is no assurance that such designation or eligibility will result in expedited review or approval. Thus, even if we or our Founded Entities do receive breakthrough therapy or fast track designation, we or our Founded Entities may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw breakthrough therapy or fast track designation if it believes that the therapeutic no longer meets the qualifying criteria. Our business may be harmed if we are unable to avail ourselves of these or any other expedited development and regulatory pathways.

We may not be able to obtain or maintain orphan drug designation or exclusivity for our therapeutic candidates.

Regulatory authorities in some jurisdictions, including the United States, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States, or if the disease or condition affects more than 200,000 individuals in the United States and there is no reasonable expectation that the cost of developing the drug for the type of disease or condition will be recovered from sales of the product in the United States.

Orphan drug designation entitles a party to financial incentives, such as tax advantages and user fee waivers. Additionally, if a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same disease or condition for seven years, except in certain circumstances, such as a showing of clinical superiority (i.e., another product is safer, more effective or makes a major contribution to patient care) over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity. Competitors, however, may receive approval of different products for the same disease or condition for which the orphan product has exclusivity, or obtain approval for the same product but for a different disease or condition than that for which the orphan product has exclusivity.

We have obtained orphan drug designation in the United States for LYT-200 for the treatment of pancreatic cancer, and we may also seek orphan drug designation for other of our therapeutic candidates in the future. We may not be the first to obtain regulatory approval of any therapeutic candidate for its orphan-designated disease or condition and may therefore not obtain orphan drug exclusivity. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an disease or condition broader than the orphan-designated disease or condition or may be lost if the FDA later determines that the request for orphan designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Orphan drug designation does not ensure that we will receive marketing exclusivity in a particular market, and we cannot assure you that any future application for orphan drug designation with respect to any other therapeutic candidate will be granted. Orphan drug designation neither shortens the development time or regulatory review time of a drug, nor gives the drug any advantage in the regulatory review or approval process.

If we or our Founded Entities are unable to successfully validate, develop and obtain regulatory clearance, authorization or approval for companion diagnostic tests for any future drug candidates that require or would commercially benefit from such tests, or experience significant delays in doing so, we or our Founded Entities may not realize the full commercial potential of these drug candidates.

In connection with the clinical development of the therapeutic candidates within our Wholly Owned Pipeline or Founded Entities' therapeutic candidates for certain indications, we or our Founded Entities may work with collaborators to develop or obtain access to in vitro companion diagnostic tests to identify patient subsets within a disease category who may derive selective and meaningful benefit from our drug candidates. For example, we may elect to develop companion diagnostics for LYT-200 and LYT-210. To be successful, we, our Founded Entities or our collaborators will need to address a number of scientific, technical, regulatory and logistical challenges. The FDA, the EMA and comparable foreign regulatory authorities regulate in vitro companion diagnostics as medical devices and, under that regulatory framework, will likely require the conduct of clinical trials to demonstrate the safety and effectiveness of any diagnostics we or our Founded Entities may develop, which we expect will require separate regulatory clearance, authorization or approval prior to commercialization. In addition, if safe and effective use of a therapeutic product depends on an in vitro companion diagnostic, the FDA generally will require approval, authorization or clearance of that diagnostic, known as a companion diagnostic, before or at the same time that the FDA approves the therapeutic product.

We or our Founded Entities may rely on third parties for the design, development and manufacture of companion diagnostic tests for our Wholly Owned Programs or our Founded Entities' therapeutic candidates that may require such tests. If we or our Founded Entities enter into such collaborative agreements, we will be dependent on the sustained cooperation and effort of our future collaborators in developing and obtaining approval for these companion diagnostics. It may be necessary to resolve issues such as selectivity/specificity, analytical validation, reproducibility, or clinical validation of companion diagnostics during the development and regulatory clearance, authorization or approval processes. Moreover, even if data from preclinical studies and early clinical trials appear to support development of a companion diagnostic for a therapeutic candidate, data generated in later clinical trials may fail to support the analytical and clinical validation of the companion diagnostic. We, our Founded Entities and our future collaborators may encounter difficulties in developing, obtaining regulatory clearance, authorization or approval for, manufacturing and commercializing companion diagnostics similar to those we face with respect to the therapeutic candidates within our Wholly Owned Pipeline themselves, including issues with achieving regulatory clearance, authorization or approval, production of sufficient quantities at commercial scale and with appropriate quality standards, and in gaining market acceptance. If we or our Founded Entities are unable to successfully develop companion diagnostics for these therapeutic candidates, or experience delays in doing so, the development of these therapeutic candidates may be adversely affected, these therapeutic candidates may not obtain marketing approval, and we may not realize the full commercial potential of any of these therapeutic candidates that obtain marketing approval. As a result, our business, results of operations and financial condition could be materially harmed. In addition, a diagnostic company with whom we or our Founded Entities contract may decide to discontinue selling or manufacturing the companion diagnostic test that we anticipate using in connection with development and commercialization of our Wholly Owned Programs or our Founded Entities' therapeutic candidates or our relationship with such diagnostic company may otherwise terminate. We or our Founded Entities may not be able to enter into arrangements with another diagnostic company to obtain supplies of an alternative diagnostic test for use in connection with the development and commercialization of our Wholly Owned Programs or our Founded Entities' therapeutic candidates or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of our or our Founded Entities' therapeutic candidates.

For any cleared, authorized or approved therapeutic, we or our Founded Entities will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we or our Founded Entities may be subject to penalties if we or our Founded Entities fail to comply with regulatory requirements or experience unanticipated problems with the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates.

Gelesis' Plenity and Akili's EndeavorRx are, and any of the therapeutic candidates within our Wholly Owned Programs or our Founded Entities' therapeutic candidates that are cleared, authorized or approved will be, subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities.

Manufacturers and manufacturers' facilities are required to comply with extensive requirements imposed by the FDA, the EMA and other comparable foreign regulatory authorities, including ensuring that quality control and manufacturing procedures conform to current good manufacturing practices, or cGMP, regulations. As such, we and our CMOs are subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any marketing authorization, and any future 510(k), de novo classification, PMA, NDA, BLA or marketing authorization application, or MAA, or equivalent application. We and our CMOs are also subject to requirements pertaining to the registration of our manufacturing facilities and the listing of our and our Founded Entities' therapeutics and therapeutic candidates with the FDA; continued complaint, adverse event and malfunction reporting; corrections and removals reporting; and labeling and promotional requirements. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production and quality control. Gelesis' and Akili's marketing authorizations for Plenity and EndeavorRx, respectively, are and any regulatory clearances, authorization or approvals that we may receive for the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates will be, subject to limitations on the cleared, authorized or approved indicated uses for which the therapeutic may be marketed and promoted or to the conditions of approval. Any regulatory clearances, authorizations or approvals that we may receive for the therapeutic candidates within our Wholly Owned Pipeline may contain requirements for potentially costly post-marketing testing, such as Phase 4 clinical trials and surveillance to monitor the safety and efficacy of a drug therapeutic. We are required to report certain adverse reactions and production problems, if any, to the FDA, the EMA and other comparable foreign regulatory authorities. Any new legislation addressing drug or medical safety issues could result in delays in therapeutic development or commercialization, or increased costs to assure compliance.

The FDA and other agencies, including the U.S. Department of Justice, and for certain therapeutics, the Federal Trade Commission, closely regulate and monitor the marketing, labeling, advertising and promotion of therapeutics to ensure that they are manufactured, marketed and

distributed only for the cleared, authorized or approved indications and in accordance with the provisions of the cleared, authorized or approved labeling. We are, and will be, required to comply with requirements concerning advertising and promotion for the therapeutic candidates within our Wholly Owned Pipeline, if cleared, authorized or approved. For example, promotional communications with respect to prescription drugs and medical devices are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the therapeutic's label or labeling. We may not promote our therapeutics for indications or uses for which they do not have approval, authorization or clearance.

The holder of a cleared 510(k), de novo classification, or an approved NDA, BLA, PMA, MAA or equivalent marketing authorization must submit new or supplemental applications and obtain clearance, authorization or approval for certain changes to the approved therapeutic, therapeutic labeling, or manufacturing process. For example, any modification to Plenity or EndeavorRx that could significantly affect its safety or effectiveness or that would constitute a major change in its intended use could require a new 510(k) clearance, de novo classification or approval of PMA application. Delays in obtaining required clearances or approvals would harm our ability to introduce new or enhanced therapeutic in a timely manner, which in turn would harm our or our Founded Entities' future growth. Failure to submit a new or supplemental application and to obtain approval for certain changes prior to marketing the modified therapeutic may require a recall or to stop selling or distributing the marketed therapeutic as modified, and may lead to significant enforcement actions.

In the European Economic Area, or the EEA, any medical devices will need to comply with the Essential Requirements set forth in the new Medical Device Regulation (EU) 2017/745, which became fully applicable on May 26, 2021. Compliance with these requirements is a prerequisite to be able to affix the CE mark to a therapeutic, without which a therapeutic cannot be marketed or sold in the EEA. To demonstrate compliance with the Essential Requirements and obtain the right to affix the CE mark, we or our Founded Entities must undergo a conformity assessment procedure, which varies according to the type of medical device and its classification. The conformity assessment procedure requires the intervention of a Notified Body (except for certain class I devices), which is an organization designated by a competent authority of an EEA country to conduct conformity assessments. The Notified Body issues a CE Certificate of Conformity following successful completion of a conformity assessment procedure and quality management system audit conducted in relation to the medical device and its manufacturer and their conformity with the Essential Requirements. This Certificate entitles the manufacturer to affix the CE mark to its medical therapeutics after having prepared and signed a related EC Declaration of Conformity. In June 2020, Gelesis received a CE Mark for Plenity as a class III medical device indicated for weight loss in overweight and obese adults with a Body Mass Index of 25-40 kg/m2, when used in conjunction with diet and exercise. Also in June 2020, Akili received a CE Mark for EndeavorRx as a prescription-only digital therapeutic software intended for the treatment of attention and inhibitory control deficits in paediatric patients with ADHD.

We or our Founded Entities could also be required to conduct post-marketing clinical trials to verify the safety and efficacy of our or our Founded Entities' therapeutics in general or in specific patient subsets. If original marketing approval of a drug or biologic was obtained via an accelerated approval pathway, we or our Founded Entities could be required to conduct a successful post-marketing clinical trial to confirm clinical benefit for our or our Founded Entities' therapeutics. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing clearance, authorization or approval.

If a regulatory agency discovers previously unknown problems with a therapeutic, such as AEs of unanticipated severity or frequency, or problems with the facility where the therapeutic is manufactured, or disagrees with the promotion, marketing or labeling of a therapeutic, such regulatory agency may impose restrictions on that therapeutic or us, including requiring withdrawal of the therapeutic from the market. If we or our Founded Entities fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things:

- issue warning letters that would result in adverse publicity;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approvals;
- suspend any of our or our Founded Entities' ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications submitted by us or our Founded Entities;
- impose restrictions on our operations, including closing our CMOs' facilities;
- seize or detain therapeutics; or
- require a recall.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our therapeutics. If regulatory sanctions are applied or if regulatory clearance, authorization or approval is withdrawn, the value of our company and our operating results will be adversely affected.

The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory clearance, authorization or approval of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If these legislative or administrative actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses.

If, for any of our Wholly Owned Programs that are cleared or approved, we are found to have improperly promoted off-label uses of those therapeutics, we may become subject to significant liability. The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription therapeutics, if cleared, authorized or approved. In particular, while the FDA permits the dissemination of truthful and non-misleading information about a cleared, authorized or approved therapeutic, a manufacturer may not promote a therapeutic for uses that are not cleared, authorized or approved by the FDA or such other regulatory agencies as reflected in the therapeutic's cleared, authorized or approved labeling. If we are found to have promoted such off-label uses, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees, corporate integrity agreements or permanent injunctions under which specified promotional conduct must be changed or curtailed. If we cannot successfully manage the promotion of the therapeutic candidates within our Wholly Owned Pipeline, if cleared, authorized or approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

Risks Related to Manufacturing our Therapeutic Candidates or Those of our Founded Entities

Certain of the therapeutic candidates being developed by us or our Founded Entities are novel, complex and difficult to manufacture. We could experience manufacturing problems that result in delays in our development or commercialization programs or otherwise harm our business.

The manufacturing processes our CMOs use to produce our and our Founded Entities' therapeutic candidates are complex and in certain cases novel. Several factors could cause production interruptions, including inability to develop novel manufacturing processes, equipment malfunctions, facility contamination, raw material shortages or contamination, natural disasters, disruption in utility services, human error or disruptions in the operations of our suppliers, including acquisition of the supplier by a third party or declaration of bankruptcy. For example, Vedanta has its own proprietary cGMP manufacturing facilities for certain therapeutic candidates, including VE202, VE303, VE800 and VE416. Creating defined consortia of live microbial therapeutics for these therapeutic candidates is inherently complex, and therefore can be vulnerable to delays. The expertise required to manufacture these therapeutic candidates is unique to Vedanta, and as a result, it would be difficult and time consuming to find an alternative CMO. In addition, manufacturing of clinical supply for certain of our therapeutic candidates is dependent on third party CMOs, and manufacturing such therapeutic candidates is inherently complex. As another example, we are advancing LYT-100 for potential treatment of complications that persist following the resolution of COVID-19 infection. COVID-19 has been widespread, and any approved treatments related to COVID-19 could face issues manufacturing sufficient quantities to meet demand. Additionally, two vaccines for COVID-19 have received full approval by the FDA and one other vaccine for COVID-19 was granted Emergency Use Authorization by the FDA. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots for the therapeutics needed for our and our Founded Entities' clinical trials or therapeutics which could lead to delays in these trials or supply shortages of therapeutics.

Some of our and our Founded Entities' therapeutic candidates include biologics, some of which have physical and chemical properties that cannot be fully characterized. As a result, assays of the finished product may not be sufficient to ensure that the therapeutic candidate is consistent from lot-to-lot or will perform in the intended manner. Accordingly, our CMOs must employ multiple steps to control the manufacturing process to assure that the process is reproducible and the therapeutic candidate is made strictly and consistently in compliance with the process. Problems with the manufacturing process, even minor deviations from the normal process, could result in therapeutic defects or manufacturing failures that result in lot failures, therapeutic recalls, product liability claims or insufficient inventory to conduct clinical trials or supply commercial markets. We or our Founded Entities may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet the FDA, the EMA or other applicable standards or specifications with consistent and acceptable production yields and costs.

In addition, the FDA, the EMA and other foreign regulatory authorities may require us or our Founded Entities to submit samples of any lot of any approved therapeutic together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA, the EMA or other foreign regulatory authorities may require that we or our Founded Entities not distribute a lot until the agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the therapeutic that could result in lot failures or therapeutic recalls. Lot failures or therapeutic recalls could cause us or our Founded Entities to delay therapeutic launches or clinical trials, which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects.

Our CMOs also may encounter problems hiring and retaining the experienced scientific, quality assurance, quality-control and manufacturing personnel needed to operate our manufacturing processes, which could result in delays in production or difficulties in maintaining compliance with applicable regulatory requirements.

Any problems in our CMOs' manufacturing process or facilities could result in delays in planned clinical trials and increased costs, and could make us a less attractive collaborator for potential partners, including larger biotechnology companies and academic research institutions, which could limit access to additional attractive development programs. Problems in our manufacturing process could restrict our ability to meet potential future market demand for therapeutics.

We do not currently have nor do we plan to acquire the infrastructure or capability internally to manufacture our clinical drug supplies for use in the conduct of our clinical trials, and we lack the resources and the capability to manufacture the therapeutic candidates within our Wholly Owned Pipeline on a clinical or commercial scale. Instead, we rely on our third-party manufacturing partners for the production of the active pharmaceutical ingredient, or API, and drug formulation. The facilities used by our third-party manufacturers to manufacture our therapeutic candidates that we may develop must be successfully inspected by the applicable regulatory authorities, including the FDA, after we submit any NDA or BLA to the FDA.

We are currently completely dependent on our third-party manufacturers for the production of certain of our therapeutic candidates in accordance with cGMPs, which include, among other things, quality control, quality assurance and the maintenance of records and documentation.

Although we have entered into agreements for the manufacture of clinical supplies for such therapeutic candidates, our third-party manufacturers may not perform as agreed, may be unable to comply with these cGMP requirements and with FDA, state and foreign regulatory requirements or may terminate its agreement with us. If any of our third-party manufacturers cannot successfully manufacture material that conforms to our specifications and the applicable regulatory authorities' strict regulatory requirements, pass regulatory inspection or maintain a compliance status acceptable to the FDA or state or foreign regulatory authorities, our NDAs or BLAs will not be approved. In addition, although we are ultimately responsible for ensuring therapeutic quality, we have no direct day-to-day control over our third-party manufacturers' ability to maintain adequate quality control, quality assurance and qualified personnel. If our third-party manufacturers are unable to satisfy the regulatory requirements for the manufacture of our therapeutics, if approved, or if our suppliers or third-party manufacturers decide they no longer want to manufacture our therapeutics, we will need to find alternative manufacturing facilities, which would be time-consuming and significantly impact our ability to develop, obtain regulatory approval for or market our therapeutics, if approved. If we are required to change contract manufacturers for any reason, we will be required to show that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturing process or procedure will produce our therapeutic candidate according to specifications previously submitted to the FDA or another regulatory authority. We might be unable to identify manufacturers for long-term clinical and commercial supply on acceptable terms or at all. Manufacturers are subject to ongoing periodic announced and unannounced inspection by the FDA and other governmental authorities to ensure compliance with government regulations. As a result, our third-party manufacturers may be subject to increased scrutiny.

If we were to experience an unexpected loss of supply for clinical development or commercialization, we could experience delays in our ongoing or planned clinical trials as our third-party manufacturers would need to manufacture additional quantities of our clinical and commercial supply and we may not be able to provide sufficient lead time to enable our third-party manufacturers to schedule a manufacturing slot, or to produce the necessary replacement quantities. This could result in delays in progressing our clinical development activities and achieving regulatory approval for our therapeutics, which could materially harm our business.

The manufacture of pharmaceutical therapeutics is complex and requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. We and our contract manufacturers must comply with cGMP regulations and guidelines. Manufacturers of pharmaceutical therapeutics often encounter difficulties in production, particularly in scaling up and validating initial production. These problems include difficulties with production costs and yields, quality control, including stability of the product, quality assurance testing, operator error, shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. Furthermore, if microbial, viral or other contaminations are discovered in our therapeutics or in the manufacturing facilities in which our therapeutics, if approved, are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. We cannot assure you that any stability or other issues relating to the manufacture of any of our therapeutics will not occur in the future. Additionally, our manufacturers may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. If our manufacturers were to encounter any of these difficulties, or otherwise fail to comply with their contractual obligations, our ability to provide any therapeutic candidates to patients in clinical trials would be jeopardized. Any delay or interruption in the supply of clinical trial supplies could delay the completion of clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials completely.

Any adverse developments affecting clinical or commercial manufacturing of our therapeutics may result in shipment delays, inventory shortages, lot failures, therapeutic withdrawals or recalls, or other interruptions in the supply of our therapeutics or therapeutic candidates. We may also have to take inventory write-offs and incur other charges and expenses for therapeutics or therapeutic candidates that fail to meet specifications, undertake costly remediation efforts or seek more costly manufacturing alternatives. Accordingly, failures or difficulties faced at any level of our supply chain could materially adversely affect our business and delay or impede the development and commercialization of any of our therapeutics or therapeutic candidates and could have a material adverse effect on our business, prospects, financial condition and results of operations.

Our or our Founded Entities' therapeutics must be manufactured in accordance with federal, state and international regulations, and we or our Founded Entities could be forced to recall our or our Founded Entities' medical devices or terminate production if we or our Founded Entities fail to comply with these regulations.

The methods used in, and the facilities used for, the manufacture of medical device therapeutics of our Founded Entities, including Gelesis, Akili, Follica and Sonde, must comply with the FDA's cGMPs for medical devices, known as Quality System Regulation, or QSR, which is a complex regulatory scheme that covers the procedures and documentation of, among other requirements, the design, testing, validation, verification, complaint handling, production, process controls, quality assurance, labeling, supplier evaluation, packaging, handling, storage, distribution, installation, servicing and shipping of medical devices. Furthermore, we and our Founded Entities are required to verify that our suppliers maintain facilities, procedures and operations that comply with our quality standards and applicable regulatory requirements. The FDA enforces the QSR through, among other oversight methods, periodic announced or unannounced inspections of medical device manufacturing facilities, which may include the facilities of subcontractors, suppliers or CMOs. Our and our Founded Entities' therapeutics are also subject to similar state regulations and various laws and regulations of foreign countries governing manufacturing.

Our or our Founded Entities' third-party manufacturers may not take the necessary steps to comply with applicable regulations or our or our Founded Entities' specifications, which could cause delays in the delivery of our therapeutics. In addition, failure to comply with applicable FDA requirements or later discovery of previously unknown problems with our or our Founded Entities' therapeutics or manufacturing processes could result in, among other things: warning letters or untitled letters; civil penalties; suspension or withdrawal of approvals or clearances; seizures or recalls of

our or our Founded Entities' therapeutics; total or partial suspension of production or distribution; administrative or judicially imposed sanctions; the FDA's refusal to grant pending or future clearances or approvals for our or our Founded Entities' therapeutics; clinical holds; refusal to permit the import or export of our or our Founded Entities' therapeutics; and criminal prosecution of us or our employees. Any of these actions could significantly and negatively impact supply of our or our Founded Entities' therapeutics. If any of these events occurs, our reputation could be harmed, we could be exposed to product liability claims and we or our Founded Entities could lose customers and suffer reduced revenue and increased costs.

Risks Related to Commercialization

If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any therapeutic candidates we may develop, we may not be successful in commercializing those therapeutic candidates if and when they are approved.

We do not have a sales or marketing infrastructure or the capabilities for sale, marketing, or distribution of pharmaceutical therapeutics. To achieve commercial success for any approved therapeutic for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to third parties. In the future, we may choose to build a focused sales, marketing, and commercial support infrastructure to market and sell the therapeutic candidates within our Wholly Owned Pipeline, if and when they are approved. We may also elect to enter into collaborations or strategic partnerships with third parties to engage in commercialization activities with respect to selected therapeutic candidates, indications or geographic territories, including territories outside the United States, although there is no guarantee we will be able to enter into these arrangements even if the intent is to do so.

There are risks involved with both establishing our own commercial capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force or reimbursement specialists is expensive and time consuming and could delay any therapeutic launch. If the commercial launch of a therapeutic candidate for which we recruit a sales force and establish marketing and other commercialization capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition commercialization personnel.

Factors that may inhibit our efforts to commercialize any approved therapeutic on our own include:

- the inability to recruit and retain adequate numbers of effective sales, marketing, reimbursement, customer service, medical affairs, and other support personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future approved therapeutics;
- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement, and other acceptance by payors;
- the inability to price therapeutics at a sufficient price point to ensure an adequate and attractive level of profitability;
- restricted or closed distribution channels that make it difficult to distribute our therapeutics to segments of the patient population;
- the lack of complementary therapeutics to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive therapeutic lines; and
- unforeseen costs and expenses associated with creating an independent commercialization organization.

If we enter into arrangements with third parties to perform sales, marketing, commercial support, and distribution services, our therapeutic revenue or the profitability of therapeutic revenue may be lower than if we were to market and sell any therapeutics we may develop internally. In addition, we may not be successful in entering into arrangements with third parties to commercialize the therapeutic candidates within our Wholly Owned Pipeline or may be unable to do so on terms that are favorable to us or them. We may have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our therapeutics effectively or may expose us to legal and regulatory risk by not adhering to regulatory requirements and restrictions governing the sale and promotion of prescription drug therapeutics, including those restricting off-label promotion. If we do not establish commercialization capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing the therapeutic candidates within our Wholly Owned Pipeline, if approved.

Even if any current or future therapeutic candidate of ours receives regulatory clearance or approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success, in which case we may not generate significant revenues or become profitable.

We have never commercialized a therapeutic, and even if any current or future therapeutic candidate of ours is approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Physicians may be reluctant to take their patients off their current medications and switch their treatment regimen. Further, patients often acclimate to the treatment regime that they are currently taking and do not want to switch unless their physicians recommend switching therapeutics or they are required to switch due to lack of coverage and adequate reimbursement. In addition, even if we are able to demonstrate our Wholly Owned Programs' safety and efficacy to the FDA and other regulators, safety or efficacy concerns in the medical community may hinder market acceptance.

Efforts to educate the medical community and third-party payors on the benefits of the therapeutic candidates within our Wholly Owned Pipeline may require significant resources, including management time and financial resources, and may not be successful. The degree of market acceptance of the therapeutic candidates within our Wholly Owned Pipeline, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of the therapeutic;
- the potential advantages of the therapeutic compared to competitive therapies;
- the prevalence and severity of any side effects;
- whether the therapeutic is designated under physician treatment guidelines as a first-, second- or third-line therapy;
- our ability, or the ability of any future collaborators, to offer the therapeutic for sale at competitive prices;
- the therapeutic's convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try, and of physicians to prescribe, the therapeutic;
- limitations or warnings, including distribution or use restrictions contained in the therapeutic's approved labelling;
- the strength of sales, marketing and distribution support;
- changes in the standard of care for the targeted indications for the therapeutic; and
- availability and adequacy of coverage and reimbursement from government payors, managed care plans and other third-party payors.

Sales of medical therapeutics also depend on the willingness of physicians to prescribe the treatment, which is likely to be based on a determination by these physicians that the therapeutics are safe, therapeutically effective and cost effective. In addition, the inclusion or exclusion of therapeutics from treatment guidelines established by various physician groups and the viewpoints of influential physicians can affect the willingness of other physicians to prescribe the treatment. We cannot predict whether physicians, physicians' organizations, hospitals, other healthcare providers, government agencies or private insurers will determine that our therapeutic is safe, therapeutically effective and cost effective as compared with competing treatments. If any therapeutic candidates we develop do not achieve an adequate level of acceptance, we may not generate significant therapeutic revenue, and we may not become profitable.

Any failure by any current or future therapeutic candidate of ours that obtains regulatory approval to achieve market acceptance or commercial success would adversely affect our business prospects. In addition, any negative perception of one of our Founded Entities or any therapeutic candidates marketed or commercialized by them may adversely affect our reputation in the marketplace or among industry participants and our business prospects.

The insurance coverage and reimbursement status of newly-approved therapeutics is uncertain. The therapeutic candidates within our Wholly Owned Pipeline may become subject to unfavorable pricing regulations, third-party coverage and reimbursement practices, or healthcare reform initiatives, which would harm our business. Failure to obtain or maintain coverage and adequate reimbursement for new or current therapeutics could limit our ability to market those therapeutics and decrease our ability to generate revenue.

The regulations that govern marketing approvals, pricing, coverage, and reimbursement for new drugs and other medical therapeutics vary widely from country to country. In the United States, healthcare reform legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a therapeutic before it can

be marketed. In many countries, the pricing review period begins after marketing or therapeutic licensing approval is granted. In some foreign markets, pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a therapeutic in a particular country, but then be subject to price regulations that delay our commercial launch of the therapeutic, possibly for lengthy time periods, and negatively impact the revenue we are able to generate from the sale of the therapeutic in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more therapeutics or therapeutic candidates, even if any therapeutic candidates we may develop obtain marketing approval.

Our ability to successfully commercialize our therapeutics and therapeutic candidates also will depend in part on the extent to which coverage and adequate reimbursement for these therapeutics and related treatments will be available from government health administration authorities, private health insurers, and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. The availability of coverage and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford treatments such as gene therapy therapeutics. Sales of these or other therapeutic candidates that we may identify will depend substantially, both domestically and abroad, on the extent to which the costs of the therapeutic candidates within our Wholly Owned Pipeline will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. If coverage and adequate reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our therapeutics or therapeutic candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. In many countries, the prices of medical therapeutics are subject to varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for medicines, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for the therapeutic candidates within our Wholly Owned Pipeline. Accordingly, in markets outside the United States, the reimbursement for therapeutics may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenues and profits.

There is also significant uncertainty related to the insurance coverage and reimbursement of newly approved therapeutics and coverage may be more limited than the purposes for which the medicine is approved by the FDA or comparable foreign regulatory authorities. In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. No uniform policy of coverage and reimbursement for therapeutics exists among third-party payors and coverage and reimbursement levels for therapeutics can differ significantly from payor to payor. As a result, the coverage determination process is often a time consuming and costly process that may require us to provide scientific and clinical support for the use of our therapeutics to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. It is difficult to predict what CMS will decide with respect to reimbursement for fundamentally novel therapeutics such as ours, as there is no body of established practices and precedents for these new therapeutics. Reimbursement agencies in Europe may be more conservative than CMS. For example, a number of cancer drugs have been approved for reimbursement in the United States and have not been approved for reimbursement in certain European countries. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved therapeutics we may develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize therapeutic candidates, and our overall financial condition. As noted above, in the United States we plan to have various programs to help patients afford our therapeutics, including patient assistance programs and co-pay coupon programs for eligible patients.

Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Our inability to promptly obtain coverage and profitable reimbursement rates third-party payors for any approved therapeutics that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize therapeutics and our overall financial condition.

Increasingly, third-party payors are requiring that pharmaceutical companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical therapeutics. We cannot be sure that reimbursement will be available for any therapeutic candidate that we commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any therapeutic or therapeutic candidate for which we obtain marketing approval. In order to obtain reimbursement, physicians may need to show that patients have superior treatment outcomes with our therapeutics compared to standard of care drugs, including lower-priced generic versions of standard of care drugs. We expect to experience pricing pressures in connection with the sale of any of the therapeutic candidates within our Wholly Owned Pipeline, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new therapeutics. Additionally, we may develop companion diagnostic tests for use with our Wholly Owned Programs or our Founded Entities' therapeutic candidates. We, or our Founded Entities or our collaborators may be required to obtain coverage and reimbursement for these tests separate and apart from the coverage and reimbursement we seek for our Wholly Owned Programs or our Founded Entities' therapeutic candidates, once approved. Even if we or our Founded Entities obtain regulatory approval or clearance for such companion diagnostics, there is significant uncertainty regarding our ability to obtain coverage and adequate reimbursement for the same reasons applicable to our Wholly Owned Programs or our Founded Entities' therapeutic candidates. Medicare reimbursement methodologies, whether under Part A, Part B, or clinical laboratory fee schedule may be amended from time to time, and we cannot predict what effect any change to these methodologies would have on any therapeutic candidate or companion diagnostic for which we receive approval.

We have no sales, distribution, or marketing capabilities, and may invest significant financial and management resources to establish these capabilities. If we are unable to establish such capabilities or enter into agreements with third parties to market and sell our future therapeutics, if approved, we may be unable to generate any revenues.

Given our stage of development, we have no sales, distribution, or marketing capabilities. To successfully commercialize any therapeutics that may result from our development programs, we will need to develop sales and marketing capabilities in the United States, Europe, and other regions, either on our own or with others. We may enter into strategic alliances with other entities to utilize their mature marketing and distribution capabilities, but we may be unable to enter into marketing agreements on favorable terms, if at all. If our future strategic collaborators do not commit sufficient resources to commercialize our future therapeutics, if any, and we are unable to develop the necessary marketing capabilities on our own, we may be unable to generate sufficient therapeutic revenue to sustain our business. We will be competing with many companies that currently have extensive and well-funded marketing and sales operations. Without a significant internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

Risks Related to Compliance with Healthcare Laws

If we fail to comply with healthcare laws, we could face substantial penalties and our business, operations and financial conditions could be adversely affected.

Healthcare providers, physicians and third-party payors in the United States and elsewhere play a primary role in the recommendation and prescription of pharmaceutical therapeutics. Arrangements with healthcare providers, third-party payors and customers can expose pharmaceutical manufacturers to broadly applicable fraud and abuse and other healthcare laws and regulations, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act, or the FCA, which may constrain the business or financial arrangements and relationships through which such companies sell, market and distribute pharmaceutical therapeutics. In particular, the promotion, sales and marketing of healthcare items

and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of ownership, pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials. The applicable federal and state healthcare laws and regulations laws that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment of up to ten years, and exclusion from government healthcare programs. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers, on the one hand, and prescribers, purchasers and formulary managers, on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. On December 2, 2020, the Office of Inspector General, or OIG, published further modifications to the federal Anti-Kickback Statute. Under the final rules, OIG added safe harbor protections under the Anti-Kickback Statute for certain coordinated care and value-based arrangements among clinicians, providers, and others. This rule (with exceptions) became effective January 19, 2021. Implementation of this change and new safe harbors for point-of-sale reductions in price for prescription pharmaceutical therapeutics and pharmacy benefit manager service fees are currently under review by the Biden administration and may be amended or repealed. We continue to evaluate what effect, if any, the rule will have on our business
- federal civil and criminal false claims laws and civil monetary penalty laws, including the False Claims Act, which impose criminal and civil penalties, including through civil "qui tam" or "whistleblower" actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other federal health care programs that are false or fraudulent; knowingly making or causing a false statement material to a false or fraudulent claim or an obligation to pay money to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing such an obligation. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. When an entity is determined to have violated the federal civil False Claims Act, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating HIPAA without actual knowledge of the statute or specific intent to violate it;
- the federal civil monetary penalties laws, which impose civil fines for, among other things, the offering or transfer or remuneration to a Medicare or state healthcare program beneficiary if the person knows or should know it is likely to influence the beneficiary's selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state healthcare program, unless an exception applies;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose, among other things, requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions;
- the federal Physician Payments Sunshine Act, created under the ACA, and its implementing regulations, which require manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the U.S. Department of Health and Human Services, or HHS, under the Open Payments Program, information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- federal price reporting laws, which require manufacturers to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on approved therapeutics; and
- analogous state and foreign laws and regulations, such as state and foreign anti-kickback, false claims, consumer protection and unfair competition laws which may apply to pharmaceutical business practices, including but not limited to, research, distribution, sales and marketing arrangements as well as submitting claims involving healthcare items or services reimbursed by any third-party payer, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government that otherwise restricts payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to file reports with states regarding pricing and marketing information, such as the tracking and reporting of gifts, compensations and other remuneration and items of value provided to healthcare professionals and entities; state and local laws requiring the registration of pharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and are often not pre-empted by HIPAA, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities, including compensation of physicians with stock or stock options, could, despite efforts to comply, be subject to challenge under one or more of such laws. Additionally, FDA or foreign regulators may not agree that we have mitigated any risk of bias in our clinical trials due to payments or equity interests provided to investigators or institutions which could limit a regulator's acceptance of those clinical trial data in support of a marketing application. Moreover, efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, disgorgement, monetary fines, exclusion from participation in Medicare, Medicaid and other federal healthcare programs, integrity and oversight agreements to resolve allegations of non-compliance, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of any of the therapeutic candidates within our Wholly Owned Pipeline outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

Failure to comply with health and data protection laws and regulations could lead to government enforcement actions (which could include civil or criminal penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business.

We and any potential collaborators may be subject to federal, state, and foreign data protection laws and regulations (i.e., laws and regulations that address privacy and data security). In the United States, numerous federal and state laws and regulations, including federal health information privacy laws, state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), that govern the collection, use, disclosure and protection of health-related and other personal information could apply to our operations or the operations of our collaborators. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA, as amended by HITECH. Depending on the facts and circumstances, we could be subject to civil, criminal, and administrative penalties if we knowingly obtain, use, or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

Compliance with U.S. and international data protection laws and regulations, including the General Data Protection Regulation 2016/679, or GDPR, in the European Union, could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Failure to comply with these laws and regulations could result in government enforcement actions (which could include civil, criminal and administrative penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects, employees and other individuals about whom we or our potential collaborators obtain personal information, as well as the providers who share this information with us, may limit our ability to collect, use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

Healthcare legislative measures aimed at reducing healthcare costs may have a material adverse effect on our business and results of operations.

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates or any future therapeutic candidates, restrict or regulate post-approval activities and affect our or our Founded Entities' ability to profitably sell any therapeutic for which we or our Founded Entities obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our or our Founded Entities' business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to therapeutic labeling; (iii) the recall or discontinuation of our therapeutics; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

In the United States, there have been and continue to be a number of legislative initiatives and judicial challenges to contain healthcare costs. For example, in March 2010, the Affordable Care Act, or the ACA, was passed, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacted the U.S. pharmaceutical industry. The ACA, among other things, subjects biological therapeutics to potential competition by lower-cost biosimilars, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, and creates a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70 percent point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

Payment methodologies may be subject to changes in healthcare legislation and regulatory challenges. For example, in order for a drug therapeutic to receive federal reimbursement under the Medicaid or Medicare Part B programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. In December 2018, the CMS published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of the federal district court litigation regarding the method CMS uses to determine this risk adjustment. Since then, the ACA risk adjustment program payment parameters have been updated annually.

Since the enactment of the ACA, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. The Tax Cuts and Jobs Act of 2017, or the Tax Act, includes a provision that repealed effective January 1, 2019 the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, or the Texas District Court Judge, ruled that the individual mandate is a critical and inseverable feature of the ACA, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the ACA are invalid as well. The former Trump Administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the Texas District Court Judge issued an order staying the judgment pending appeal. On December 18, 2019, the U.S. Court of Appeals for the 5th Circuit ruled that the individual mandate was unconstitutional but remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. On March 2, 2020, the U.S. Supreme Court granted the petitions for writs of certiorari to review the case, and held oral arguments on November 10, 2020. Pending a decision, the ACA remains in effect, but it is unclear at this time what effect these developments will have on the status of the ACA. We will continue to evaluate the effect that the ACA and its possible repeal and replacement has on our business.

Since January 2017, former President Trump signed various Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. On October 13, 2017, former President Trump signed an Executive Order terminating the cost-sharing subsidies that reimburse insurers under the ACA. The former Trump administration concluded that cost-sharing reduction, or CSR, payments to insurance companies required under the ACA have not received necessary appropriations from Congress and announced that it would discontinue these payments immediately until those appropriations are made. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. On August 14, 2020, the U.S. Court of Appeals for the Federal Circuit ruled in two separate cases that the federal government is liable for the full amount of unpaid CSRs for the years preceding and including 2017. For CSR claims made by health insurance companies for years 2018 and later, further litigation will be required to determine the amounts due, if any. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. This decision was appealed to the U.S. Supreme Court, which on April 27, 2020, reversed the U.S. Court of Appeals for the Federal Circuit's decision and remanded the case to the U.S. Court of Federal Claims, concluding the government has an obligation to pay these risk corridor payments under the relevant formula. The U.S. federal government has since started sending third-party payors owed payments. It is not clear what effect these rulings will have on our business, but we will continue to monitor any developments.

Moreover, on January 22, 2018, former President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. However, on December 20, 2019, the U.S. President signed into law the Further Consolidated Appropriations Act (H.R. 1865), which repeals the Cadillac tax, the health insurance provider tax, and the medical device excise tax. The Bipartisan Budget Act of 2018, also amended the ACA, effective January 1, 2019, by increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and closing the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." In addition, CMS published a final rule on April 25, 2019 that gave states greater flexibility, starting in 2020, in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, resulted in aggregate reductions of Medicare payments to providers of 2 percent per fiscal year, which went into effect in 2013, and, due to subsequent legislative amendments, will remain in effect through 2030 unless additional Congressional action is taken. However, pursuant to the Coronavirus Aid, Relief and Economic

Security Act, or CARES Act, and due to subsequent legislation, these Medicare sequester reductions were suspended from May 1, 2020 through March 31, 2021 due to the COVID-19 pandemic. Proposed legislation, if passed, would extend this suspension until the end of the pandemic. The American Taxpayer Relief Act of 2012 further reduced Medicare payments to several types of providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

There has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the former Trump administration's budget for fiscal year 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. On March 10, 2020, the former Trump administration sent "principles" for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases. Additionally, the former Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their therapeutics and reduce the out of pocket costs of drug therapeutics paid by consumers. The U.S. Department of HHS has already started the process of soliciting feedback on some of these measures and, at the same time, is immediately implementing others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. However, it is unclear whether the Biden administration will challenge, reverse, revoke or otherwise modify these executive and administrative actions.

In addition, on May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug therapeutics that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug therapeutics available to eligible patients as a result of the Right to Try Act.

In 2020, former President Trump announced several executive orders related to prescription drug pricing that seek to implement several of the administration's proposals. The FDA released a final rule on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, CMS issued an Interim Final Rule implementing the Most Favored Nation, or MFN, Model under which Medicare Part B reimbursement rates will be calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. The MFN Model regulations mandate participation by identified Part B providers and would have applied to all U.S. states and territories for a seven-year period beginning January 1, 2021, and ending December 31, 2027. However, in response to a lawsuit filed by several industry groups, on December 28, the U.S. District Court for the Northern District of California issued a nationwide preliminary injunction enjoining government defendants from implementing the MFN Rule pending completion of notice-and-comment procedures under the Administrative Procedure Act. On January 13, 2021, in a separate lawsuit brought by industry groups in the U.S. District of Maryland, the government defendants entered a joint motion to stay litigation on the condition that the government would not appeal the preliminary injunction granted in the U.S. District Court for the Northern District of California and that performance for any final regulation stemming from the MFN Interim Final Rule shall not commence earlier than 60 days after publication of that regulation in the Federal Register. Further, authorities in Canada have passed rules designed to safeguard the Canadian drug supply from shortages. If implemented, importation of drugs from Canada and the MFN Model may materially and adversely affect the price we receive for any of our therapeutic candidates. Additionally, on December 2, 2020, HHS published a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to an order entered by the U.S. District Court for the District of Columbia, the portion of the rule eliminating safe harbor protection for certain rebates related to the sale or purchase of a pharmaceutical therapeutic from a manufacturer to a plan sponsor under Medicare Part D has been delayed to January 1, 2023. Further, implementation of this change and new safe harbors for point-of-sale reductions in price for prescription pharmaceutical therapeutics and pharmacy benefit manager service fees are currently under review by the Biden administration and may be amended or repealed.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological therapeutic pricing, including price or patient reimbursement constraints, discounts, restrictions on certain therapeutic access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical therapeutics and which suppliers will be included in their prescription drug and other healthcare programs. Furthermore, there has been increased interest by third-party payors and governmental authorities in reference pricing systems and publication of discounts and list prices.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at containing or lowering the cost of healthcare. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our therapeutic. Such reforms could have an adverse effect on anticipated revenue from therapeutic candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop therapeutic candidates. We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates, if approved;
- our ability to receive or set a price that we believe is fair for our therapeutics;
- our ability to generate revenue and achieve or maintain profitability;
- the amount of taxes that we are required to pay; and
- the availability of capital.

Other healthcare reform measures may be adopted in the future, and may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, lower reimbursement, and new payment methodologies. This could lower the price that we receive for any approved therapeutic. Any denial in coverage or reduction in reimbursement from Medicare or other government-funded programs may result in a similar denial or reduction in payments from private payors, which may prevent us from being able to generate sufficient revenue, attain profitability or commercialize the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates, if approved. Litigation and legislative efforts to change or repeal the ACA are likely to continue, with unpredictable and uncertain results.

Risks Related to Competition

We face significant competition in an environment of rapid technological and scientific change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer, more advanced or more effective than ours, which may negatively impact our ability to successfully market or commercialize any therapeutic candidates we may develop and ultimately harm our financial condition.

The development and commercialization of new drug therapeutics is highly competitive. We may face competition with respect to any therapeutic candidates that we seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization.

There are a number of major pharmaceutical and biotechnology companies that are currently pursuing the development and commercialization of potential medicines targeting similar treatment areas as we are. If any of our competitors receive FDA approval before we do, the therapeutic candidates within our Wholly Owned Pipeline would not be the first

treatment on the market, and our market share may be limited. In addition to competition from other companies targeting our target indications, any therapeutics we may develop may also face competition from other types of therapies.

Many of our current or potential competitors, either alone or with their strategic partners, have:

- greater financial, technical, and human resources than we have at every stage of the discovery, development, manufacture, and commercialization of therapeutics;
- more extensive resources for preclinical testing, conducting clinical trials, obtaining regulatory approvals, and in manufacturing, marketing, and selling drug therapeutics;
- therapeutics that have been approved or are in late stages of development; and
- collaborative arrangements in our target markets with leading companies and research institutions.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize therapeutics that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any therapeutics that we may develop. Furthermore, currently approved therapeutics could be discovered to have application for treatment of our targeted disease indications or similar indications, which could give such therapeutics significant regulatory and market timing advantages over the therapeutic candidates within our Wholly Owned Pipeline. Our competitors may also obtain FDA, EMA or other comparable foreign regulatory approval for their therapeutics more rapidly than we may obtain approval for ours and may obtain orphan therapeutic exclusivity from the FDA for indications that we are targeting, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, therapeutics or technologies developed by our competitors may render our potential therapeutic candidates uneconomical or obsolete and we may not be successful in marketing any therapeutic candidates we may develop against competitors.

In addition, we could face litigation or other proceedings with respect to the scope, ownership, validity and/or enforceability of our patents relating to our competitors' therapeutics and our competitors may allege that our therapeutics infringe, misappropriate or otherwise violate their intellectual property. The availability of our competitors' therapeutics could limit the demand, and the price we are able to charge, for any therapeutics that we may develop and commercialize.

The therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates for which we or our Founded Entities intend to seek approval as biologic therapeutics may face competition sooner than anticipated.

If we or our Founded Entities are successful in achieving regulatory approval to commercialize any biologic therapeutic candidate we or our Founded Entities develop alone or with collaborators, it may face competition from biosimilar therapeutics. In the United States, certain of the therapeutic candidates within our Wholly Owned Pipeline and our Founded Entities' therapeutic candidates are regulated by the FDA as biologic therapeutics subject to approval under the BLA pathway. The Biologics Price Competition and Innovation Act of 2009, or BPCIA, created an abbreviated pathway for the approval of biosimilar and interchangeable biologic therapeutics following the approval of an original BLA. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an existing brand therapeutic. Under the BPCIA, an application for a biosimilar therapeutic may not be submitted until four years following the date that the reference therapeutic was first licensed by the FDA. In addition, the approval of a biosimilar therapeutic may not be made effective by the FDA until 12 years after the reference therapeutic was first licensed by the FDA. During this 12-year period of exclusivity, another company may still market a competing version of the reference therapeutic if the FDA approves a full BLA for the competing therapeutic containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their therapeutic.

We believe that any of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates that are approved as a biological therapeutic under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider such therapeutic candidates to be reference therapeutics for competing therapeutics, potentially creating the opportunity for generic competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. Moreover, the extent to which a biosimilar therapeutic, once approved, will be substituted for any one of our, our Founded Entities' or our collaborators' reference therapeutics in a way that is similar to traditional generic substitution for non-biologic therapeutics is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing. If competitors are able to obtain marketing approval for biosimilars referencing any therapeutics that we or our Founded Entities develop alone or with collaborators that may be approved, such therapeutics may become subject to competition from such biosimilars, with the attendant competitive pressure and potential adverse consequences.

Risks Related to Reliance on Third Parties

We are currently party to and may seek to enter into additional collaborations, licenses and other similar arrangements and may not be successful in maintaining existing arrangements or entering into new ones, and even if we are, we may not realize the benefits of such relationships.

We are currently parties to license and collaboration agreements with a number of universities and pharmaceutical companies and expect to enter into additional agreements as part of our business strategy. The success of our current and any future collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborations are subject to numerous risks, which may include risks that:

- collaborators may have significant discretion in determining the efforts and resources that they will apply to collaborations;
- collaborators may not pursue development and commercialization of the therapeutic candidates within our Wholly Owned Pipeline or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in their strategic focus due to their acquisition of competitive therapeutics or their internal development of competitive therapeutics, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial, abandon a therapeutic candidate, repeat or conduct new clinical trials or require a new formulation of a therapeutic candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, therapeutics that compete directly or indirectly with our therapeutics or therapeutic candidates;
- a collaborator with marketing, manufacturing and distribution rights to one or more therapeutics may not commit sufficient resources to or otherwise not perform satisfactorily in carrying out these activities;
- we could grant exclusive rights to our collaborators that would prevent us from collaborating with others;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that cause the delay or termination of the research, development or commercialization of our current or future therapeutic candidates or that results in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated, which may result in a need for additional capital to pursue further development or commercialization of the applicable current or future therapeutic candidates;
- collaborators may own or co-own intellectual property covering therapeutics that result from our collaboration with them, and in such cases, we would not have the exclusive right to develop or commercialize such intellectual property;
- disputes may arise with respect to the ownership of any intellectual property developed pursuant to our collaborations; and
- a collaborator's sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings.

Additionally, we may seek to enter into additional collaborations, joint ventures, licenses and other similar arrangements for the development or commercialization of the therapeutic candidates within our Wholly Owned Pipeline, due to capital costs required to develop or commercialize the therapeutic candidate or manufacturing constraints. We may not be successful in our efforts to establish such collaborations for the therapeutic candidates within our Wholly Owned Pipeline because our R&D pipeline may be insufficient, the therapeutic candidates within our Wholly Owned

Pipeline may be deemed to be at too early of a stage of development for collaborative effort or third parties may not view the therapeutic candidates within our Wholly Owned Pipeline as having the requisite potential to demonstrate safety and efficacy or significant commercial opportunity. In addition, we face significant competition in seeking appropriate strategic partners, and the negotiation process can be time consuming and complex. Further, any future collaboration agreements may restrict us from entering into additional agreements with potential collaborators. We cannot be certain that, following a strategic transaction or license, we will achieve an economic benefit that justifies such transaction.

Even if we are successful in our efforts to establish such collaborations, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such collaborations if, for example, development or approval of a therapeutic candidate is delayed, the safety of a therapeutic candidate is questioned or sales of an approved therapeutic candidate are unsatisfactory.

In addition, any potential future collaborations may be terminable by our strategic partners, and we may not be able to adequately protect our rights under these agreements. Furthermore, strategic partners may negotiate for certain rights to control decisions regarding the development and commercialization of the therapeutic candidates within our Wholly Owned Pipeline, if approved, and may not conduct those activities in the same manner as we do. Any termination of collaborations we enter into in the future, or any delay in entering into collaborations related to the therapeutic candidates within our Wholly Owned Pipeline, could delay the development and commercialization of the therapeutic candidates within our Wholly Owned Pipeline and reduce their competitiveness if they reach the market, which could have a material adverse effect on our business, financial condition and results of operations.

Collaborative relationships with third parties could cause us to expend significant resources and give rise to substantial business risk with no assurance of financial return.

We anticipate relying upon strategic collaborations for marketing and commercializing our existing therapeutic candidates, and we may rely even more on strategic collaborations for R&D of other therapeutic candidates or discoveries. We may sell therapeutic offerings through strategic partnerships with pharmaceutical and biotechnology companies. If we are unable to establish or manage such strategic collaborations on terms favorable to us in the future, our R&D efforts and potential to generate revenue may be limited.

If we enter into R&D collaborations during the early phases of therapeutic development, success will in part depend on the performance of research collaborators. We will not directly control the amount or timing of resources devoted by research collaborators to activities related to therapeutic candidates. Research collaborators may not commit sufficient resources to our R&D programs. If any research collaborator fails to commit sufficient resources, the preclinical or clinical development programs related to the collaboration could be delayed or terminated. Also, collaborators may pursue existing or other development-stage therapeutics or alternative technologies in preference to those being developed in collaboration with us. Finally, if we fail to make required milestone or royalty payments to collaborators or to observe other obligations in agreements with them, the collaborators may have the right to terminate or stop performance of those agreements.

Establishing strategic collaborations is difficult and time-consuming. Our discussions with potential collaborators may not lead to the establishment of collaborations on favorable terms, if at all. Potential collaborators may reject collaborations based upon their assessment of our financial, regulatory or intellectual property position. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. Even if we successfully establish new collaborations, these relationships may never result in the successful development or commercialization of therapeutic candidates or the generation of sales revenue. To the extent that we enter into collaborative arrangements, the related therapeutic revenues are likely to be lower than if we directly marketed and sold therapeutics. Such collaborators may also consider alternative therapeutic candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for any future therapeutic candidate.

Management of our relationships with collaborators will require:

- significant time and effort from our management team;
- coordination of our marketing and R&D programs with the marketing and R&D priorities of our collaborators; and
- effective allocation of our resources to multiple projects.

We rely on third parties to assist in conducting our clinical trials and some aspects of our research and preclinical testing, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research, or testing.

We currently rely and expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions, and clinical investigators, to conduct some aspects of research and preclinical testing and clinical trials. Any of these third parties may terminate their engagements with us or be unable to fulfill their contractual obligations. If any of our relationships with these third parties terminate, we may not be able to enter into arrangements with alternative third parties on commercially reasonable terms, or at all. If we need to enter into alternative arrangements, it would delay therapeutic development activities.

Further, although our reliance on these third parties for clinical development activities limits our control over these activities, we remain responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards. For example, notwithstanding the obligations of a CRO for a trial of one of the therapeutic candidates within our Wholly Owned Pipeline, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with requirements, commonly referred to as GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. The FDA enforces these GCPs through periodic inspections of trial sponsors, principal investigators, clinical trial sites and IRBs. If we or our third-party contractors fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving the therapeutic candidates within our Wholly Owned Pipeline, which would delay the regulatory approval process. We cannot be certain that, upon inspection, the FDA will determine that any of our clinical trials comply with GCPs. We are also required to register certain clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. NIH and FDA recently signaled the government's willingness to begin enforcing those requirements against non-compliant clinical trial sponsors. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, the third parties conducting clinical trials on our behalf are not our employees, and except for remedies available to us under our agreements with such contractors, we cannot control whether or not they devote sufficient time, skill and resources to our ongoing development programs. These contractors may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug or medical device development activities, which could impede their ability to devote appropriate time to our clinical programs. If these third parties, including clinical investigators, do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we may not be able to obtain, or may be delayed in obtaining, regulatory approvals for the therapeutic candidates within our Wholly Owned Pipeline. If that occurs, we will not be able to, or may be delayed in our efforts to, successfully commercialize the therapeutic candidates within our Wholly Owned Pipeline. In such an event, our financial results and the commercial prospects for any therapeutic candidates that we seek to develop could be harmed, our costs could increase and our ability to generate revenues could be delayed, impaired or foreclosed.

Our or our Founded Entities' use of third parties to manufacture the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates and other therapeutic candidates that we or our Founded Entities may develop for preclinical studies and clinical trials may increase the risk that we or our Founded Entities will not have sufficient quantities of our or our Founded Entities' therapeutic candidates, therapeutics, or necessary quantities of such materials on time or at an acceptable cost.

With respect to certain of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates, we and certain of our Founded Entities do not currently have, nor do we plan to acquire, the infrastructure or capability internally to manufacture drug supplies for our ongoing clinical trials or any future clinical trials that we or our Founded Entities may conduct, and we and our Funded Entities lack the resources to manufacture any therapeutic candidates on a commercial scale. We rely, and expect to continue to rely, on third-party manufacturers to produce our and certain of our Founded Entities' therapeutic candidates or other therapeutic candidates that we or our Founded Entities may

identify for clinical trials, as well as for commercial manufacture if any therapeutic candidates receive marketing authorization. Although we and our Founded Entities generally do not begin a clinical trial unless we or our Founded Entities believe we have a sufficient supply of a therapeutic candidate to complete the trial, any significant delay or discontinuity in the supply of a therapeutic candidate, or the raw material components thereof, for an ongoing clinical trial due to the need to replace a third-party manufacturer could considerably delay the clinical development and potential regulatory authorization of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates, which could harm our business and results of operations.

We or our Founded Entities may be unable to identify and appropriately qualify third-party manufacturers or establish agreements with third-party manufacturers or do so on acceptable terms. Even if we or our Founded Entities are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for sourcing of raw materials, components, and such other goods as may be required for execution of its manufacturing processes and the oversight by the third party of its suppliers;
- reliance on the third party for regulatory compliance and quality assurance for the manufacturing activities each performs;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of proprietary information, including trade secrets and know-how; and
- the possible termination or non-renewal of the agreement by the third party at a time that is costly or inconvenient for us or our Founded Entities.

Furthermore, all of our CMOs are engaged with other companies to supply and/or manufacture materials or therapeutics for such companies, which exposes our manufacturers to regulatory risks for the production of such materials and therapeutics. The facilities used by our contract manufacturers to manufacture our drug, or medical device therapeutic candidates are subject to review by the FDA pursuant to inspections that will be conducted after we submit an NDA, BLA, PMA application or other marketing application to the FDA. We do not control the manufacturing process of, and are to some extent dependent on, our contract manufacturing partners for compliance with the regulatory requirements, known as cGMP requirements for manufacture of drug, biologic and device therapeutics. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, we will not be able to secure or maintain regulatory authorization for the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates manufactured at these manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA, the EMA or another comparable foreign regulatory agency does not approve these facilities for the manufacture of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates or if any agency withdraws its approval in the future, we or our Founded Entities may need to find alternative manufacturing facilities, which would negatively impact our or our Founded Entities' ability to develop, obtain regulatory authorization for or market the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates, if cleared or approved.

The therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates may compete with other therapeutic candidates and marketed therapeutics for access to manufacturing facilities. Any performance failure on the part of our or our Founded Entities' existing or future manufacturers could delay clinical development, marketing approval or commercialization. Our and certain of our Founded Entities' current and anticipated future dependence upon others for the manufacturing of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates may adversely affect our future profit margins and our ability to commercialize any therapeutic candidates that receive marketing clearance or approval on a timely and competitive basis.

If the contract manufacturing facilities on which we and certain of our Founded Entities' rely do not continue to meet regulatory requirements or are unable to meet our or our Founded Entities' supply demands, our business will be harmed.

All entities involved in the preparation of therapeutic candidates for clinical trials or commercial sale, including our and certain of our Founded Entities' existing CMOs for the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates, are subject to extensive regulation. Components of a finished drug or biologic therapeutic approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with cGMP, or similar regulatory requirements outside the United States. These regulations govern manufacturing processes and procedures, including recordkeeping, and the implementation and operation of quality systems to control and assure the quality of investigational therapeutics and therapeutics approved for sale. Similarly, medical devices must be manufactured in accordance with QSR. Poor control of production processes can lead to the introduction of contaminants or to inadvertent changes in the properties or stability of Gelesis' Plenity, Akili's EndeavorRx, our Founded Entities' other therapeutic candidates or the therapeutic candidates within our Wholly Owned Pipeline. Our or our Founded Entities' failure, or the failure of third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us or our Founded Entities, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, suspension of production, seizures or recalls of therapeutic candidates or marketed drugs or devices, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect clinical or commercial supplies of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates.

We and/or our CMOs must supply all necessary documentation, as applicable, in support of a marketing application, such as an NDA, BLA, PMA or MAA, on a timely basis and must adhere to regulations enforced by the FDA and other regulatory agencies through their facilities inspection program. Some of our CMOs have never produced a commercially approved pharmaceutical therapeutic and therefore have not obtained the requisite regulatory authority approvals to do so. The facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates or any of our other potential therapeutics. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates or our other potential therapeutics or the associated quality systems for compliance with the regulations applicable to the activities being conducted. Although we oversee the CMOs, we cannot control the manufacturing process of, and are completely dependent on, our CMO partners for compliance with the regulatory requirements. If these facilities do not pass a pre-approval plant inspection, regulatory approval of the therapeutics may not be granted or may be substantially delayed until any violations are corrected to the satisfaction of the regulatory authority, if ever.

The regulatory authorities also may, at any time following clearance or approval of a therapeutic for sale, audit the manufacturing facilities of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our therapeutic specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time consuming for us or a third party to implement, and that may include the temporary or permanent suspension of a clinical study or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

Additionally, if supply from one approved manufacturer is interrupted, an alternative manufacturer would need to be qualified. For drug and biologic therapeutics, as applicable, an NDA, BLA supplement or MAA variation, or equivalent foreign regulatory filing, is also required, which could result in further delay. Similarly, for medical devices, a new marketing application or supplement may be required. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause us or our Founded Entities to incur higher costs and could cause the delay or termination of clinical trials, regulatory submissions, required approvals, or commercialization of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates. Furthermore, if our or our Founded Entities' suppliers fail to meet contractual requirements and we or our Founded Entities are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our or our Founded Entities' clinical trials may be delayed or we or our Founded Entities could lose potential revenue.

Risks Related to Our Intellectual Property

Risks Related to Our Intellectual Property Protection

If we or our Founded Entities are unable to obtain and maintain sufficient intellectual property protection for our or our Founded Entities' existing therapeutic candidates or any other therapeutic candidates that we or they may identify, or if the scope of the intellectual property protection we or they currently have or obtain in the future is not sufficiently broad, our competitors could develop and commercialize therapeutic candidates similar or identical to ours, and our ability to successfully commercialize our existing therapeutic candidates and any other therapeutic candidates that we or they may pursue may be impaired.

As is the case with other pharmaceutical and biopharmaceutical companies, our success depends in large part on our ability to obtain and maintain protection of the intellectual property we may own solely and jointly with others, particularly patents, in the United States and other countries with respect to our Wholly Owned Programs or our Founded Entities' therapeutic candidates and technology. We and our Founded Entities seek to protect our proprietary position by filing patent applications in the United States and abroad related to our and our Founded Entities' existing therapeutic candidates, our various proprietary technologies, and any other therapeutic candidates or technologies that we or they may identify.

Obtaining, maintaining and enforcing pharmaceutical and biopharmaceutical patents is costly, time consuming and complex, and we may not be able to file or prosecute all necessary or desirable patent applications, or maintain, enforce or license patents that may issue from such patent applications, at a reasonable cost or in a timely manner. It is also possible that we could fail to identify patentable aspects of our R&D output before it is too late to obtain patent protection. Although we take reasonable measures, we have systems in place to remind us of filing and prosecution deadlines, and we employ outside firms and rely on outside counsel to monitor patent deadlines, we may miss or fail to meet a patent deadline, including in a foreign country, which could negatively impact our patent rights and harm our competitive position, business, and prospects. We may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the rights to patents licensed to third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal, technological and factual questions and has in recent years been the subject of much litigation. The standards that the U.S. Patent and Trademark Office, or the USPTO, and its foreign counterparts use to grant patents are not always applied predictably or uniformly. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States, or vice versa. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, which can prevent a patent from issuing from a pending application or later invalidate or narrow the scope of an issued patent. For example, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued that protect our Wholly Owned Programs or our Founded Entities' therapeutic candidates, in whole or in part, or which effectively prevent others from commercializing competitive therapeutic candidates. Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our patents by developing similar or alternative therapeutic candidates in a non-infringing manner.

In addition, the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical therapeutic candidates to ours, or limit the duration of the patent protection of our Wholly Owned Programs or our Founded Entities' therapeutic candidates. For example, we may be subject to a third-party preissuance submission of prior art to the USPTO, or become involved in opposition, derivation, reexamination, inter partes review, post-grant review or interference proceedings challenging our owned or licensed patent rights. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our Wholly Owned Programs or our Founded Entities' therapeutic candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize drugs without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future therapeutic candidates.

Furthermore, our and our Founded Entities' intellectual property rights may be subject to a reservation of rights by one or more third parties. We are party to a license agreement with New York University related to certain intellectual property underlying our LYT-200 and LYT-210 therapeutic candidates which is subject to certain rights of the government, including march-in rights, to such intellectual property due to the fact that the research was funded at least in part by the U.S. government. We are also party to other license agreements for intellectual property underlying certain of our therapeutic candidates and programs. Additionally, our Founded Entities Akili, Follica, Vedanta, Sonde, Alivio and Vor, are party to license agreements with academic institutions pursuant to which such Founded Entities have in-licensed certain intellectual property underlying various of their therapeutic candidates. While these license agreements are exclusive, they contain provisions pursuant to which the government has certain rights, including march-in rights, to such patents and technologies due to the fact that the research was funded at least in part by the U.S. government. When new technologies are developed with government funding, the government generally obtains certain rights in any resulting patents, including a non-exclusive license authorizing the government to use the invention or to have others use the invention on its behalf. These rights may permit the government to disclose our information to third parties and to exercise march-in rights to use or allow third parties to use our technology. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture therapeutics embodying such inventions in the United States. Any exercise by the government of such rights or by any third party of its reserved rights could harm our competitive position, business, financial condition, results of operations, and prospects.

If our or our Founded Entities' trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our or our Founded Entities' registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We and our Founded Entities may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential collaborators or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we and our Founded Entities are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. We and our Founded Entities may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our or our Founded Entities' trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Our or our Founded Entities' efforts to enforce or protect our proprietary rights related to trademarks, trade names, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our competitive position, business, financial condition, results of operations and prospects.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect or enforce intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we and our Founded Entities may not be able to prevent third parties from practicing our inventions in all countries

outside the United States, or from selling or importing therapeutics made using our inventions in and into the United States or other jurisdictions. Competitors may use our and our Founded Entities' technologies in jurisdictions where we have not obtained patent protection to develop their own therapeutics and may also export infringing therapeutics to territories where we have patent protection, but enforcement is not as strong as that in the United States. These therapeutics may compete with our or our Founded Entities' therapeutics and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology and pharmaceutical therapeutics, which could make it difficult for us to stop the infringement of our or our Founded Entities' patents or marketing of competing therapeutics in violation of our proprietary rights generally. Proceedings to enforce our or our Founded Entities' patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our or our Founded Entities' patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us or our Founded Entities. We may not prevail in any lawsuits that we or our Founded Entities initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

In some jurisdictions including European Union countries, compulsory licensing laws compel patent owners to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we, our Founded Entities or any of our licensors are forced to grant a license to third parties under patents relevant to our or our Founded Entities' business, or if we, our Founded Entities or our licensors are prevented from enforcing patent rights against third parties, our competitive position may be substantially impaired in such jurisdictions.

Our or our Founded Entities' proprietary rights may not adequately protect our technologies and therapeutic candidates, and do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our or our Founded Entities' intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our or our Founded Entities' business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- others may be able to make therapeutics that are the same as or similar to the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates but that are not covered by the claims of the patents that we or our Founded Entities own or have exclusively licensed;
- others, including inventors or developers of our or our Founded Entities' owned or in-licensed patented technologies who may become involved with competitors, may independently develop similar technologies that function as alternatives or replacements for any of our or our Founded Entities' technologies without infringing our intellectual property rights;
- we, our Founded Entities or our licensors or our other collaboration partners might not have been the first to conceive and reduce to practice the inventions covered by the patents or patent applications that we or our Founded Entities own or license or will own or license;
- we, our Founded Entities or our licensors or our other collaboration partners might not have been the first to file patent applications covering certain of the patents or patent applications that we or they own or have obtained a license, or will own or will have obtained a license;
- we, our Founded Entities or our licensors may fail to meet obligations to the U.S. government with respect to in-licensed patents and patent applications funded by U.S. government grants, leading to the loss of patent rights;
- it is possible that our or our Founded Entities' pending patent applications will not result in issued patents;
- it is possible that there are prior public disclosures that could invalidate our, our Founded Entities' or our licensors' patents;
- issued patents that we or our Founded Entities own or exclusively license may not provide us with any competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our or our Founded Entities' competitors might conduct R&D activities in countries where we do not have patent rights, or in countries where R&D safe harbor laws exist, and then use the information learned from such activities to develop competitive therapeutics for sale in our major commercial markets;
- ownership, validity or enforceability of our, our Founded Entities' or our licensors' patents or patent applications may be challenged by third parties; and
- the patents of third parties or pending or future applications of third parties, if issued, may have an adverse effect on our business.

Risks Related to Our License Arrangements

The failure to maintain our licenses and realize their benefits may harm our business.

We have acquired and in-licensed certain of our technologies from third parties. We may in the future acquire, in-license or invest in additional technology that we believe would be beneficial to our business. We are subject to a number of risks associated with our acquisition, in-license or investment in technology, including the following:

- diversion of financial and managerial resources from existing operations;
- successfully negotiating a proposed acquisition, in-license or investment in a timely manner and at a price or on terms and conditions favorable to us;
- successfully combining and integrating a potential acquisition into our existing business to fully realize the benefits of such acquisition;
- the impact of regulatory reviews on a proposed acquisition, in-license or investment; and
- the outcome of any legal proceedings that may be instituted with respect to the proposed acquisition, in-license or investment.

If we fail to properly evaluate potential acquisitions, in-licenses, investments or other transactions associated with the creation of new R&D programs or the maintenance of existing ones, we might not achieve the anticipated benefits of any such transaction, we might incur costs in excess of what we anticipate, and management resources and attention might be diverted from other necessary or valuable activities.

Our or our Founded Entities' rights to develop and commercialize our Wholly Owned Programs or our Founded Entities' therapeutic candidates are subject in part to the terms and conditions of licenses granted to us and our Founded Entities by others, and the patent protection, prosecution and enforcement for some of our Wholly Owned Programs or our Founded Entities' therapeutic candidates may be dependent on our and our Founded Entities' licensors.

We and our Founded Entities currently are reliant upon licenses of certain intellectual property rights and proprietary technologies from third parties that are important or necessary to the development of our and our Founded Entities' proprietary technologies, including technologies related to our Wholly Owned Programs and our Founded Entities' therapeutic candidates. These licenses, and other licenses we and they may enter into in the future, may not provide adequate rights to use such intellectual property and proprietary technologies in all relevant fields of use or in all territories in which we or our Founded Entities may wish to develop or commercialize technology and therapeutic candidates in the future. Licenses to additional third-party proprietary technology or intellectual property rights that may be required for our or our Founded Entities' development programs may not be available in the future or may not be available on commercially reasonable terms. In that event, we or our Founded Entities may be required to expend significant time and resources to redesign our proprietary technology or therapeutic candidates or to develop or license replacement technology, which may not be feasible on a technical or commercial basis. If we and our Founded Entities are unable to do so, we may not be able to develop and commercialize technology and therapeutic candidates in fields of use and territories for which we are not granted rights pursuant to such licenses, which could harm our competitive position, business, financial condition, results of operations and prospects significantly.

In some circumstances, we and our Founded Entities may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain and enforce the patents, covering technology that we or our Founded Entities license from third parties. In addition, some of our or our Founded Entities' agreements with our licensors require us to obtain consent from the licensor before we can enforce patent rights, and our licensor may withhold such consent or may not provide it on a timely basis. Therefore, we cannot be certain that our licensors or collaborators will prosecute, maintain, enforce and defend

such intellectual property rights in a manner consistent with the best interests of our business, including by taking reasonable measures to protect the confidentiality of know-how and trade secrets, or by paying all applicable prosecution and maintenance fees related to intellectual property registrations for any of our Wholly Owned Programs or our Founded Entities' therapeutic candidates and proprietary technologies. We and our Founded Entities also cannot be certain that our licensors have drafted or prosecuted the patents and patent applications licensed to us in compliance with applicable laws and regulations, which may affect the validity and enforceability of such patents or any patents that may issue from such applications. This could cause us to lose rights in any applicable intellectual property that we in-license, and as a result our ability to develop and commercialize therapeutic candidates may be adversely affected and we may be unable to prevent competitors from making, using and selling competing therapeutics.

In addition, our or our Founded Entities' licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights. In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future therapeutics, if any, the amounts may be significant. The amount of our and our Founded Entities' future royalty obligations will depend on the technology and intellectual property we and our Founded Entities use in therapeutic candidates that we successfully develop and commercialize, if any. Therefore, even if we or our Founded Entities successfully develop and commercialize therapeutic candidates, we may be unable to achieve or maintain profitability. In addition, we or our Founded Entities may seek to obtain additional licenses from our licensors and, in connection with obtaining such licenses, we may agree to amend our existing licenses in a manner that may be more favorable to the licensors, including by agreeing to terms that could enable third parties (potentially including our competitors) to receive licenses to a portion of the intellectual property rights that are subject to our or our Founded Entities' existing licenses. Any of these events could have a material adverse effect on our or our Founded Entities' competitive position, business, financial conditions, results of operations, and prospects.

If we or our Founded Entities fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or these agreements are terminated or we or our Founded Entities otherwise experience disruptions to our business relationships with our licensors, we could lose intellectual property rights that are important to our business.

We are party to various agreements that we depend on to develop our Wholly Owned Programs or our Founded Entities' therapeutic candidates and various proprietary technologies, and our rights to use currently licensed intellectual property, or intellectual property to be licensed in the future, are or will be subject to the continuation of and our and our Founded Entities' compliance with the terms of these agreements. For example, under certain of our and our Founded Entities' license agreements we and our Founded Entities are required to use commercially reasonable efforts to develop and commercialize therapeutic candidates covered by the licensed intellectual property rights, maintain the licensed intellectual property rights, and achieve certain development milestones, each of which could result in termination in the event we or our Founded Entities fail to comply.

In spite of our efforts, our or our Founded Entities' licensors might conclude that we have materially breached our obligations under such license agreements and might therefore terminate the license agreements, thereby removing or limiting our or our Founded Entities' ability to develop and commercialize therapeutics and technology covered by these license agreements.

Moreover, disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our Wholly Owned Programs or our Founded Entities' therapeutic candidates, technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our or our Founded Entities' collaborative development relationships;
- our and our Founded Entities' diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our and our Founded Entities' licensors and us and our Founded Entities and our partners; and
- the priority of invention of patented technology.

In addition, certain provisions in our and our Founded Entities' license agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the agreement, either of which could have a material adverse effect on our or our Founded Entities' business, financial condition, results of operations and prospects. Moreover, if disputes over intellectual property that we or our Founded Entities have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected therapeutic candidates, which could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

Third-party claims of intellectual property infringement may prevent or delay our development and commercialization efforts.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. However, our research, development and commercialization activities may be subject to claims that we infringe or otherwise violate patents or other intellectual property rights owned or controlled by third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, derivation, oppositions, inter partes review and post-grant review before the USPTO, and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are pursuing development candidates. Our competitors in both the United States and abroad, many of which have substantially greater resources and have made substantial investments in patent portfolios and competing technologies, may have applied for or obtained or may in the future apply for or obtain, patents that will prevent, limit or otherwise interfere with our ability to make, use and sell, if approved, the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates. In addition, many companies in the biotechnology and pharmaceutical industries have employed intellectual property litigation as a means to gain an advantage over their competitors. As the biotechnology and pharmaceutical industries expand and more patents are issued, and as we gain greater visibility and market exposure as a public company, the risk increases that our existing therapeutic candidates and any other therapeutic candidates that we or our Founded Entities may identify may be subject to claims of infringement of the patent rights of third parties.

There may be other third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our or our Founded Entities' existing therapeutic candidates and any other therapeutic candidates that we or they may identify. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our or our Founded Entities' existing therapeutic candidates and any other therapeutic candidates that we or they may identify may infringe. In addition, third parties may obtain patents in the future and claim that use of our or our Founded Entities' technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of our or our Founded Entities' existing therapeutic candidates and any other therapeutic candidates that we or they may identify, any molecules formed during the manufacturing process, or any final therapeutic itself, the holders of any such patents may be able to block our ability to commercialize such therapeutic candidate unless we obtained a license under the applicable patents, or until such patents expire. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our Wholly Owned Programs or our Founded Entities' therapeutic candidates. Furthermore, the scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history and can involve other factors such as expert opinion. Our analysis of these issues, including interpreting the relevance or the scope of claims in a patent or a pending application, determining applicability of such claims to our proprietary technologies or therapeutic candidates, predicting whether a third party's pending patent application will issue with claims of relevant scope, and determining the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our or our Founded Entities' ability to develop and market the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates. We do not always conduct independent reviews of pending patent applications of and patents issued to third parties.

Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our or our Founded Entities' formulations, processes for manufacture or methods of use, including any combination therapies, the holders of any such patents may be able to block our or

our Founded Entities' ability to develop and commercialize the applicable therapeutic candidate unless we obtained a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all, or it may be non-exclusive, which could result in our competitors gaining access to the same intellectual property.

Parties making claims against us or our Founded Entities may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our or our Founded Entities' existing therapeutic candidates and any other therapeutic candidates that we may identify. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of management and employee resources from our business. In the event of a successful claim of infringement against us or our Founded Entities, we or our Founded Entities may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing therapeutics or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

Parties making claims against us or our Founded Entities may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

Risks Related to Our Patents

Patent terms may be inadequate to protect our competitive position on therapeutic candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional or international patent application filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our Wholly Owned Programs or our Founded Entities' therapeutic candidates are obtained, once the patent life has expired, we or our Founded Entities may be open to competition from competitive therapeutics, including generics or biosimilars. Given the amount of time required for the development, testing and regulatory review of new therapeutic candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our or our Founded Entities' owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing therapeutics similar or identical to ours.

If we or our Founded Entities are not able to obtain patent term extension or non-patent exclusivity in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation, thereby potentially extending the marketing exclusivity term of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates, one or more of the U.S. patents covering each of such therapeutic candidates or the use thereof may be eligible for up to five years of patent term extension under the Hatch-Waxman Act. The Hatch-Waxman Act allows a maximum of one patent to be extended per new drug application, or NDA, for an FDA approved therapeutic as compensation for the patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of therapeutic approval and only those claims covering such approved drug therapeutic, a method for using it or a method for manufacturing it may be extended. Patent term extension also may be available in certain foreign countries upon regulatory approval of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates. Nevertheless, we or our Founded Entities may not be granted patent term extension either in the United States or in any foreign country because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request.

If we or our Founded Entities are unable to obtain patent term extension or restoration, or the term of any such extension is less than our request, the period during which we will have the right to exclusively market our therapeutic may be shortened and our competitors may obtain approval of competing therapeutics following our patent expiration sooner, and our revenue could be reduced, possibly materially.

Further, for certain of our and our Founded Entities' licensed patents, we and our Founded Entities do not have the right to control prosecution, including filing with the USPTO, a petition for patent term extension under the Hatch-Waxman Act. Thus, if one of our or our Founded Entities' licensed patents is eligible for patent term extension under the Hatch-Waxman Act, we may not be able to control whether a petition to obtain a patent term extension is filed with, or whether a patent term extension is obtained from, the USPTO.

Also, there are detailed rules and requirements regarding the patents that may be submitted to the FDA for listing in the Approved Drug Products with Therapeutic Equivalence Evaluations, or the Orange Book. We or our Founded Entities may be unable to obtain patents covering the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates that contain one or more claims that satisfy the requirements for listing in the Orange Book. Even if we or our Founded Entities submit a patent for listing in the Orange Book, the FDA may decline to list the patent, or a manufacturer of generic drugs may challenge the listing. If or when one of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates is approved and a patent covering that therapeutic candidate is not listed in the Orange Book, a manufacturer of generic drugs would not have to provide advance notice to us of any abbreviated new drug application, or ANDA, filed with the FDA to obtain permission to sell a generic version of such therapeutic candidate.

Issued patents covering our Wholly Owned Programs or our Founded Entities' therapeutic candidates could be found invalid or unenforceable if challenged in courts or patent offices.

If we, our Founded Entities or one of our licensing partners initiated legal proceedings against a third party to enforce a patent covering one or more of our Wholly Owned Programs or our Founded Entities' therapeutic candidates, the defendant could counterclaim that the patent covering the relevant therapeutic candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including subject matter eligibility, novelty, nonobviousness, written description or enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post grant review, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in revocation or amendment to our or our Founded Entities' patents in such a way that they no longer cover our Wholly Owned Programs or our Founded Entities' therapeutic candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our Wholly Owned Programs or our Founded Entities' therapeutic candidates. Such a loss of patent protection could have a material adverse impact on our business.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our and our Founded Entities' ability to protect our therapeutics.

Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to a patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith America Invents Act, or the America Invents Act, enacted in September 2011, the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013, but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us and our Founded Entities to be cognizant of the time from invention to filing of a patent application and be diligent in filing patent applications, but circumstances could prevent us from promptly filing patent applications on our inventions. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we, our Founded Entities or our licensors were the first to either (i) file any patent application related to our

Wholly Owned Programs or our Founded Entities' therapeutic candidates or (ii) invent any of the inventions claimed in our, our Founded Entities or our licensor's patents or patent applications.

The America Invents Act also includes a number of significant changes that affect the way patent applications are prosecuted and also may affect patent litigation. These include allowing third party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, inter partes review, and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Therefore, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our Founded Entities' owned or in-licensed patent applications and the enforcement or defense of our or our Founded Entities' owned or in-licensed issued patents, all of which could have a material adverse effect on our competitive position, business, financial condition, results of operations, and prospects.

In addition, the patent positions of companies in the development and commercialization of pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court and Federal Circuit rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We and our Founded Entities have systems in place to remind us to pay these fees, and we and our Founded Entities employ outside firms and rely on outside counsel to pay these fees due to the USPTO and non-U.S. patent agencies. However, we and our Founded Entities cannot guarantee that our licensors have similar systems and procedures in place to pay such fees. In addition, the USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

Risks Related to Confidentiality

If we are unable to protect the confidentiality of our trade secrets, the value of our technology could be materially adversely affected and our business would be harmed.

We and our Founded Entities consider proprietary trade secrets, confidential know-how and unpatented know-how to be important to our business. We and our Founded Entities may rely on trade secrets and confidential know-how to protect our technology, especially where patent protection is believed by us to be of limited value. However, trade secrets and confidential know-how are difficult to protect, and we have limited control over the protection of trade secrets and confidential know-how used by our licensors, collaborators and suppliers. Because we have relied in the past on third parties to manufacture the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates, because we may continue to do so in the future, and because we expect to collaborate with third parties on the development of our current therapeutic candidates and any future therapeutic candidates we develop, we may, at times, share trade secrets with them. We also conduct joint R&D programs that may require us to share trade secrets under the terms of our R&D partnerships or similar agreements. Under such circumstances, trade secrets and confidential know-how can be difficult to maintain as confidential.

We and our Founded Entities seek to protect our confidential proprietary information, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and collaborators. These agreements are designed to protect our proprietary information. However, we cannot be certain that such agreements have been entered into with all relevant parties, and we cannot be certain that our and our Founded Entities' trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. For example, any of these parties may breach the agreements and disclose proprietary information, including trade secrets, and we may not be able to obtain adequate remedies for such breaches. We and our Founded Entities also seek to preserve the integrity and confidentiality of our confidential proprietary information by maintaining physical security of our premises and physical and electronic security of our information technology systems, but it is possible that these security measures could be breached. If any of our or our Founded Entities' confidential proprietary information were to be lawfully obtained or independently developed by a competitor, we or our Founded Entities would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position.

Unauthorized parties may also attempt to copy or reverse engineer certain aspects of our or our Founded Entities' therapeutics that we consider proprietary. We or our Founded Entities may not be able to obtain adequate remedies in the event of such unauthorized use. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Trade secrets will also over time be disseminated within the industry through independent development, the publication of journal articles and the movement of personnel skilled in the art from company to company or academic to industry scientific positions. Though our or our Founded Entities' agreements with third parties typically restrict the ability of our advisors, employees, collaborators, licensors, suppliers, third-party contractors and consultants to publish data potentially relating to our trade secrets, our agreements may contain certain limited publication rights. In addition, if any of our or our Founded Entities' trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position. Despite employing the contractual and other security precautions described above, the need to share trade secrets increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of such information may be greatly reduced and our competitive position, business, financial condition, results of operations, and prospects would be harmed.

We or our Founded Entities may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

As is common in the biotechnology and pharmaceutical industries, we and our Founded Entities employ individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we and our Founded Entities try to ensure that our employees, consultants and independent contractors do not use the proprietary information or know-how of others in their work for us, we or our Founded Entities may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any of our employee's former employer or other third parties. Litigation may be necessary to defend against these claims. If we or our Founded Entities fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we or our Founded Entities are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Risks Related to Challenges or Lawsuits Related to Intellectual Property

We may become involved in lawsuits to protect or enforce our or our Founded Entities' patents or other intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our or our Founded Entities' patents or other intellectual property. Our and our Founded Entities' ability to enforce our

patent or other intellectual property rights depends on our ability to detect infringement. It may be difficult to detect infringers who do not advertise the components or methods that are used in connection with their therapeutics and services. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's therapeutic or service. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded if we were to prevail may not be commercially meaningful. If we were to initiate legal proceedings against a third party to enforce a patent covering one or more of our Wholly Owned Programs or our Founded Entities' therapeutic candidates, the defendant could counterclaim that the patent covering our or our Founded Entities' therapeutic candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including subject matter eligibility, novelty, nonobviousness, written description or enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable. Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our or our Founded Entities' patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. Our defense of litigation or interference or derivation proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue clinical trials, continue research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring therapeutic candidates to market. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our or our Founded Entities' confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could adversely impact the price of our ADSs. Furthermore, any of the foregoing could have a material adverse effect on our financial condition, results of operations, and prospects.

We and our Founded Entities may be subject to claims challenging the inventorship of our patents and other intellectual property.

Our and our Founded Entities' agreements with employees and our personnel policies provide that any inventions conceived by an individual in the course of rendering services to us shall be our exclusive property. Although our policy is to have all such individuals complete these agreements, we may not obtain these agreements in all circumstances, and individuals with whom we have these agreements may not comply with their terms. The assignment of intellectual property may not be automatic upon the creation of an invention and despite such agreement, such inventions may become assigned to third parties. In the event of unauthorized use or disclosure of our trade secrets or proprietary information, these agreements, even if obtained, may not provide meaningful protection, particularly for our trade secrets or other confidential information.

We, our Founded Entities or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patents, trade secrets, or other intellectual property as an inventor or co-inventor. For example, we, our Founded Entities or our licensors may have inventorship disputes arising from conflicting obligations of employees, consultants or others who are involved in developing our Wholly Owned Programs or our Founded Entities' therapeutic candidates. Litigation may be necessary to defend against these and other claims challenging inventorship of our, our Founded Entities' or our licensors' ownership of our owned or in-licensed patents, trade secrets or other intellectual property. If we, our Founded Entities or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our Wholly Owned Programs or our Founded Entities' therapeutic candidates. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Any of the foregoing could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects.

Risks Related to the COVID-19 Pandemic

The COVID- 19 pandemic has impacted, and will likely continue to impact, our business, including our clinical trials and preclinical studies, and may materially and adversely affect our business in the future.

Public health crises such as pandemics or other global emergencies could adversely impact our business. In response to the spread of COVID-19 and governmental shelter-in-place orders, we encouraged our administrative employees to work outside of our offices and allowed staff in our laboratory facilities to operate under applicable government orders and protocols designed to protect their health and safety. Many of these restrictions have since been eased or lifted in a phased-in approach over time. However, these government policies and directives are subject to change, including that additional, more restrictive orders, proclamations and/or directives may be issued in the future, as the effects and spread of the COVID-19 pandemic continue to evolve.

As a result of the COVID-19 outbreak or any future pandemics, we have experienced, and may in the future experience, disruptions that severely impact our business, clinical trials and preclinical studies, including:

- delays or difficulties in enrolling patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- delays or disruptions in non-clinical experiments due to unforeseen circumstances at contract research organizations, or CROs, and vendors along their supply chain;
- increased rates of patients withdrawing from our clinical trials following enrollment as a result of contracting COVID-19, being forced to quarantine, or not accepting home health visits;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures (particularly any procedures that may be deemed non-essential), which may impact the integrity of subject data and clinical study endpoints;
- interruption or delays in the operations of the FDA and comparable foreign regulatory agencies, which may impact review and approval timelines;
- interruption of, or delays in receiving, supplies of our therapeutic candidates from our contract manufacturing organizations due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems; and
- limitations on employee resources that would otherwise be focused on the conduct of our preclinical studies and clinical trials, including because of sickness of employees or their families, the desire of employees to avoid contact with large groups of people, an increased reliance on working from home or mass transit disruptions.

These and other factors arising from the COVID-19 pandemic could worsen in countries that are already afflicted with COVID-19, could continue to spread to additional countries, or could return to countries where the pandemic has been partially contained, each of which could further adversely impact our ability to conduct clinical trials and our business generally, and could have a material adverse impact on our operations and financial condition and results.

In addition, the trading prices for biopharmaceutical companies have been highly volatile as a result of the COVID-19 pandemic. As a result, if we require any further capital we may face difficulties raising capital through sales of our common stock or such sales may be on unfavorable terms. The COVID-19 outbreak continues to rapidly evolve. The extent to which the outbreak may impact our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the outbreak, travel restrictions and actions to contain the outbreak or treat its impact, such as social distancing and quarantines or lock-downs in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

To the extent the COVID-19 pandemic adversely affects our business and financial results, it may also have the effect of heightening many of the other risks described in this "Risk Factors" section, such as those relating to our clinical development operations, the supply chain for our ongoing and planned clinical trials, and the availability of governmental and regulatory authorities to conduct inspections of our clinical trial sites, review materials submitted by us in support of our applications for regulatory approval and grant approval for our therapeutic candidates.

We may not be successful in our efforts to develop LYT-100 for the treatment of Long COVID respiratory complications and related sequelae.

We have initiated and fully enrolled a global, randomized, double-blind, placebo-controlled Phase 2 trial designed to evaluate the efficacy, safety and tolerability of LYT-100 in adults with post-acute COVID-19 respiratory complications. The primary endpoint is a standardized test of how far a patient can walk in six minutes. Secondary endpoints, including pharmacokinetics, inflammatory biomarkers, imaging, and patient-reported outcomes will also be evaluated.

Given the rapidity of the onset of the COVID-19 pandemic, scientific and medical research on the SARS-CoV-2 virus is ongoing and evolving. We cannot be certain that the evidence that we believe suggests that LYT-100 may be beneficial to these patients will be established in a clinical trial. The failure of LYT-100 to demonstrate safety and efficacy in these patients could negatively impact the perception of us and LYT-100 by investors and it is possible that unexpected safety issues could occur in these COVID-19 patients. Any such safety issues could affect our development plans for LYT-100 in other indications.

Risks Related to Our Business and Industry

We attempt to distribute our scientific, execution and financing risks across a variety of therapeutic areas, indications, programs and modalities that relate to the brain, immune system and gastrointestinal system and the interface between them. However, our assessment of, and approach to, risk may not be comprehensive or effectively avoid delays or failures in one or more of our programs. Failures in one or more of our programs could adversely impact other programs and have a material adverse impact on our business, results of operations and ability to fund our business.

We are dedicated to discovering, developing and commercializing highly differentiated medicines for devastating diseases, including inflammatory, fibrotic and immunological conditions, intractable cancers, lymphatic and gastrointestinal diseases and neurological and neuropsychological disorders, among others. Across the entire portfolio, we established the underlying programs and platforms that have resulted in 27 therapeutics and therapeutic candidates that are being advanced within our Wholly Owned Programs or by our Founded Entities. Of these therapeutics and therapeutic candidates, 16 are clinical-stage and two have been cleared for marketing by the FDA and granted marketing authorization in the EEA and in other countries that recognize the CE Mark. Our publicly-listed Founded Entities, Karuna, Vor and Gelesis, are advancing seven of these therapeutic candidates, including two that are currently in Phase 3/Pivotal studies, as well as one FDA-authorized therapeutic. Our privately-held Founded Entities, Akili, Vedanta, Follica, Sonde and Entrega, are advancing 13 other therapeutic candidates, including two that are expected to enter a pivotal study. Finally, we are advancing seven therapeutic candidates within our Wholly Owned Pipeline, including one therapeutic candidate that is being advanced in collaboration with a pharmaceutical company, with two Phase 2 and two Phase 1 clinical trials underway. We and our Founded Entities have relationships with several pharmaceutical companies or their investment arms to advance some of the programs and platforms underlying these therapeutics and therapeutic candidates. As our and certain of our Founded Entities' therapeutic candidates progress through clinical development, we or others may determine that certain of our risk allocation decisions were incorrect or insufficient, that individual programs or our science in general has technology or biology risks that were unknown or underappreciated, or that we have allocated resources across our programs in such a way that did not maximize potential value creation. All of these risks may relate to our current and future programs sharing similar science and infrastructure, and in the event material decisions in any of these areas turn out to have been incorrect or under-optimized, we may experience a material adverse impact on our business and ability to fund our operations.

Our business is highly dependent on the clinical advancement of our programs and our success in identifying potential therapeutic candidates across the brain, immune and gastrointestinal therapeutic areas. Delay or failure to advance our programs could adversely impact our business.

We are developing new medicines based on the lymphatic system and the brain, immune and gastrointestinal therapeutic areas. Over time, our and our Founded Entities' preclinical and clinical work led us to identify potential synergies across target therapeutic indications in the brain, immune and gastrointestinal areas, generating a broad portfolio of therapeutic candidates across multiple programs. Even if a particular program is successful in any phase of development, such program could fail at a later phase of development, and other programs within the same therapeutic area may still fail at any phase of development including at phases where earlier programs in that therapeutic area were successful. This may be a result of technical challenges unique to that program or due to biology risk, which is unique to every program. As we progress our programs through clinical development, there may be new technical challenges that arise that cause an entire program or a group of programs within an area of focus in the brain, immune and gastrointestinal therapeutic areas to fail. While we aim to segregate risk across programs, and in certain cases among our Founded Entities, there may be foreseen and unforeseen risks across the therapeutic candidates within our Wholly Owned Pipeline and programs being developed by our Founded Entities in whole or in part. In addition, if any one or more of our clinical programs encounter safety, tolerability, or efficacy problems, developmental delays, regulatory issues, or other problems, our business could be significantly harmed.

Our future success depends on our ability to retain key employees, directors, consultants and advisors and to attract, retain and motivate qualified personnel.

Our ability to compete in the highly competitive biotechnology industry depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on the management, R&D, clinical, financial and business development expertise of our executive officers, our directors, as well as the other members of our scientific and clinical teams, including Daphne Zohar, our chief executive officer, Bharatt Chowrira, our president and chief business, legal and operating officer, George Farmer, our chief financial officer, Eric Elenko, our chief innovation and strategy officer, Joseph Bolen, our chief scientific officer, and Julie Krop, our chief medical officer. The loss of the services of any of our executive officers and other key personnel, and our inability to find suitable replacements could result in delays in therapeutic development and our financial condition and results of operations could be materially adversely affected.

Furthermore, each of our executive officers may terminate their employment with us at any time. Recruiting and retaining qualified scientific and clinical personnel and, if we progress the development of the therapeutic candidates within our Wholly Owned Pipeline toward scaling up for commercialization, sales and marketing personnel, will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval for and commercialize the therapeutic candidates within our Wholly Owned Pipeline. Competition to hire qualified personnel in our industry is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. Furthermore, to the extent we hire personnel from competitors, we may be subject to allegations that they have been improperly solicited or that they have divulged proprietary or other confidential information, or that their former employers own their research output. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions.

In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We will need to expand our organization and we may experience difficulties in managing this growth, which could disrupt our operations.

As we mature, we expect to expand our full-time employee base and to hire more consultants and contractors. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time toward managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional therapeutic candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenues could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize therapeutic candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

Because we are developing multiple programs and therapeutic candidates and are pursuing a variety of target indications and treatment modalities, we may expend our limited resources to pursue a particular therapeutic candidate and fail to capitalize on development opportunities or therapeutic candidates that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and personnel resources, we may forgo or delay pursuit of opportunities with potential target indications or therapeutic candidates that later prove to have greater commercial

potential than our current and planned development programs and therapeutic candidates. Our resource allocation decisions may cause us to fail to capitalize on viable commercial therapeutics or profitable market opportunities. Our spending on current and future research and development programs and other future therapeutic candidates for specific indications may not yield any commercially viable future therapeutic candidates. If we do not accurately evaluate the commercial potential or target market for a particular therapeutic candidate, we may be required to relinquish valuable rights to that therapeutic candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such future therapeutic candidates.

Additionally, we may pursue additional in-licenses or acquisitions of development-stage assets or programs, which entails additional risk to us. For example, in 2019 we acquired LYT-100, which is the most advanced therapeutic candidate in our Wholly Owned Pipeline and to which we are investing significant resources for its development. Identifying, selecting and acquiring promising therapeutic candidates requires substantial technical, financial and human resources expertise. Efforts to do so may not result in the actual acquisition or license of a successful therapeutic candidate, potentially resulting in a diversion of our management's time and the expenditure of our resources with no resulting benefit. For example, if we are unable to identify programs that ultimately result in approved therapeutics, we may spend material amounts of our capital and other resources evaluating, acquiring and developing therapeutics that ultimately do not provide a return on our investment.

Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any therapeutic candidates that we may develop.

We face an inherent risk of product liability exposure related to the testing of therapeutic candidates in human clinical trials and will face an even greater risk if we commercially sell any therapeutics that we may develop. If we cannot successfully defend ourselves against claims that the therapeutic candidates within our Wholly Owned Pipeline or medicines caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any therapeutic candidates or medicines that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize the therapeutic candidates within our Wholly Owned Pipeline.

Although we maintain product liability insurance, including coverage for clinical trials that we sponsor, it may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage as we commence additional clinical trials and if we successfully commercialize any therapeutic candidates. The market for insurance coverage is increasingly expensive, and the costs of insurance coverage will increase as our clinical programs increase in size. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

The increasing use of social media platforms presents new risks and challenges.

Social media is increasingly being used to communicate about our and our Founded Entities' clinical development programs and the diseases our therapeutics are being developed to treat, and we intend to utilize appropriate social media in connection with our commercialization efforts following approval of the therapeutic candidates within our Wholly Owned Pipeline. Social media practices in the biopharmaceutical industry continue to evolve and regulations relating to such use are not always clear. This evolution creates uncertainty and risk of noncompliance with regulations applicable to our business. For example, patients may use social media channels to comment on their experience in an ongoing blinded clinical study or to report an alleged adverse event. When such disclosures occur, there is a risk that we fail to monitor and comply with applicable adverse event reporting obligations or we may not be able to defend our business or the public's legitimate interests in the face of the political and market pressures generated by social media due to restrictions on what we may say about the therapeutic candidates within our Wholly Owned Pipeline. There is also a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us on any social networking website. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face regulatory actions or incur other harm to our business.

Our and our Founded Entities' employees, independent contractors, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of fraud, misconduct or other illegal activity by our employees, independent contractors, consultants, commercial partners and vendors as well as the employees, independent contractors, consultants, commercial partners and vendors of our Founded Entities. Misconduct by these parties could include intentional, reckless and negligent conduct that fails to: comply with the laws of the FDA and comparable foreign regulatory authorities; provide true, complete and accurate information to the FDA and comparable foreign regulatory authorities; comply with manufacturing standards we have established; comply with healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws; or report financial information or data accurately or to disclose unauthorized activities. If we or our Founded Entities obtain FDA approval of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates and begin commercializing those therapeutics in the United States, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. In particular, research, sales, marketing, education and other business arrangements in the healthcare industry are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, educating, marketing and promotion, sales and commission, certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

Employee litigation and unfavorable publicity could negatively affect our future business.

Our employees may, from time to time, bring lawsuits against us regarding injury, creating a hostile work place, discrimination, wage and hour disputes, sexual harassment, or other employment issues. In recent years, there has been an increase in the number of discrimination and harassment claims generally. Coupled with the expansion of social media platforms and similar devices that allow individuals access to a broad audience, these claims have had a significant negative impact on some businesses. Certain companies that have faced employment- or harassment-related lawsuits have had to terminate management or other key personnel, and have suffered reputational harm that has negatively impacted their business. If we were to face any employment-related claims, our business could be negatively affected.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste therapeutics. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research,

development or therapeutic efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Cyber-attacks or other failures in our telecommunications or information technology systems, or those of our collaborators, contract research organizations, third-party logistics providers, distributors or other contractors or consultants, could result in information theft, data corruption and significant disruption of our business operations.

We, our collaborators, our CROs, third-party logistics providers, distributors and other contractors and consultants utilize information technology, or IT, systems and networks to process, transmit and store electronic information in connection with our business activities. As use of digital technologies has increased, cyber incidents, including third parties gaining access to employee accounts using stolen or inferred credentials, computer malware, viruses, spamming, phishing attacks or other means, and deliberate attacks and attempts to gain unauthorized access to computer systems and networks, have increased in frequency and sophistication. These threats pose a risk to the security of our, our collaborators', our CROs', third-party logistics providers', distributors' and other contractors' and consultants' systems and networks, and the confidentiality, availability and integrity of our data. There can be no assurance that we will be successful in preventing cyber-attacks or successfully mitigating their effects. Similarly, there can be no assurance that our collaborators, CROs, third-party logistics providers, distributors and other contractors and consultants will be successful in protecting our clinical and other data that is stored on their systems. Although to our knowledge we have not experienced any such material system failure or material security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of development programs and business operations.

Any cyber-attack, data breach or destruction or loss of data could result in a violation of applicable U.S. and international privacy, data protection and other laws, and subject us to litigation and governmental investigations and proceedings by federal, state and local regulatory entities in the United States and by international regulatory entities, resulting in exposure to material civil and/or criminal liability. Further, our general liability insurance and corporate risk program may not cover all potential claims to which we are exposed and may not be adequate to indemnify us for all liability that maybe imposed; and could have a material adverse effect on our business and prospects. For example, the loss of clinical trial data from completed or ongoing clinical trials for any of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates could result in delays in our development and regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, we may suffer reputational harm or face litigation or adverse regulatory action as a result of cyber-attacks or other data security breaches and may incur significant additional expense to implement further data protection measures.

Changes in funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new therapeutics and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new therapeutics or take action with respect to other regulatory matters can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept payment of user fees, and statutory, regulatory, and policy changes. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. The priorities of the FDA may also influence the ability of the FDA to take action on regulatory matters, for example the FDA's budget and funding levels and ability to hire and retain key personnel.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved, or for other actions to be taken, by relevant government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Similarly, a prolonged government shutdown could prevent the timely review of our patent applications by the USPTO, which could delay the issuance of any U.S. patents to which we might otherwise be entitled. Further, in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Separately, foreign and domestic inspections by the FDA were largely on hold during the COVID-19 pandemic. Should the FDA determine that an inspection is necessary for approval of a marketing application and an inspection cannot be completed during the review cycle due to restrictions on travel or for other reasons, the FDA has stated that it generally intends to issue a complete response letter. Further, if there is inadequate information to make a determination on the acceptability of a facility, the FDA may defer action on the application until an inspection can be completed. For example, in 2020, several companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic or for other reasons and may experience delays in their regulatory activities. If a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Future shutdowns or other disruptions could also affect other government agencies such as the SEC, which may also impact our business by delaying review of our public filings, to the extent such review is necessary, and our ability to access the public markets.

We or the third parties upon whom we depend may be adversely affected by a natural disaster and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our third-party CMOs, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, could have a material adverse effect on our business, financial condition, results of operations and prospects.

We will continue to incur increased costs as a result of operating as a U.S.-listed public company, and our management will be required to devote substantial time to new compliance initiatives.

As a U.S. public company, and particularly now that we are no longer an emerging growth company, we have incurred and will continue to incur significant legal, accounting and other expenses that we did not incur as a public company listed on the LSE. In addition, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and rules subsequently implemented by the SEC and Nasdaq have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance.

Pursuant to Section 404, we are required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404, we have and continue to be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk we will not be able to conclude that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Risks Related to Our International Operations

As a company based in the United Kingdom, we are subject to economic, political, regulatory and other risks associated with international operations.

As a company based in the United Kingdom, our business is subject to risks associated with being organized outside of the United States. While the majority of our operations are in the United States and our functional

currency is the U.S. dollar, our future results could be harmed by a variety of international factors, including:

- economic weakness, including inflation, or political instability in particular non-U.S. economies and markets;
- differing and changing regulatory requirements;
- difficulties in compliance with different, complex and changing laws, regulations and court systems of multiple jurisdictions and compliance with a wide variety of foreign laws, treaties and regulations;
- changes in a specific country's or region's political or economic environment, including, but not limited to, the implications of one or more of the following occurring the decision of the United Kingdom:
- future activities subject to the terms of the Trade and Cooperation Agreement between the United Kingdom and the European Union effective May 1, 2021, which has not impacted our results to-date;
- a second referendum on Scottish independence from the United Kingdom; and/or
- a snap general election; and
- negative consequences from changes in tax laws.

Unfavorable global economic conditions, including conditions resulting from the COVID-19 pandemic, could adversely affect our business, financial condition or results of operations.

Our ability to invest in and expand our business and meet our financial obligations, to attract and retain third-party contractors and collaboration partners and to raise additional capital depends on our operating and financial performance, which, in turn, is subject to numerous factors, including the prevailing economic and political conditions and financial, business and other factors beyond our control, such as the rate of unemployment, the number of uninsured persons in the United States, political influences and inflationary pressures. For example, an overall decrease in or loss of insurance coverage among individuals in the United States as a result of unemployment, underemployment or the repeal of certain provisions of the ACA, may decrease the demand for healthcare services and pharmaceuticals. If fewer patients are seeking medical care because they do not have insurance coverage, we and our Founded Entities may experience difficulties in any eventual commercialization of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates and our business, results of operations, financial condition and cash flows could be adversely affected.

In addition, our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets upon which pharmaceutical and biopharmaceutical companies such as us are dependent for sources of capital. In the past, global financial crises have caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn could result in a variety of risks to our business, including a reduced ability to raise additional capital when needed on acceptable terms, if at all, and weakened demand for the therapeutic candidates within our Wholly Owned Pipeline. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

The COVID-19 pandemic has had, and will continue to have, an unfavorable impact on global economic conditions, including a decrease in or loss of insurance coverage among individuals in the United States, an increase in unemployment, volatility in markets, and other negative impacts that have arisen or will arise over the course of the COVID-19 pandemic.

Our international operations may expose us to business, regulatory, political, operational, financial, pricing and reimbursement and economic risks associated with doing business outside of the United States.

Our business strategy incorporates potential international expansion to target patient populations outside the United States. If we or our Founded Entities receive regulatory approval for and commercialize any of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates in patient populations outside the United States, we may hire sales representatives and conduct physician and patient association outreach activities outside of the United States. Doing business internationally involves a number of risks, including, but not limited to:

- multiple, conflicting, and changing laws and regulations such as privacy regulations, tax laws, export and import restrictions, employment laws, regulatory requirements, and other governmental approvals, permits, and licenses;
- failure by us to obtain and maintain regulatory approvals for the use of our therapeutics in various countries;
- additional potentially relevant third-party patent rights;
- complexities and difficulties in obtaining protection and enforcing our intellectual property;
- difficulties in staffing and managing foreign operations;
- complexities associated with managing multiple payor reimbursement regimes, government payors, or patient self-pay systems;
- limits in our ability to penetrate international markets;
- financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our therapeutics, and exposure to foreign currency exchange rate fluctuations;
- natural disasters, political and economic instability, including wars, such as the developing conflict between Russia and Ukraine, terrorism, and political unrest, outbreak of disease, boycotts, curtailment of trade, and other business restrictions;
- certain expenses including, among others, expenses for travel, translation, and insurance; and
- regulatory and compliance risks that relate to maintaining accurate information and control over sales and activities that may fall within the purview of the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, its books and records provisions, or its anti-bribery provisions.

Any of these factors could significantly harm our potential international expansion and operations and, consequently, our results of operations.

European data collection is governed by restrictive regulations governing the use, processing and cross-border transfer of personal information.

In the event we decide to conduct clinical trials or continue to enroll subjects in our ongoing or future clinical trials in the European Union, we may be subject to additional privacy restrictions. The collection and use of personal health data in the European Union is governed by the provisions of the General Data Protection Regulation (EU) 2016/679, or GDPR. This directive imposes several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, notification of data processing obligations to the competent national data protection authorities and the security and confidentiality of the personal data. The GDPR also imposes strict rules on the transfer of personal data out of the European Union to the United States. Failure to comply with the requirements of the Data Protection Directive, which governs the collection and use of personal health data in the European Union, the GDPR, and the related national data protection laws of the European Union Member States may result in fines and other administrative penalties. The GDPR introduced new data protection requirements in the European Union and substantial fines for breaches of the data protection rules. The GDPR regulations may impose additional responsibility and liability in relation to personal data that we process and we may be required to put in place additional mechanisms ensuring compliance with these and/or new data protection rules. This may be onerous and adversely affect our business, financial condition, prospects and results of operations.

We are subject to the U.K. Bribery Act 2010, or the Bribery Act, the U.S. Foreign Corrupt Practices Act of 1977 (as amended) ("FCPA") and other anti-corruption laws, as well as export control laws, import and customs laws, trade and economic sanctions laws and other laws governing our operations.

Our operations are subject to anti-corruption laws, including the Bribery Act, the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. §201, the U.S. Travel Act, and other anti-corruption laws that apply in countries where we do business. These laws generally prohibit us and our employees and intermediaries acting on our behalf from corruptly authorizing, promising, offering, or providing, directly or indirectly, anything else of value, to government officials or other persons to obtain or retain business or gain some other business advantage. The Bribery Act also prohibits: (i) "commercial" bribery of private parties, in addition to bribery involving domestic or foreign officials; (ii) the acceptance of bribes, as well as the giving of bribes, and (iii) "facilitation payments", meaning generally low level payments designed to secure or expedite routine governmental actions or other conduct to which persons are already under obligations to perform. The Bribery Act also creates an offence applicable corporate entities for failure to prevent bribery by our employees, officers, directors and other third parties acting on our behalf, to which the only defence is to maintain "adequate procedures" designed to prevent such acts of bribery.

In the future, we and our strategic partners may operate in jurisdictions that pose a heightened risk of potential Bribery Act or FCPA violations, and we may participate in collaborations and relationships with third parties whose conduct could potentially subject us to liability under the Bribery Act, FCPA or other anti-corruption laws, even if we do not explicitly authorize or have actual knowledge of such activities. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the

governments of the United Kingdom and the United States, and authorities in the European Union and its member states, including applicable export control regulations, economic sanctions and embargoes on certain countries, regions, and persons, import and customs requirements and currency exchange regulations, collectively referred to as the Trade Control laws. Compliance with Trade Control Laws regarding the import and export of our products may create delays in the introduction of our products in international markets, and, in some cases, prevent the export of our products to some countries altogether.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the Bribery Act, the FCPA or other legal requirements, including Trade Control laws. If we are not in compliance with the Bribery Act, the FCPA and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement, debarment from debarment from government contracts as well as other sanctions and remedial measures, and may also result in collateral litigation. These consequences could have an adverse impact on our business, financial condition, results of operations and liquidity. Likewise, any investigation of any potential violations of the Bribery Act, the FCPA, other anti-corruption laws or Trade Control laws by United Kingdom, United States or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition. In addition, responding to any enforcement action may result in a significant diversion of management's attention and resources and significant defense costs and other professional fees.

The United Kingdom's withdrawal from the European Union may have a negative effect on global economic conditions, financial markets and our business, which could reduce the price of our ADSs.

On June 23, 2016, the United Kingdom held a referendum in which a majority of the eligible members of the electorate voted for the United Kingdom to leave the European Union. The United Kingdom's withdrawal from the European Union is commonly referred to as Brexit. In October 2019, a withdrawal agreement, or the Withdrawal Agreement, setting out the terms of the United Kingdom's exit from the European Union, and a political declaration on the framework for the future relationship between the United Kingdom and European Union was agreed between the UK and EU governments. Under the terms of the EU Withdrawal Agreement, the United Kingdom withdrew from membership of the European Union on 31 January 2020 and entered into a 'transition period', or the Transition Period, during which the majority of rights and obligations associated with membership of the European Union continued to apply to the United Kingdom; however, this expired on December 31, 2020. The United Kingdom and the European Union have signed a EU-UK Trade and Cooperation Agreement, which became provisionally applicable on January 1, 2021 and formally applicable effective May 1, 2021. This agreement provides details on how some aspects of the United Kingdom and European Union's relationship will operate going forwards however there are still many uncertainties.

These developments have had and may continue to have a significant adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. In particular, it could also lead to a period of considerable uncertainty in relation to the UK financial and banking markets. As a result of this uncertainty, global financial markets could experience significant volatility, which could adversely affect the market price of our ADSs. Asset valuations, currency exchange rates and credit ratings may also be subject to increased market volatility.

We may also face new regulatory costs and challenges that could have an adverse effect on our operations. The United Kingdom will lose the benefits of global trade agreements negotiated by the European Union on behalf of its members, which may result in increased trade barriers that could make our doing business in Europe more difficult. In addition, currency exchange rates in the pound sterling and the euro with respect to each other and the U.S. dollar have already been adversely affected by Brexit. Furthermore, now that the Transition Period has expired, Great Britain will no longer be covered by the centralized procedure for obtaining EEA-wide marketing authorization from the EMA and a separate process for authorization of drug therapeutics, including the therapeutic candidates within our Wholly Owned Pipeline, will be required in Great Britain, resulting in an authorization covering the United Kingdom or Great Britain only. For a period of two years from January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA (the UK medicines and medical devices regulator) may rely on a decision taken by the European Commission on the approval of a new marketing authorization in the centralized procedure, in order to more quickly grant a Great Britain marketing authorization. A separate application will, however, still be required. The MHRA has published a series of guidance notes on how the process for authorization of medicines will now work, however exactly what implications this will have in practice remain unclear.

Risks Related to Our Equity Securities and ADSs

The market price of our ADSs has been and will likely continue to be highly volatile, and you could lose all or part of your investment.

The market price of our ADSs has been and will likely continue to be volatile. The stock market in general, and the market for biopharmaceutical companies in particular, has experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your ADSs at or above the purchase price. The market price for our ADSs may be influenced by many factors, including:

- adverse results or delays in our preclinical studies or clinical trials;
- reports of AEs or other negative results in clinical trials of third parties' therapeutic candidates that target the therapeutic candidates within our Wholly Owned Pipeline's or our Founded Entities' therapeutic candidates' target indications;
- an inability for us to obtain additional funding on reasonable terms or at all;
- any delay in submitting an IND, BLA or NDA for the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates and any adverse development or perceived adverse development with respect to the FDA's review of that IND, BLA or NDA;
- failure to develop successfully and commercialize the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates;
- announcements we make regarding our current therapeutic candidates, acquisition of potential new therapeutic candidates and companies and/or in-licensing;
- failure to maintain our or our Founded Entities' existing license arrangements or enter into new licensing and collaboration agreements;
- failure by us, our Founded Entities or our licensors to prosecute, maintain or enforce our intellectual property rights;
- changes in laws or regulations applicable to future therapeutics;
- inability to obtain adequate clinical or commercial supply for the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates or the inability to do so at acceptable prices;
- adverse regulatory decisions, including failure to reach agreement with applicable regulatory authorities on the design or scope of our planned clinical trials;
- failure to obtain and maintain regulatory exclusivity for the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates;
- regulatory approval or commercialization of new therapeutics or other methods of treating our target disease indications by our competitors;
- failure to meet or exceed financial projections we may provide to the public or to the investment community;
- publication of research reports or comments by securities or industry analysts;
- the perception of the pharmaceutical and biotechnology industries by the public, legislatures, regulators and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us, our Founded Entities our strategic collaboration partners or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our or our Founded Entities' ability to obtain patent protection for our technologies;
- additions or departures of our key scientific or management personnel;
- significant lawsuits, including patent or shareholder litigation, against us;
- changes in the market valuations of similar companies;
- adverse developments relating to any of the above or additional factors with respect to our Founded Entities;
- sales or potential sales of substantial amounts of our ADSs; and
- trading volume of our ADSs.

In addition, companies trading in the stock market in general, and Nasdaq, in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our ADSs, regardless of our actual operating performance. Since our ADSs were initially sold in November 2020 at a price of $33.00 per ADS, our ADS price has fluctuated significantly, ranging from an intraday low of $21.95 to an intraday high of $63.95 for the period beginning November 16, 2020, our first day of trading on The Nasdaq Global Market, through March 31, 2022. If the market price of our ADSs does not exceed the price at which you acquired them, you may not

realize any return on your investment in us and may lose some or all of your investment.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our ADS price and trading volume could decline.

The trading market for our ADSs and ordinary shares depends in part on the research and reports that securities or industry analysts publish about us or our business. If no or few securities or industry analysts cover our company, the trading price for our ADSs and ordinary shares would be negatively impacted. If one or more of the analysts who covers us downgrades our equity securities or publishes incorrect or unfavorable research about our business, the price of our ordinary shares and ADSs would likely decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, or downgrades our securities, demand for our ordinary shares and ADSs could decrease, which could cause the price of our ordinary shares and ADSs or their trading volume to decline.

Future sales, or the possibility of future sales, of a substantial number of our securities could adversely affect the price of the shares and dilute shareholders.

Sales of a substantial number of our ADSs in the public market could occur at any time, subject to certain restrictions described below. If our existing shareholders sell, or indicate an intent to sell, substantial amounts of our securities in the public market, the trading price of the ADSs could decline significantly and could decline below the original purchase price. As of March 31, 2022, we had 287,841,508 outstanding ordinary shares. Ordinary shares subject to outstanding options under our equity incentive plans and the ordinary shares reserved for future issuance under our equity incentive plans will become eligible for sale in the public market in the future, subject to certain legal and contractual limitations.

Holders of ADSs are not treated as holders of our ordinary shares.

If you purchase an ADS, you will become a holder of ADSs with underlying ordinary shares in a company incorporated under English law. Holders of ADSs are not treated as holders of our ordinary shares, unless they withdraw the ordinary shares underlying their ADSs in accordance with the deposit agreement and applicable laws and regulations. The depositary is the holder of the ordinary shares underlying the ADSs. Holders of ADSs therefore do not have any rights as holders of our ordinary shares, other than the rights that they have pursuant to the deposit agreement. See "Description of Securities Other Than Equity Securities" in our Annual Report on Form 20-F.

Holders of ADSs may be subject to limitations on the transfer of their ADSs and the withdrawal of the underlying ordinary shares.

ADSs are transferable on the books of the depositary. However, the depositary may close its books at any time or from time to time when it deems expedient in connection with the performance of its duties. The depositary may refuse to deliver, transfer or register transfers of ADSs generally when our books or the books of the depositary are closed, or at any time if we or the depositary think it is advisable to do so because of any requirement of law, government or governmental body, or under any provision of the deposit agreement, or for any other reason, subject to the right of ADS holders to cancel their ADSs and withdraw the underlying ordinary shares. Temporary delays in the cancellation of your ADSs and withdrawal of the underlying ordinary shares may arise because the depositary has closed its transfer books or we have closed our transfer books, the transfer of ordinary shares is blocked to permit voting at a shareholders' meeting or we are paying a dividend on our ordinary shares. In addition, ADS holders may not be able to cancel their ADSs and withdraw the underlying ordinary shares when they owe money for fees, taxes and similar charges and when it is necessary to prohibit withdrawals in order to comply with any laws or governmental regulations that apply to ADSs or to the withdrawal of ordinary shares or other deposited securities. See "Description of Securities Other Than Equity Securities" in our Annual Report on Form 20-F.

ADS holders may not be entitled to a jury trial with respect to claims arising under the deposit agreement, which could result in less favorable outcomes to the plaintiff(s) in any such action.

The deposit agreement governing the ADSs representing our ordinary shares provides that, to the fullest extent permitted by law, holders and beneficial owners of ADSs irrevocably waive the right to a jury trial of any claim they may have against us or the depositary arising out of or relating to the ADSs or the deposit agreement.

If this jury trial waiver provision is not permitted by applicable law, an action could proceed under the terms of the deposit agreement with a jury trial. If we or the depositary opposed a jury trial demand based on the waiver, the court would determine whether the waiver was enforceable based on the facts and circumstances of that case in accordance with the applicable state and federal law. To our knowledge, the enforceability of a contractual pre-dispute jury trial waiver in connection with claims arising under the federal securities laws has not been finally adjudicated by the U.S. Supreme Court. However, we believe that a contractual pre-dispute jury trial waiver provision is generally enforceable, including under the laws of the State of New York, which govern the deposit agreement, by a federal or state court in the City of New York, which has non-exclusive jurisdiction over matters arising under the deposit agreement. In determining whether to enforce a contractual pre-dispute jury trial waiver provision, courts will generally consider whether a party knowingly, intelligently and voluntarily waived the right to a jury trial. We believe that this is the case with respect to the deposit agreement and the ADSs. It is advisable that you consult legal counsel regarding the jury waiver provision before entering into the deposit agreement.

If you or any other holders or beneficial owners of ADSs bring a claim against us or the depositary in connection with matters arising under the deposit agreement or the ADSs, including claims under federal securities laws, you or such other holder or beneficial owner may not be entitled to a jury trial with respect to such claims, which may have the effect of limiting and discouraging lawsuits against us and/or the depositary. If a lawsuit is brought against us and/or the depositary under the deposit agreement, it may be heard only by a judge or justice of the applicable trial court, which would be conducted according to different civil procedures and may result in different outcomes than a trial by jury would have had, including results that could be less favorable to the plaintiff(s) in any such action, depending on, among other things, the nature of the claims, the judge or justice hearing such claims, and the venue of the hearing.

No condition, stipulation or provision of the deposit agreement or ADSs serves as a waiver by any holder or beneficial owner of ADSs or by us or the depositary of compliance with the U.S. federal securities laws and the rules and regulations promulgated thereunder.

One of our principal shareholders has a significant holding in the company which may give them influence in certain matters requiring approval by shareholders, including approval of significant corporate transactions in certain circumstances.

As of February 16, 2022, Invesco Asset Management Limited, or Invesco, held approximately 22.5 percent of our ordinary shares. Accordingly, Invesco may, as a practical matter, be able to influence certain matters requiring approval by shareholders, including approval of significant corporate transactions in certain circumstances. Such concentration of ownership may also have the effect of delaying or preventing any future proposed change in control of the Company. The trading price of the ordinary shares could be adversely affected if potential new investors are disinclined to invest in the Company because they perceive disadvantages to a large shareholding being concentrated in the hands of a single shareholder. The interests of Invesco and the investors that acquire ADSs may not be aligned. Invesco may make acquisitions of, or investments in, other businesses in the same sectors as us or our Founded Entities. These businesses may be, or may become, competitors of us or our Founded Entities. In addition, funds or other entities managed or advised by Invesco may be in direct competition with us or our Founded Entities on potential acquisitions of, or investments in, certain businesses. In addition, Invesco holds equity interests in certain of our Founded Entities where they may exert direct influence.

You will not have the same voting rights as the holders of our ordinary shares and may not receive voting materials in time to be able to exercise your right to vote.

Except as described in our Annual Report on Form 20-F and the deposit agreement, holders of the ADSs will not be able to exercise voting rights attaching to the ordinary shares represented by the ADSs. Under the terms of the deposit agreement, holders of the ADSs may instruct the depositary to vote the ordinary shares underlying their ADSs. Otherwise, holders of ADSs will not be able to exercise their right to vote unless they withdraw the ordinary shares underlying their ADSs to vote them in person or by proxy in accordance with applicable laws and regulations and our Articles of Association. Even so, ADS holders may not know about a meeting far enough in advance to withdraw those ordinary shares. If we ask for the instructions of holders of the ADSs, the depositary, upon timely notice from us, will notify ADS holders of the upcoming vote and arrange to deliver our voting materials to them. Upon our request, the depositary will mail to holders a shareholder meeting notice that contains, among other things, a statement as to the manner in which voting instructions may be given. We cannot guarantee that ADS holders will receive the voting materials in time to ensure that they can instruct the depositary to vote the ordinary shares underlying their ADSs. A shareholder is only entitled to participate in, and vote at, the meeting of shareholders, provided that it holds our ordinary shares as of the record date set for such meeting and otherwise complies with our Articles of Association. In addition, the depositary's liability to ADS holders for failing to execute voting instructions or for the manner

of executing voting instructions is limited by the deposit agreement. As a result, holders of ADSs may not be able to exercise their right to give voting instructions or to vote in person or by proxy and they may not have any recourse against the depositary or us if their ordinary shares are not voted as they have requested or if their shares cannot be voted.

You may not receive distributions on our ordinary shares represented by the ADSs or any value for them if it is illegal or impractical to make them available to holders of ADSs.

The depositary for the ADSs has agreed to pay to you any cash dividends or other distributions it or the custodian receives on our ordinary shares or other deposited securities after deducting its fees and expenses. You will receive these distributions in proportion to the number of our ordinary shares your ADSs represent. However, in accordance with the limitations set forth in the deposit agreement, it may be unlawful or impractical to make a distribution available to holders of ADSs. We have no obligation to take any other action to permit distribution on the ADSs, ordinary shares, rights or anything else to holders of the ADSs. This means that you may not receive the distributions we make on our ordinary shares or any value from them if it is unlawful or impractical to make them available to you. These restrictions may have an adverse effect on the value of your ADSs.

Because we do not have immediate plans to pay any cash dividends on our ADSs, capital appreciation, if any, may be your sole source of gains and you may never receive a return on your investment.

Under current English law, a company's accumulated realized profits must exceed its accumulated realized losses (on a non-consolidated basis) before dividends can be declared and paid. Therefore, we must have sufficient distributable profits before declaring and paying a dividend. We have not paid dividends in the past on our ordinary shares. We have not announced any immediate plans to pay any cash dividends. As a result, capital appreciation, if any, on our ADSs will be your sole source of gains for the foreseeable future, and you would suffer a loss on your investment if you were unable to sell your ADSs at or above the price that you initially paid for them. Investors seeking cash dividends should not purchase our ADSs.

Risks Related to Our Corporate Status

We are no longer an "emerging growth company" and, as a result, are subject to certain enhanced disclosure requirements.

Because the market value of our equity securities held by non-affiliates exceeded $700.0 million as of June 30, 2021, among other things, we no longer qualified as an emerging growth company as of December 31, 2021. As a result, we are subject to certain requirements that apply to other public companies but did not previously apply to us due to our status as an emerging growth company, such as the auditor attestation requirements under Section 404 of the Sarbanes Oxley Act. Compliance with these enhanced disclosure requirements will increase our costs and could negatively affect our results of operations and financial condition.

We are not, and do not intend to become, regulated as an "investment company" under the Investment Company Act of 1940, as amended, or the 1940 Act and if we were deemed an "investment company" under the 1940 Act, applicable restrictions could make it impractical for us to continue our business as contemplated and could have a material adverse effect on our business.

The 1940 Act and the rules thereunder contain detailed parameters for the organization and operation of investment companies. Among other things, the 1940 Act and the rules thereunder limit or prohibit transactions with affiliates, impose limitations on the issuance of debt and equity securities and impose certain governance requirements. We have not been and do not intend to become regulated as an investment company, and we intend to conduct our activities so that we will not be deemed to be an investment company under the 1940 Act. In order to ensure that we are not deemed to be an investment company, we may be limited in the assets that we may continue to own and, further, may need to dispose of or acquire certain assets at such times or on such terms as may be less favorable to us than in the absence of such requirement. If anything were to happen which would cause us to be deemed to be an investment company under the 1940 Act (such as significant changes in the value of our Founded Entities or a change in circumstance that results in a reclassification of our interests in our Founded Entities for purposes of the 1940 Act), the requirements imposed by the 1940 Act could make it impractical for us to continue our business as currently conducted, which would materially adversely affect our business, results of operations and financial condition. In addition, if we were to become inadvertently subject to the 1940 Act, any violation of the 1940 Act could subject us to material adverse consequences, including potentially significant regulatory penalties and the possibility that certain of our contracts could be deemed unenforceable.

As a foreign private issuer, we are exempt from a number of rules under the U.S. securities laws and are permitted to file less information with the SEC than a U.S. company. This may limit the information available to holders of ADSs or our ordinary shares.

We are a "foreign private issuer," as defined in the SEC's rules and regulations and, consequently, we are not subject to all of the disclosure requirements applicable to public companies organized within the United States. For example, we are exempt from certain rules under the Exchange Act, that regulate disclosure obligations and procedural requirements related to the solicitation of proxies, consents or authorizations applicable to a security registered under the Exchange Act, including the U.S. proxy rules under Section 14 of the Exchange Act. In addition, our officers and directors are exempt from the reporting and "short-swing" profit recovery provisions of Section 16 of the Exchange Act and related rules with respect to their purchases and sales of our securities. Moreover, while we currently make annual and semi-annual filings with respect to our listing on the LSE, we will not be required to file periodic reports and financial statements with the SEC as frequently or as promptly as U.S. domestic issuers and will not be required to file quarterly reports on Form 10-Q or current reports on Form 8-K under the Exchange Act. Accordingly, there will be less publicly available information concerning our company than there would be if we were not a foreign private issuer.

As a foreign private issuer, we are permitted to adopt certain home country practices in relation to corporate governance matters that differ significantly from Nasdaq corporate governance listing standards. These practices may afford less protection to shareholders than they would enjoy if we complied fully with corporate governance listing standards.

As a foreign private issuer listed on Nasdaq, we are subject to corporate governance listing standards. However, rules permit a foreign private issuer like us to follow the corporate governance practices of its home country. Certain corporate governance practices in the United Kingdom, which is our home country, may differ significantly from corporate governance listing standards. For example, neither the corporate laws of the United Kingdom nor our articles of association require a majority of our directors to be independent and we could include non-independent directors as members of our nomination and remuneration committee, though a majority is required, and our independent directors would not necessarily hold regularly scheduled meetings at which only independent directors are present. Currently, we follow home country practice to the maximum extent possible. Therefore, our shareholders may be afforded less protection than they otherwise would have under corporate governance listing standards applicable to U.S. domestic issuers. See "Governance" of this Annual Report and Accounts and "Item 16G—Corporate Governance" of our Annual Report on Form 20-F.

We may lose our foreign private issuer status in the future, which could result in significant additional cost and expense.

While we currently qualify as a foreign private issuer, the determination of foreign private issuer status is made annually on the last business day of an issuer's most recently completed second fiscal quarter and, accordingly, the next determination will be made with respect to us on June 30, 2022.

In the future, we would lose our foreign private issuer status if we to fail to meet the requirements necessary to maintain our foreign private issuer status as of the relevant determination date. For example, if more than 50 percent of our securities are held by U.S. residents and more than 50 percent of the members of our executive committee or members of our board of directors are residents or citizens of the United States, we could lose our foreign private issuer status.

The regulatory and compliance costs to us under U.S. securities laws as a U.S. domestic issuer may be significantly more than costs we incur as a foreign private issuer. If we are not a foreign private issuer, we will be required to file periodic reports and registration statements on U.S. domestic issuer forms with the SEC, which are more detailed and extensive in certain respects than the forms available to a foreign private issuer. We would be required under current SEC rules to prepare our financial statements in accordance with U.S. GAAP, rather than IFRS, and modify certain of our policies to comply with corporate governance practices associated with U.S. domestic issuers. Such conversion of our financial statements to U.S. GAAP will involve significant time and cost. In addition, we may lose our ability to rely upon exemptions from certain corporate governance requirements on U.S. stock exchanges that are available to foreign private issuers such as the ones described above and exemptions from procedural requirements related to the solicitation of proxies.

Risks Related to Our Internal Controls

We have identified a material weakness in our internal control over financial reporting in connection with the audit of our consolidated financial statements in accordance with the standards of the PCAOB and U.S. securities laws. If we fail to implement and maintain effective internal control over financial reporting, we may be unable to accurately report our results of operations, meet our reporting obligations or prevent fraud.

Section 404 of the Sarbanes-Oxley Act requires that our management assess our internal control over financial reporting and that we include a report of management on our internal control over financial reporting in our annual reports on Form 20-F. As disclosed in more detail under Item 15 "Controls and Procedures" of this Report, we have concluded that our internal control over financial reporting was ineffective as of December 31, 2021 due to a material weakness that was unremediated as of December 31, 2021 and is described in Item 15.

A material weakness is a deficiency, or combination of control deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the annual or interim financial statements will not be prevented or detected on a timely basis. The material weakness relates to our risk assessment process over the design and implementation of our management review controls over the valuation of financial instruments, the completeness and accuracy of related sensitivity disclosures, the valuation of share based payment liabilities and completeness and the accuracy of the tax provision. There was insufficient precision in and documentation of the performance of such review controls resulting in controls not being designed in a way to sufficiently address the level of aggregation and criteria for investigation. Additionally, management did not completely identify the information used in the control and did not design sufficient controls to address the relevance and reliability of such information. We concluded that a similar material weakness existed as of December 31, 2020, and this material weakness continued to exist at December 31, 2021. We intend to take further steps to implement our remediation plan, including the implementation of more robust procedures to identify and document relevant risks at an appropriately disaggregated level and more detailed management review controls to mitigate such risks. While we expect to continue to implement our remediation plan through 2022, we cannot be certain as to when remediation will be fully completed. As with any internal control framework, we cannot be certain that these efforts will be sufficient to remediate our material weakness or prevent future material weaknesses or significant deficiencies from occurring in the future. If we are unable to successfully remediate our existing or any future material weaknesses in our internal control over financial reporting, or if we identify any additional material weaknesses, the accuracy and timing of our financial reporting may be adversely affected.

Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement or maintain these controls, or difficulties encountered in their implementation, could cause us to fail to meet our reporting obligations. In addition, any testing by us or by our independent registered public accounting firm may reveal additional deficiencies in our internal control over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement.

If we fail to achieve and maintain effective internal control over financial reporting, we could suffer material misstatements in our financial statements and fail to meet our reporting obligations, which could cause investors to lose confidence in our reported financial information. This could in turn limit our access to capital markets or lead to a decline in the trading price of our securities. We may also be required to restate our financial statements from prior periods. Additionally, ineffective internal control over financial reporting could expose us to increased risk of fraud or misuse of corporate assets and subject us to potential delisting from the stock exchange on which we list, regulatory investigations, litigation from shareholders and civil or criminal sanctions, which could have a material adverse effect on our business.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to certain reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosures due to error or fraud may occur and not be detected.

Risks Related to Tax Matters

Comprehensive tax reform legislation could adversely affect our business and financial condition.

The rules dealing with U.S. federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. For example, on December 22, 2017, the Tax Act was signed into law and enacted many significant changes to U.S. tax laws. Future guidance from the Internal Revenue Service and other tax authorities with respect to the Tax Act may affect us, and certain aspects of the Tax Act could be repealed or modified in future legislation. For example, on March 27, 2020, the "Coronavirus Aid, Relief, and Economic Security Act" or the CARES Act was signed into law, which modified certain provisions of the Tax Act and included certain changes in tax law intended to stimulate the U.S. economy in light of the COVID-19 coronavirus outbreak, including temporary beneficial changes to the treatment of net operating losses, interest deductibility limitations and payroll tax matters. It is uncertain if and to what extent various states will conform to the newly enacted federal tax law. We will continue to examine the impact tax reform legislation may have on our business.

We are treated as a U.S. domestic corporation for U.S. federal income tax purposes.

We are treated as a U.S. domestic corporation for U.S. federal income tax purposes under Section 7874(b) of the Internal Revenue Code of 1986, as amended, or the Code. As a result, we are subject to U.S. income tax on our worldwide income and any dividends paid by us to non-U.S. holders (as defined in the discussion under "Taxation in the United States" in our Annual Report on Form 20-F) will be subject to U.S. federal income tax withholding at a 30 percent rate or such lower rate as provided in an applicable treaty. Furthermore, PureTech Health plc is also resident for tax purposes in the U.K. and subject to U.K. corporation tax on its worldwide income and gains. Consequently, we may be liable for both U.S. and U.K. income tax, which could have a material adverse effect on our financial condition and results of operations.

This discussion of certain U.S. federal income tax risks is subject in its entirety to the summaries set forth in "Certain United Kingdom Tax Considerations" and "Taxation in the United States" in our Annual Report on Form 20-F

Our ability to use our net operating losses to offset future taxable income may be subject to certain limitations.

As of December 31, 2021, we had U.S. federal and state net operating loss carryforwards, or NOLs, of approximately $215.3 million and 27.9 million respectively, due to prior period losses, which, subject to the following discussion, are generally available to be carried forward to offset our future taxable income, if any, until such NOLs are used or expire. In general, under Section 382 of the Code, a corporation that undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain shareholders over a three year period, is subject to limitations on its ability to utilize its NOLs to offset future taxable income. Our existing NOLs may be subject to limitations arising from previous ownership changes, and if we undergo an ownership change, our ability to utilize NOLs could be further limited by Section 382 of the Code. Future changes in our stock ownership, some of which are outside of our control, could result in an ownership change under Section 382 of the Code. Additionally, we may no longer be able to utilize losses of our Founded Entities that have been deconsolidated or that will deconsolidate in the future. Furthermore, our ability to utilize NOLs of companies that we have acquired or may acquire in the future may be subject to limitations. In addition, under the Tax Act, the amount of post 2017 NOLs that we are permitted to deduct in any taxable year is limited to the lesser of our NOLs or 80 percent of our taxable income in such year (subject to Section 382 of the Code), where taxable income is determined without regard to the NOL deduction itself. Federal NOLs generated after December 31, 2017 are not subject to expiration and generally may not be carried back to prior taxable years, except that under the CARES Act, NOLs generated in 2018, 2019 and 2020 may be carried back five taxable years and these NOLs could fully offset prior year taxable income without the 80% taxable income limitation under the CARES Act.. There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs, or other unforeseen reasons, our existing NOLs could be unavailable to offset future income tax liabilities. In addition, changes under the Tax Act,

as amended by the CARES Act, includes changes to the U.S. federal tax rates and the rules governing NOLs that may significantly impact our ability to utilize our NOLs to offset taxable income in the future. For these reasons, we may not be able to realize a tax benefit from the use of our NOLs.

We may be unable to use net operating loss and tax credit carryforwards and certain built-in losses to reduce future U.K. tax liabilities.

As a U.K. incorporated and tax resident entity, PureTech Health plc is subject to U.K. corporate taxation on its tax-adjusted trading profits. Due to the nature of our business, PureTech Health plc has generated losses since inception and therefore we have not paid any U.K. corporation tax. Subject to numerous utilization criteria and restrictions (including those that limit the percentage of profits that can be reduced by carried forward losses and those that can restrict the use of carried forward losses where there is a change of ownership of more than half the ordinary shares of the company and a major change in the nature, conduct or scale of the trade), we expect these to be eligible for carry forward and utilization against future U.K. operating profits.

Future changes to tax laws could materially adversely affect our company and reduce net returns to our shareholders.

The tax treatment of the company is subject to changes in tax laws, regulations and treaties, or the interpretation thereof, tax policy initiatives and reforms under consideration and the practices of tax authorities in jurisdictions in which we operate, as well as tax policy initiatives and reforms related to the Organisation for Economic Co-Operation and Development's, or OECD, Base Erosion and Profit Shifting, or BEPS, Project, the European Commission's state aid investigations and other initiatives. Such changes may include (but are not limited to) the taxation of operating income, investment income, dividends received or (in the specific context of withholding tax) dividends paid. We are unable to predict what tax reform may be proposed or enacted in the future or what effect such changes would have on our business, but such changes, to the extent they are brought into tax legislation, regulations, policies or practices, could affect our financial position and overall or effective tax rates in the future in countries where we have operations, reduce post-tax returns to our shareholders, and increase the complexity, burden and cost of tax compliance.

Tax authorities may disagree with our positions and conclusions regarding certain tax positions, resulting in unanticipated costs, taxes or non-realization of expected benefits.

A tax authority may disagree with tax positions that we have taken, which could result in increased tax liabilities. For example, HM Revenue & Customs, or HMRC, the Internal Revenue Service or another tax authority could challenge our allocation of income by tax jurisdiction and the amounts paid between certain of our Founded Entities pursuant to our intercompany arrangements and transfer pricing policies, including amounts paid with respect to our intellectual property development. Similarly, a tax authority could assert that we are subject to tax in a jurisdiction where we believe we have not established a taxable connection, often referred to as a "permanent establishment" under international tax treaties, and such an assertion, if successful, could increase our expected tax liability in one or more jurisdictions. A tax authority may take the position that material income tax liabilities, interest and penalties are payable by us, in which case, we expect that we might contest such assessment. Contesting such an assessment may be lengthy and costly and if we were unsuccessful in disputing the assessment, the implications could increase our anticipated effective tax rate, where applicable.

Shareholder protections found in provisions under the U.K. City Code on Takeovers and Mergers, or the Takeover Code, will not apply if our securities are no longer admitted to trading on a regulated market or a multilateral trading facility in the United Kingdom or on any stock exchange in the Channel Islands or the Isle of Man and our place of management and control is considered to change to outside the United Kingdom.

We are registered as a public limited company incorporated in England and Wales and have our ordinary shares admitted to trading on a regulated market in the United Kingdom (being the main market of the LSE). Accordingly, we are currently subject to the Takeover Code and, as a result, our shareholders are entitled to the benefit of certain takeover offer protections provided under the Takeover Code. The Takeover Code provides a framework within which takeovers of companies are regulated and conducted. If, at the time of a takeover offer, we have de-listed from the main market of the LSE (and do not maintain a listing of securities on any other regulated market or a multilateral trading facility in the United Kingdom or on any stock exchange in the Channel Islands or the Isle of Man) and the Panel on Takeovers and Mergers determine that we do not have our place of central management and control in the United Kingdom, then the Takeover Code may not apply to us and our shareholders would not be entitled to the benefit of the various protections that the Takeover Code affords. In particular, we would not be subject to the rules regarding mandatory takeover bids. The following is a brief summary of some of the most important rules of the Takeover Code:

- when any person acquires, whether by a series of transactions over a period of time or not, an interest in shares which (taken together with shares already held by that person and an interest in shares held or acquired by persons acting in concert with him or her) carry 30 percent or more of the voting rights of a company that is subject to the Takeover Code, that person is generally required to make a mandatory offer to all the holders of any class of equity share capital or other class of transferable securities carrying voting rights in that company to acquire the balance of their interests in the company;
- when any person who, together with persons acting in concert with him or her, is interested in shares representing not less than 30 percent but does not hold more than 50 percent of the voting rights of a company that is subject to the Takeover Code, and such person, or any person acting in concert with him or her, acquires an additional interest in shares which increases the percentage of shares carrying voting rights in which he or she is interested, then such person is generally required to make a mandatory offer to all the holders of any class of equity share capital or other class of transferable securities carrying voting rights of that company to acquire the balance of their interests in the company;
- a mandatory offer triggered in the circumstances described in the two paragraphs above must be in cash (or be accompanied by a cash alternative) and at not less than the highest price paid within the preceding 12 months to acquire any interest in shares in the company by the person required to make the offer or any person acting in concert with him or her;
- in relation to a voluntary offer (i.e. any offer which is not a mandatory offer), when interests in shares representing 10 percent or more of the shares of a class have been acquired for cash by an offeror (i.e., a bidder) and any person acting in concert with it in the offer period and the previous 12 months, the offer must be in cash or include a cash alternative for all shareholders of that class at not less than the highest price paid for any interest in shares of that class by the offeror and by any person acting in concert with it in that period. Further, if an offeror acquires for cash any interest in shares during the offer period, a cash alternative must be made available at not less than the highest price paid for any interest in the shares of that class;
- if the offeror acquires an interest in shares in an offeree company (i.e., a target) at a price higher than the value of the offer, the offer must be increased to not less than the highest price paid for the interest in shares so acquired;
- the offeree company must obtain competent advice as to whether the terms of any offer are fair and reasonable and the substance of such advice must be made known to all the shareholders, together with the opinion of the board of directors of the offeree company;
- special or favorable deals for selected shareholders are not permitted, except in certain circumstances where independent shareholder approval is given and the arrangements are regarded as fair and reasonable in the opinion of the financial adviser to the offeree;
- all shareholders must be given the same information;
- each document published in connection with an offer by or on behalf of the offeror or offeree must state that the directors of the offeror or the offeree, as the case may be, accept responsibility for the information contained therein;
- profit forecasts, quantified financial benefits statements and asset valuations must be made to specified standards and must be reported on by professional advisers;
- misleading, inaccurate or unsubstantiated statements made in documents or to the media must be publicly corrected immediately;
- actions during the course of an offer by the offeree company, which might frustrate the offer are generally prohibited unless shareholders approve these plans. Frustrating actions would include, for example, lengthening the notice period for directors under their service contract or agreeing to sell off material parts of the target group;
- stringent and detailed requirements are laid down for the disclosure of dealings in relevant securities during an offer, including the prompt disclosure of positions and dealing in relevant securities by the parties to an offer and any person who is interested (directly or indirectly) in 1 percent or more of any class of relevant securities; and
- employees of both the offeror and the offeree company and the trustees of the offeree company's pension scheme must be informed about an offer. In addition, the offeree company's employee representatives and pension scheme trustees have the right to have a separate opinion on the effects of the offer on employment appended to the offeree board of directors' circular or published on a website.

Company information

Directors, Secretary and Advisors to PureTech

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www.puretechhealth.com

Board of Directors
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(Independent Non-Executive Director)
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Non-Executive Director)
Ms. Kiran Mazumdar-Shaw
(Independent Non-Executive Director)
Ms. Sharon Barber-Lui
(Independent Non-Executive Director)
Dr. Bharatt Chowrira
(President and Chief Business,
Legal & Operating Officer)

Company Secretary
Dr. Bharatt Chowrira

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Gelesis, Inc. and subsidiaries

Consolidated financial statements as of and for the years ended December 31, 2021 and 2020

GELESIS, INC.
INDEX TO FINANCIAL STATEMENTS

KPMG LLP
Two Financial Center 60 South Street
Boston, MA 02111

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
Gelesis, Inc.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Gelesis, Inc. and subsidiaries (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations, comprehensive loss, non-controlling interest, redeemable convertible preferred stock and stockholders' deficit, and cash flows for each of the years then ended, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the years then ended, in conformity with U.S. generally accepted accounting principles.

Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses from operations and has a net capital deficiency that raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB and in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ KPMG LLP

We have served as the Company's auditor since 2015.

Boston, Massachusetts
March 24, 2022

GELESIS, INC.
CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share data)

	December 31, 2021	December 31, 2020
ASSETS		
Current assets:		
Cash and cash equivalents	$ 28,397	$ 48,144
Marketable securities	—	23,998
Accounts receivable	731	818
Grants receivable	9,172	8,116
Inventories	13,503	5,122
Prepaid expenses and other current assets	14,203	6,677
Total current assets	66,006	92,875
Property and equipment, net	58,515	46,895
Operating lease right-of-use assets	2,016	2,167
Intangible assets, net	15,680	17,947
Other assets	4,084	3,959
Total assets	$ 146,301	$ 163,843
LIABILITIES, REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' DEFICIT		
Current liabilities:		
Accounts payable, including due to related party of $147 and $93, respectively	$ 10,066	$ 8,322
Accrued expenses and other current liabilities, including due to related party of $5,664 and $109 respectively	13,660	7,320
Deferred income	32,370	624
Operating lease liabilities	541	421
Convertible promissory notes due to related party, held at fair value	27,128	—
Notes payable	1,950	254
Warrant liabilities	15,821	581
Total current liabilities	101,536	17,522
Deferred income	8,914	8,276
Operating lease liabilities	1,519	1,780
Notes payable, including due to related party of $16,523 and $18,936, respectively	35,131	34,002
Warrant liabilities	—	11,518
Other long-term liabilities, including due to related party of $2,416 and $7,457, respectively	5,588	11,729
Total liabilities	152,688	84,827
Commitments and contingencies (Note 19)		
Noncontrolling interest	11,855	12,429
Redeemable convertible preferred stock, $0.0001 par value – authorized 19,957,625 and 19,957,625 shares at December 31, 2021 and 2020, respectively		
Series A-1 – 1,711,755 shares designated; 1,689,193 and 1,636,971 shares issued and outstanding at December 31, 2021 and 2020; aggregate liquidation preference of $7,505 and $7,273 at December 31, 2021 and 2020, respectively	7,113	6,176
Series A-2 – 1,161,254 shares designated; 1,161,254 shares issued and outstanding at December 31, 2021 and 2020; aggregate liquidation preference of $3,030 at December 31, 2021 and 2020, respectively	3,033	3,033
Series A-3 – 1,730,874 shares designated; 1,730,874 and 1,492,685 shares issued and outstanding at December 31, 2021 and 2020; aggregate liquidation preference of $5,188 and $4,474 at December 31, 2021 and 2020, respectively	7,460	4,463
Series A-4 – 2,159,022 shares designated; 1,450,529 shares issued and outstanding at December 31, 2021 and 2020, respectively; aggregate liquidation preference of $5,473 at December 31, 2021 and 2020, respectively	2,602	2,602
Series A-5 – 1,977,114 shares designated; 1,977,114 shares issued and outstanding at December 31, 2021 and 2020; aggregate liquidation preference of $24,536 at December 31, 2021 and 2020	44,307	24,991
Series Growth – 2,538,274 shares designated; 2,538,274 shares issued and outstanding at December 31, 2021 and 2020; aggregate liquidation preference of $31,500 at December 31, 2021 and 2020	56,959	32,763
Series 2 Growth – 2,370,803 shares designated; 2,370,803 shares issued and outstanding at December 31, 2021 and 2020; aggregate liquidation preference of $30,370 at December 31, 2021 and 2020	53,201	30,684
Series 3 Growth – 6,308,529 shares designated; 5,818,895 shares issued and outstanding at December 31, 2021 and 2020, respectively; aggregate liquidation preference of $150,768 at December 31, 2021 and 2020, respectively	136,919	108,813
Stockholders' deficit:		
Common stock, $0.0001 par value – 48,595,723 shares authorized at December 31, 2021 and 2020, respectively; 2,410,552 and 2,155,490 shares issued and outstanding at December 31, 2021 and 2020, respectively	1	1
Additional paid-in capital	(64,549)	23,907
Accumulated other comprehensive income	219	938
Accumulated deficit	(265,507)	(171,784)
Total stockholders' deficit	(329,836)	(146,938)
Total liabilities, noncontrolling interest, redeemable convertible preferred stock and stockholders' deficit	$ 146,301	$ 163,843

The accompanying notes are an integral part of these consolidated financial statements.

GELESIS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
(In thousands)

	Year Ended December 31,	
	2021	**2020**
Revenue:		
Product revenue, net	$ 11,185	$ 2,708
Licensing revenue	—	18,734
Total revenue, net	11,185	21,442
Operating expenses:		
Costs of goods sold, including related party expenses of $447 and $108, respectively	9,983	2,414
Selling, general and administrative, including related party expenses of $494 and $614, respectively	71,041	28,870
Research and development, including related party expenses of $255 and $272, respectively	12,867	16,115
Amortization of intangible assets	2,267	2,267
Total operating expenses	96,158	49,666
Loss from operations	(84,973)	(28,224)
Change in the fair value of convertible promissory notes	(128)	—
Change in the fair value of warrants	(7,646)	(1,466)
Change in fair value of tranche rights liability	—	256
Interest expense, net	(1,364)	(432)
Other income, net	781	6,000
Loss before income taxes	(93,330)	(23,866)
Provision for income taxes	17	2,039
Net loss	(93,347)	(25,905)
Accretion of senior preferred stock to redemption value	(94,134)	(11,372)
Accretion of noncontrolling interest put option to redemption value	(376)	(567)
Net loss attributable to common stockholders	$ (187,857)	$ (37,844)
Net loss per share attributable to common stockholders—basic and diluted	$ (85.22)	$ (17.61)
Weighted average common shares outstanding—basic and diluted	2,204,486	2,149,182

The accompanying notes are an integral part of these consolidated financial statements.

GELESIS, INC.
CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(In thousands)

	Year Ended December 31,	
	2021	**2020**
Net loss	$ (93,347)	$ (25,905)
Other comprehensive income (loss):		
Foreign currency translation adjustment	(719)	828
Unrealized loss on marketable securities	-	(1)
Total other comprehensive (loss) income	(719)	827
Comprehensive loss	$ (94,066)	$ (25,078)

The accompanying notes are an integral part of these consolidated financial statements.

GELESIS, INC.
CONSOLIDATED STATEMENTS OF NONCONTROLLING INTEREST, REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' DEFICIT
(In thousands, except share and per share data)
The accompanying notes are an integral part of these consolidated financial statements.

		Redeemable Convertible Preferred Stock																					
	Noncontrolling Interest	Series A-1		Series A-2		Series A-3		Series A-4		Series A-5		Series Growth		Series 2 Growth		Series 3 Growth		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income	Accumulat Deficit
		Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount			
Balance at December 31, 2019	$ —	1,636,971	$6,176	1,161,254	$3,033	1,492,685	$4,463	1,439,352	$2,466	1,977,114	$24,536	2,538,274	$31,500	2,370,803	$30,370	2,973,270	$51,348	2,144,651	$1	$26,248	$111	$(145,4
Cumulative effects of adoption of accounting standards (see Note 2)																				(111)		1
Noncontrolling interest, net of issuance costs of $406	11,349																					
Issuance of common stock warrants																				4,322		
Issuance of Series 3 growth redeemable convertible preferred stock, net of issuance costs of $329 and warrant liability of $744																2,845,625	48,125					
Accretion of senior preferred stock to redemption value										455		1,263		314			9,340			(11,372)		
Exercise of Series A-4 warrants								11,177	136													
Stock based compensation expense																				4,808		
Exercise of share-based awards																		10,839		12		
Net loss																						(25,9
Accretion of noncontrolling interest put option to redemption value	567																					(5
Foreign currency translation loss	513																				828	
Unrealized loss on marketable securities																					(1)	
Balance at December 31, 2020	$12,429	1,636,971	$6,176	1,161,254	$3,033	1,492,685	$4,463	1,450,529	$2,602	1,977,114	$24,991	2,538,274	$32,763	2,370,803	$30,684	5,818,895	$108,813	2,155,490	$1	$23,907	$938	$(171,7
Accretion of senior preferred stock to redemption value											$19,316		$24,196		$22,517		$28,106			(94,134)		
Stock based compensation expense																				5,532		
Exercise of stock options																		255,062		146		
Exercise of warrants		52,222	937			238,189	2,997															
Accretion of noncontrolling interest put option to redemption value	376																					(3
Net loss																						(93,3
Foreign currency translation gain	(950)																				(719)	
Balance at December 31, 2021	$11,855	1,689,193	$7,113	1,161,254	$3,033	1,730,874	$7,460	1,450,529	$2,602	1,977,114	$44,307	2,538,274	$56,959	2,370,803	$53,201	5,818,895	$136,919	2,410,552	$1	$(64,549)	$219	$(265,5

GELESIS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year ended December 31,	
	2021	**2020**
Cash flows from operating activities:		
Net loss	$ (93,347)	$ (25,905)
Adjustments to reconcile net loss to net cash used in operating activities:		.
Amortization of intangible assets	2,267	2,267
Reduction in carrying amount of right-of-use assets	449	375
Depreciation	1,524	512
Stock-based compensation	5,532	4,808
Unrealized loss on foreign currency transactions	(37)	(589)
Noncash interest expense	173	—
Accretion on marketable securities	(1)	(6)
Amortization/accretion on long-term assets and liabilities, net	—	(4)
Change in the fair value of warrants	7,646	1,466
Change in the fair value of convertible promissory notes	128	—
Change in fair value of One S.r.l. call option	1,024	—
Gain on extinguishment of debt	—	(297)
Gain on extinguishment of preferred stock warrant	—	(157)
Change in fair value of trance rights liability	—	(256)
Deferred tax expense on intangible asset (see Note 11)	—	1,810
Changes in operating assets and liabilities:		
Account receivables	70	(729)
Grants receivable	(1,723)	(6,779)
Prepaid expenses and other current assets	(8,029)	(3,281)
Inventories	(8,645)	(3,928)
Other assets	107	(3,583)
Accounts payable	2,604	4,085
Accrued expenses and other current liabilities	8,709	151
Operating lease liabilities	(440)	(358)
Deferred income	33,140	8,242
Other long-term liabilities	(6,442)	165
Net cash used in operating activities	(55,291)	(21,991)
Cash flows from investing activities:		
Purchases of property and equipment	(19,917)	(32,212)
Maturities (purchases) of marketable securities	24,000	(23,993)
Net cash provided by (used) in investing activities	4,083	(56,205)
Cash flows from financing activities:		
Principal repayment of notes payable	(302)	(192)
Proceeds from the exercise of warrants	10	—
Proceeds from the issuance of convertible promissory notes	27,000	—
Proceeds from issuance of promissory notes (net of issuance costs of $207 and $751, respectively)	5,679	28,939
Proceeds from issuance of redeemable convertible preferred stock (net of issuance costs of $0 and $329, respectively)	—	48,815
Proceeds from exercise of share-based awards	146	12
Proceeds from issuance of noncontrolling interest	—	11,349
Net cash provided by financing activities	32,533	88,923
Effect of exchange rates on cash	(1,072)	1,643
Net decrease (increase) in cash	(19,747)	12,370
Cash and cash equivalents at beginning of year	48,144	35,774
Cash and cash equivalents at end of year	$ 28,397	$ 48,144
Noncash investing and financing activities:		
Purchases of property and equipment included in accounts payable and accrued expense	$ 1,712	$ 1,818
Deferred financing costs included in accounts payable and accrued expense	$ 773	$ —
Supplemental cash flow information:		
Lease liabilities arising from obtaining right-of-use assets	$ 305	$ —
Interest paid on notes payable	$ 1,578	$ 274

The accompanying notes are an integral part of these consolidated financial statements.

1. Nature of the Business and Basis of Presentation

Nature of Business

Gelesis, Inc., or the Company, is a commercial stage biotherapeutics company incorporated in 2006 under the laws of the State of Delaware. The Company aims to transform weight management through proprietary biomimetic hydrogel technology, inspired by the compositional and mechanical properties of raw vegetables. Since its inception, the Company has devoted substantially all of its efforts to business planning, licensing technology, research and development, commercial activities, recruiting management and technical staff and raising capital and has financed its operations through the issuance of redeemable convertible preferred and common stock, a license and collaboration agreement, supply and distribution agreements, long-term loans, convertible bridge note financings, and government grants.

The Company currently manufactures and markets its first product, Plenity®, which is based on a proprietary hydrogel technology. Plenity®, received de novo clearance from the FDA on April 12, 2019 as a Class II medical device to aid in weight management in adults with excess weight or obesity, Body Mass Index (BMI) of 25 to 40 kg/m^2, when used in conjunction with diet and exercise. In June 2019, the Company received approval to market Plenity in Europe through a Conformité Européenne (CE) mark for Plenity as a class III medical device indicated for weight loss in overweight and obese adults with a Body Mass Index (BMI) of 25-40 kg/m^2, when used in conjunction with diet and exercise. Plenity, which is available by prescription in the United States, became available for first commercial sale in May 2020 to a limited number of consumers. In October 2020 availability was increased to test commercial interest and consumer experience. Activities associated with a full commercial launch in the United States began in late 2021.

On July 19, 2021, the Company entered into a business combination agreement with Capstar Special Purpose Acquisition Corp. ("CPSR"), a special purpose acquisition company. On January 13, 2022, CPSR, a Delaware corporation and the predecessor company consummated the previously announced business combination, pursuant to the terms of the business combination Agreement, dated as of July 19, 2021 (as amended on November 8, 2021 and December 30, 2021), by and among CPSR, CPSR Gelesis Merger Sub, Inc., a Delaware corporation and wholly-owned subsidiary of CPSR (“Merger Sub”), and Gelesis, Inc.(together with its consolidated subsidiaries, “Legacy Gelesis”). Pursuant to the business combination agreement, on the closing date, (i) Merger Sub merged with and into Legacy Gelesis (the “Merger”), with Legacy Gelesis as the surviving company in the Merger, and, after giving effect to such Merger, Legacy Gelesis became a wholly-owned subsidiary of CPSR and (ii) CPSR changed its name to “Gelesis Holdings, Inc.” (together with its consolidated subsidiaries, “Gelesis Holdings”). The business combination, together with the PIPE financing and the sale of the backstop purchase shares, generated approximately $105 million in gross proceeds. On January 14, 2022, Gelesis Holdings’ securities began trading on the New York Stock Exchange under the symbols “GLS” and “GLS.W”.

The business combination was accounted for as a reverse recapitalization in conformity with accounting principles generally accepted in the United States. Under this method of accounting, CPSR has been treated as the "acquired" company for financial reporting purposes. This determination was primarily based on the Legacy Gelesis’ stockholders comprising a relative majority of the voting power of the combined company, the Legacy Gelesis’ operations prior to the acquisition comprising the only ongoing operations of Gelesis Holdings, the majority of Gelesis Holdings’ board of directors appointment by Legacy Gelesis, and Legacy Gelesis' senior management comprising a majority of the senior management of Gelesis Holdings. Accordingly, for accounting purposes, the financial statements of Gelesis Holdings will represent a continuation of the consolidated financial statements of Legacy Gelesis with the business combination being treated as the equivalent of Legacy Gelesis issuing stock for the net assets of CPSR, accompanied by a recapitalization. The net assets of CPRS will be stated at historical costs, with no goodwill or other intangible assets recorded.

Going Concern

The consolidated financial statements have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the ordinary course of business. The consolidated financial statements do not include any adjustments relating to the recoverability and classification of recorded assets and liabilities that might be necessary should the Company be unable to continue as a going concern.

The Company has a history of incurring substantial operating losses and has financed its operations in recent years primarily from the issuance of redeemable convertible preferred stock, promissory notes, government grants and collaborations and licensing arrangements. The Company expects such operating losses and negative cash flows from operations will continue in 2022. The Company expects its cash on hand as of the date of the consolidated financial statements and gross proceeds of $105 million from the business combination, together with the PIPE financing and the sale of the backstop purchase shares, will only be sufficient to meet the Company’s obligations into the first quarter of 2023, prior to considerations for any additional funding, and not at least twelve months beyond the date of issuance of the consolidated financial statements. These conditions raise substantial doubt about the Company’s ability to continue as a going concern.

The Company will need to raise additional capital in future periods to fund its operations. The Company will seek to raise necessary funds through a combination of public or private equity offerings, debt financings, strategic collaborations and licensing arrangements, government grants, or other financing mechanisms. The Company's ability to fund the completion of its ongoing and planned clinical studies, as well as its regulatory and commercial efforts, may be substantially dependent upon whether the Company can obtain sufficient funding at acceptable terms. If adequate sources of funding are not available to the Company, the Company may be required to delay, reduce or eliminate research and development programs, reduce or eliminate commercialization efforts, and reduce its headcount. Additionally, the Company is subject to risks common to companies in the biotechnology industry, including but not limited to, risks of failure of the full-scope product commercialization in targeted markets, clinical trials and preclinical studies, the impact of COVID19 pandemic on the Company's supply chain and results of operations, dependence on key personnel, protection of proprietary technology, compliance with government regulations, development by competitors of technological innovations.

2. Summary of Significant Accounting Policies

Basis of Presentation

The Company's consolidated financial statements are prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASUs") issued by the Financial Accounting Standards Board ("FASB").

The Company consolidates those entities where it has a direct and indirect controlling financial interest based on either a variable interest model or voting interest model. The Company's consolidated financial statements include the accounts of the Company, its two wholly-owned subsidiaries and a variable interest entity ("VIE"), Gelesis S.r.l., in which the Company has a controlling interest and is the primary beneficiary. The noncontrolling interest attributable to the Company's VIE is presented as a separate component from stockholders' deficit in the consolidated balance sheets and as a noncontrolling interest in the consolidated statements of noncontrolling interest, redeemable convertible preferred stock and stockholders' deficit. All intercompany balances and transactions have been eliminated in consolidation. Under the variable interest model, a controlling financial interest is determined based on which entity, if any, has (i) the power to direct the activities of the VIE that most significantly impacts the VIE's economic performance and (ii) the obligations to absorb losses that could potentially be significant to the VIE or the right to receive benefits from the VIE that could potentially be significant to the VIE. Management performs ongoing reassessments of whether changes in the facts and circumstances regarding the Company's involvement with a VIE will cause the consolidation conclusion to change. The consolidation status of a VIE may change as a result of such reassessments. Changes in consolidation status are applied prospectively in accordance with U.S. GAAP.

Use of Estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of income and expenses during the reporting period. The Company assesses the above estimates on an ongoing basis; however, actual results could materially differ from those estimates.

Subsequent Event(s)

The Company considers events or transactions that occur after the balance sheet date but before the consolidated financial statements are issued to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure. The Company evaluated all events and transactions through the date these financial statements were filed with the Security and Exchange Commission ("SEC") or were available to be issued.

Fair Value of Financial Instruments

The guidance in FASB ASC 820, *Fair Value Measurements and Disclosures* ("ASC 820"), defines fair value and establishes a fair value hierarchy that prioritizes the inputs to valuation techniques used to measure fair value. The hierarchy gives the highest priority to unadjusted quoted prices in active markets for identical assets or liabilities (Level 1 measurements) and the lowest priority to unobservable inputs (Level 3 measurements). The three levels of the fair value hierarchy are described below:

Level 1 – Inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities that the reporting entity has the ability to access at the measurement date.

Level 2 – Valuations based on quoted prices in markets that are not active or for which all significant inputs are observable, either directly or indirectly.

Level 3 – Prices or valuations that require inputs that are both significant to the fair value measurement and unobservable.

To the extent that valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

Fair value is a market-based measure considered from the perspective of a market participant rather than an entity-specific measure. Therefore, even when market assumptions are not readily available, the Company's own assumptions are set to reflect those that market participants would use in pricing the asset or liability at the measurement date. The Company uses prices and inputs that are current as of the measurement date, including during periods of market dislocation. In periods of market dislocation, the observability of prices and inputs may be reduced for many instruments. This condition could cause an instrument to be reclassified from Level 1 to Level 2 or Level 2 to Level 3.

The Company's tranche rights liability, preferred stock warrants, and call option liability (see Notes 3 and 11) are recorded at fair value on a recurring basis. The carrying amount of accounts receivable, grants receivable, accounts payable and accrued expenses are considered a reasonable estimate of their fair value, due to the short-term maturity of these instruments. The carrying amount of notes payable is also considered to be a reasonable estimate of the fair value based on the nature of the debt and that the debt bears interest at the prevailing market rate for instruments with similar characteristics. The Company's cash equivalents and marketable securities are carried at fair value, determined according to the fair value hierarchy described below (see Note 3).

Preferred Stock Warrant Liability: The Company has recorded redeemable convertible preferred stock warrants issued to investors as liabilities as the terms of the warrants are not fixed due to potential adjustments in the exercise price and/or the number of shares issuable under the warrants, and because all of the redeemable convertible preferred stock warrants are exercisable for preferred shares. Redeemable convertible preferred stock warrants are initially recorded at fair value, with gains and losses arising from subsequent changes in fair value recognized in the consolidated statements of operations at each period end while such instruments are outstanding. The Company measures fair value of redeemable convertible preferred stock warrants using a Black-Scholes option pricing model (see Notes 3 and 14).

Tranche Rights Liability: The Company has recorded tranche rights issued to investors, which is a right of the investor to purchase additional shares of redeemable convertible preferred stock in connection with an initial issuance of the underlying shares at one or more subsequent closings at a fixed agreed upon price, as liabilities pursuant to ASC 480, *Distinguishing Liabilities from Equity*. Tranche rights are initially recorded at fair value, with a corresponding offset recorded as a discount on the redeemable convertible preferred stock. Tranche rights are subsequently adjusted for settlement of the tranche rights upon issuance of the tranche shares, and from gains and losses arising from changes in fair value, which are recognized in the consolidated statements of operations at each period end while such instruments are outstanding. The Company initially measures the fair value of the tranche rights at the issuance date, and subsequently at each reporting date, using a Black-Scholes option pricing model (see Notes 3 and 14).

Noncontrolling Interests: The Company recognizes noncontrolling interest related to VIE's, in which the Company is the primary beneficiary, as temporary equity in the consolidated financial statements separate from the shareholders' equity. Changes in the shareholders' ownership interest in a subsidiary that do not result in deconsolidation are treated as equity transactions if the parent entity retains its controlling financial interest. In addition, when a subsidiary is deconsolidated, any retained noncontrolling equity investment in the former subsidiary will be initially measured at fair value and the difference between the carrying value and fair value of the retained interest will be recorded as a gain or loss.

Cash Equivalents

The Company considers all short-term, highly liquid investments with original maturities of 90 days or less at acquisition date to be cash equivalents. Cash equivalents, which consist of money market accounts purchased with original maturities of less than 90 days from the date of purchase, are stated at fair value.

Marketable Securities

The Companies classifies all investment securities as available-for-sale, as the sale of such securities may be required prior to maturity. These investment securities are carried at fair value, with unrealized gains and losses reported as accumulated other comprehensive loss until realized. The cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization and accretion, as well as interest, are included in interest income. Realized gains and losses from sale of available-for-sale securities, if any, are determined on a specific identification basic and are also included in interest income.

The Company reviews all available-for-sale securities at each period end to determine if they remain available-for-sale based on then current intent and ability to sell the security if it is required to do so. Marketable securities are subject to a periodic impairment review. The Company may recognize an impairment charge when a decline in the fair value of investments below the cost basis is determined to be other-than-temporary. The Company did not have any marketable securities deemed to be impaired at December 31, 2020 and did not have any marketable securities at December 31, 2021.

Accounts Receivable

The Company extends credit to customers based upon contractual terms or its evaluation of the customer's financial condition.

Customer accounts receivable are stated at amounts due net of applicable discounts and other contractual adjustments as well as an allowance for expected credit losses. The Company assesses the need for an allowance for expected credit losses based upon currently expected credit losses ("CECL") by considering a number of factors, including the length of time trade accounts receivable are past due, the customer's ability to pay its obligation and the condition of the general economy and the industry as a whole. The Company will write off accounts receivable when the Company determines that they are uncollectible. The Company has not historically experienced any collection issues or significant credit losses. Based on historical receipts and collections history, management has determined that an allowance for expected credit losses is not necessary at December 31, 2021 or 2020.

Government Grants

The Company recognizes grants from governmental agencies in other income on the consolidated statements of operations, gross of the expenditures that were related to the underlying project being co-funded by the grant, when there is reasonable assurance that the Company will comply with the conditions attached to the grant arrangement and payments under the grant will be received. The Company evaluates the conditions of each individual grant as of each reporting period to ensure that the Company has reached reasonable assurance of meeting the conditions of each grant arrangement and that it is expected that the grant payment will be received as a result of meeting the necessary conditions.

The Company has been awarded grants from government agencies in Italy for certain capital expenditures and expenses incurred for research and development work performed under specified programs conducted in Italy. The Company submits qualifying expenses and capital purchases for reimbursement under each specified program, which occurs after the Company has made the capital purchases and/or incurred the research and development costs. The Company records a grant receivable upon incurring such expenses, as approval and reimbursement are considered to be perfunctory once the qualifying program has been approved. Government grants are recognized in the consolidated statements of operations on a systematic basis over the periods in which the Company recognizes the related costs for which the government grant is intended to compensate. Specifically, grant income related to research and development costs is recognized as such expenses are incurred. Research and development costs that were incurred prior to the approval of a qualifying program are recognized as grant income immediately upon approval of the program by the grantor. Grant income related to qualifying capital purchases is recognized in proportion to the depreciation expense incurred on the underlying assets.

Deferred income related to capital purchases for which grant income will be recognized beyond twelve months from the balance sheet date is classified as long-term deferred income on the consolidated balance sheets and amortized to other income, net, over the same life of the related asset.

Inventory

The Company manufactures its own super-absorbent hydrogels used in Plenity® and other product candidates out of its own manufacturing facilities located in Italy. The packaging of the hydrogels is currently outsourced to contract packaging organizations for commercial and research and development purposes.

Inventories comprise raw materials, including raw materials for packaging components, work-in-process, and finished goods, which are goods that are available for sale. The Company states inventory at the lower of cost or net realizable value with the cost based on the first-in, first-out method. If the Company identifies excess, obsolete or unsalable items, it writes down its inventory to its net realizable value in the period in which the impairment is identified. These adjustments are recorded based upon various factors related to the product, including the level of product manufactured by the Company, the level of product in the distribution channel, current and projected demand, the expected shelf-life of the product and firm inventory purchase commitments. Significant shipping and handling costs incurred for inventory purchases are included in inventory and costs incurred for product shipments are recorded in cost of goods sold as incurred.

Property and Equipment

Property and equipment are stated at cost, less accumulated depreciation. Expenditures for maintenance and repairs are charged to operations as incurred whereas major betterments are capitalized as additions to property and equipment. Depreciation and amortization begin at the time the asset is placed in service, and are recorded using the straight-line method over the estimated useful lives, as follows:

Asset Category	Useful Lives
Computer equipment and software	1 – 3 years
Laboratory and manufacturing equipment	2.5 – 8.3 years
Leasehold improvements	5 – 10 years, or the remaining term of lease, if shorter
Buildings and land improvements	18 – 20 years
Land	Not depreciated

Impairment of Long-Lived Assets

The Company reviews long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of the asset may not be recoverable. When such events occur, the Company compares the carrying amounts of the assets to the undiscounted expected future cash flows the assets are expected to generate and recognizes an impairment loss equal to the excess of the carrying value over the fair value of the related asset. For the years ended December 31, 2021 and 2020, there were no indicators of impairment.

Intangible Assets

Intangible assets with estimable useful lives, or definite-lived intangibles, are carried at cost and are amortized on a straight-line basis over their estimated useful lives and reviewed for impairment upon certain triggering events. We routinely review the remaining estimated useful lives of definite-lived intangible assets. If we reduce the estimated useful life assumption, the remaining unamortized balance is amortized over the revised estimated useful life.

Redeemable Convertible Preferred Stock

The Company has classified redeemable convertible preferred stock as temporary equity in the consolidated balance sheets due to certain change in control clauses that are outside of the Company's control, including liquidation, sale, or transfer of control of the Company, as holders of the redeemable convertible preferred stock could cause redemption of the shares in these situations. The Company accretes the carrying values of the classes of redeemable convertible preferred stock that are mandatorily redeemable to the redemption values. The Company does not accrete the carrying values of the classes of redeemable convertible preferred stock that are not mandatorily redeemable to the redemption values since a liquidation event, sale, or transfer is not considered probable. Subsequent adjustments of the carrying values to the ultimate redemption values will be made only if and when it becomes probable that such a liquidation event will occur.

Leases

The Company determines if an arrangement is a lease at contract inception under ASC 842 – *Leases*. Operating lease assets represent a right to use an underlying asset for the lease term and operating lease liabilities represent an obligation to make lease payments arising from the lease. The Company recognizes operating lease assets and liabilities at the commencement date of the lease based upon the present value of lease payments over the lease term. When determining the lease term, the Company includes options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option. As the discount rate implicit in the leases was typically not readily determinable, the Company utilized the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. incremental borrowing rate (IBR).

The Company has elected to apply the practical expedient to account for lease and non-lease components as a single lease component for new and modified leases commencing after adoption election. The Company has also elected not to recognize leases with an initial term of 12 months or less on the consolidated balance sheets, instead, those lease payments are recognized in the consolidated statements of operations on a straight-line basis over the lease term.

Revenue Recognition

Product Revenue

The Company commercializes Plenity in the U.S. markets principally through synergistic partnerships with online pharmacies and telehealth providers, which in turn sell Plenity directly to patients based on prescriptions. Outside the U.S., the Company primarily seeks collaborations with strategic partners to market Plenity and obtain necessary regulatory approvals as necessary.

Product revenue is recognized by the Company in an amount that reflects the consideration which the Company expects to receive in exchange for those goods or services when the customer obtains control of the product, which occurs at a point in time, when the product is received by the Company's customers.

Reserves for Variable Consideration

Revenues from product sales are recorded as product revenue at the net sales price (transaction price), which includes estimates of variable consideration that are reimbursable to customers for which reserves are established and which result from (a) shipping charges to end-users, (b) pharmacy dispensing and platform fees, (c) merchant and processing fees, (d) promotional discounts offered by the Company to end-users, and (e) reserves for expected product quality returns. These reserves for contractual adjustments are based on the amounts earned or to be claimed on the related sales and are classified as reductions of accounts receivable (if the amount is payable to the customer) or a current liability (if the amount is payable to a party other than the customer). Where appropriate, these estimates take into consideration a range of possible outcomes that are probability-weighted for relevant factors such as the Company's historical experience, current contractual and statutory requirements, specific known market events and trends, industry data and forecasted customer buying and payment patterns. Overall, these reserves reflect the Company's best estimates of the amount of consideration to which the Company is entitled based on the terms of the contract(s). The amount of variable consideration that is included in the transaction price may be constrained and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from the Company's estimates. If actual results in the future vary from the Company's estimates, the Company will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known. The Company has no plan to seek government or commercial payor reimbursements in the US or the overseas markets. Therefore, reserves for variable consideration do not contain any components related to government and payor rebates or chargebacks.

Product Returns

The Company generally does not accept customer returns, except for product quality related cases. The Company evaluates quality related returns and adjust the corresponding product warranty reserves and liabilities at least quarterly and at the end of each reporting period.

License and Collaboration Revenues

The Company recognizes revenue from product sales and collaboration arrangements in accordance with ASC 606, *Revenue from Contracts with Customers* (“ASC 606”). Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to be entitled to in exchange for those goods or services. To determine the appropriate amount of revenue to be recognized for arrangements determined to be within the scope of ASC 606, the Company performs the following five steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect consideration it expects to be entitled to in exchange for the goods or services it transfers to the customer.

Performance obligations are promised goods or services in a contract to transfer a distinct good or service to the customer and are considered distinct when (i) the customer can benefit from the good or service on its own or together with other readily available resources and (ii) the promised good or service is separately identifiable from other promises in the contract. In assessing whether promised goods or services are distinct, the Company considers factors such as the stage of development of the underlying intellectual property, the capabilities of the customer to develop the intellectual property on its own or whether the required expertise is readily available, and whether the goods or services are integral or dependent to other goods or services in the contract. For performance obligations which consist of the Company’s materials, shipping and distribution activities occur prior to the transfer of control of the Company’s materials and are considered activities to fulfill the Company’s promise to deliver goods to the customers.

The Company has entered and anticipates to enter future license, collaboration and/or distribution agreements, which are within the scope of ASC 606, to manufacture and commercialize product(s). The terms of these agreements typically contain multiple promises or obligations, which may include: (i) manufacturing and supply of covered products, and (ii) regulatory support activities to be provided to the collaboration partner relating to the covered product(s). Payments to the Company under these agreements may include payments based upon the achievement of certain milestones and royalties on any resulting net product sales.

The Company first evaluates collaboration arrangements to determine whether the arrangement (or part of the arrangement) represents a collaborative arrangement pursuant to ASC Topic 808, *Collaborative Arrangements,* based on the risks and rewards and activities of the parties pursuant to the contractual arrangement. The Company accounts for collaborative arrangements (or elements within the contract that are deemed part of a collaborative arrangement), which represent a collaborative relationship and not a customer relationship, outside the scope of ASC 606. The Company's collaborations primarily represent revenue arrangements. The Company uses judgment to determine whether milestones or other variable consideration, except for sales-based royalties, should be included in the transaction price. The transaction price is allocated to each performance obligation on a relative standalone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. The Company utilizes key assumptions to determine the standalone selling price, which may include other comparable transactions, pricing considered in negotiating the transaction and the estimated costs. For performance obligations which consist of licenses and other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress. As of and for the two years ended December 31, 2021, there were no performance obligations to be satisfied over time for recognition purposes.

Amounts received prior to revenue recognition are recorded as deferred income. Amounts expected to be recognized as revenue within the twelve months following the balance sheet date are classified as current portion of deferred income in the accompanying consolidated balance sheets. Amounts not expected to be recognized as revenue within the twelve months following the balance sheet date are classified as deferred income, net of current portion. Amounts recognized as revenue, but not yet received or invoiced are generally recognized as contract assets.

Cost of goods sold

Cost of goods sold includes the cost of manufacturing our proprietary superabsorbent hydrogels for Plenity for which revenue was recognized during the period, as well as the associated costs for encapsulation, packaging, shipment, supply management and quality assurance. Expenses from royalty agreements on net product sales are also recognized as a component of cost of goods sold during the period in which the associated revenues are recognized. A portion of depreciation with respect to property and equipment directly utilized in manufacturing Plenity units is recognized as a component of cost of goods sold over the depreciable life of the asset.

Selling, General and Administrative Costs

Selling, general and administrative costs are expensed as incurred. Selling, general and administrative costs include sales and marketing costs incurred as a result of the commercialization of the Company’s products, payroll and personnel expense, stock-based compensation expense, and costs of programs and infrastructure necessary for the general conduct of the Company’s business.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development costs include payroll and personnel expense, stock-based compensation expense, consulting costs, external contract research and development expenses, as well as depreciation and utilities. Prepaid research and development costs are deferred and amortized over the service period, as the services are provided.

Stock-Based Compensation

Effective January 1, 2020, the Company accounts for all stock-based compensation awards granted to employees and non-employees in accordance with ASC 718, *Compensation – Stock Compensation*. The Company’s stock-based compensation consist primarily of stock options. The measurement date for share-based awards is the date of grant, and stock-based compensation costs are recognized as expense over the respective requisite service periods, which are typically the vesting period. The fair value of each stock option grant is estimated as of the date of grant using the Black-Scholes option-pricing model that requires management to apply judgment and make estimates, including:

- *exercise price:* In determining the exercise prices for options granted, the Board of Directors has considered the fair value of the common stock as of each grant date. The fair value of the common stock underlying the stock options has been determined by the Board of Directors at each award grant date based upon the estimated fair value of the Company’s

common stock as determined by an independent third-party valuation firm. The specialists at this valuation firm considered a variety of factors including the Company's financial position and historical financial performance, the status of technological developments within the Company's products, the composition and ability of the current clinical and management team, an evaluation or benchmark of the Company's competition, the current business climate in the marketplace, the illiquid nature of the common stock, arm's length sales of the Company's capital stock (including Series Preferred), the effect of the rights and preferences of the preferred stockholders, and the prospects of a liquidity event, among others.

- *expected volatility:* As the Company is a privately-owned company, there is not sufficient historical volatility for the expected term of the options. Therefore, the Company used an average historical share price volatility based on an analysis of reported data for a peer group of comparable companies for which historical information is available. For these analyses, the Company selects companies with comparable characteristics to itself including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. The Company computes the historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of its stock-based awards. The Company intends to consistently apply this process using representative companies until a sufficient amount of historical information regarding the volatility of its own share price becomes available;
- risk-free interest rate, which is based on the U.S. Treasury yield curve in effect at the time of grant commensurate with the expected term assumption;
- expected term, which is calculated using the simplified method, as prescribed by the Securities and Exchange Commission Staff Accounting Bulletin No. 107, *Share-Based Payment,* as the Company has insufficient historical information regarding its stock options to provide a basis for an estimate. Under this approach, the weighted-average expected life is presumed to be the average of the contractual term of ten years and the weighted-average vesting term of the stock options, taking into consideration multiple vesting tranches;
- dividend yield, which is zero based on the fact that the Company never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future.

Prior to the adoption of Accounting Standards ASU No. 2018-07, *Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting* ("ASU No. 2018-07"), the measurement date for non-employee awards was generally the date the services were completed, resulting in financial reporting period adjustments to stock-based compensation during the vesting terms for changes in the fair value of the awards. Since the adoption of ASU 2018-07 on January 1, 2020, the measurement date for non-employee awards is the date of grant without changes in the fair value of the award. Stock-based compensation costs for non-employees are recognized as expense over the vesting period. Stock-based compensation expense is classified in the consolidated statements of operations based on the function to which the related services are provided. Forfeitures are recorded as they occur.

Income Taxes

The consolidated financial statements reflect provisions for federal, state, local and foreign income taxes. Deferred tax assets and liabilities are recognized based on temporary differences between the financial reporting and income tax basis of assets and liabilities using rates anticipated to be in effect when such temporary differences reverse. A change in tax rates is recognized in income in the period of the enactment date. A valuation allowance against net deferred tax assets is required if, based upon the available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

The Company also assesses the probability that the positions taken or expected to be taken in its income tax returns will be sustained by taxing authorities. A "more likely than not" (more than 50%) recognition threshold must be met before a tax benefit can be recognized. Tax positions that are more likely than not to be sustained on examination by the taxing authorities, based on the technical merits of the position, are reflected in the Company's consolidated financial statements. Tax positions are measured as the largest amount of tax benefit that is greater than 50% likely of being realized upon settlement with a taxing authority that has full knowledge of all relevant information. The difference between the benefit recognized for a position and the tax benefit claimed on a tax return is referred to as an unrecognized tax benefit. Potential interest and penalties associated with such uncertain tax positions are recorded as a component of income tax expense.

Foreign Currency Translation

The financial statements of each of the Company's subsidiaries with a functional currency other than the U.S. dollar are translated into U.S. dollars using period-end exchange rates for assets and liabilities, historical exchange rates for stockholders' equity and weighted average exchange rates for operating results. Translation gains and losses are included in accumulated other comprehensive income (loss) in stockholders' equity. Foreign currency transaction gains and losses are included in other (expense) income, net in the results of operations.

Concentrations of Credit Risk and Off -Balance-Sheet Risk

The Company has no significant off-balance-sheet risk such as foreign exchange contracts, option contracts, or other foreign hedging arrangements. Financial instruments that potentially expose the Company to concentrations of credit risk primarily consist of cash and cash equivalents, investments, accounts receivable and unbilled account receivables.

The Company's cash balances, trade receivables, and grants receivable subject the Company to significant concentrations of credit risk. Periodically, the Company maintains deposits in government insured financial institutions in excess of government insured limits. The Company deposits its cash in financial institutions that it believes have high credit quality and has not experienced any losses on such accounts and does not believe it is exposed to any significant credit risk on cash. The Company's grants receivable are due from government agencies, which the Company believes to have high credit quality. The Company has a limited number of commercial customers. The Company monitors the creditworthiness of customers to whom it grants credit terms and has not experienced any credit losses.

Earnings (Loss) per Share

The Company computes basic earnings (loss) per share by dividing income (loss) attributable to common stockholders by the weighted average number of shares of common stock outstanding. During periods of income, the Company allocates participating securities a proportional share of income determined by dividing total weighted average participating securities by the sum of the total weighted average common shares and participating securities (the "two-class method"). The Company's restricted stock and various series of preferred stocks participate in dividends declared by the Company and are therefore considered to be participating securities. Participating securities have the effect of diluting both basic and diluted earnings per share during periods of income. During periods of loss, the Company allocates no loss to participating securities because they have no contractual obligation to share in the losses of the Company. The Company computes diluted earnings (loss) per share after giving consideration to the dilutive effect of stock options and warrants that are outstanding during the period, except where such non-participating securities would be anti-dilutive.

Segment Information

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker, or decision-making group, in making decisions on how to allocate resources and assess performance. The Company's chief operating decision maker is the chief executive officer. The Company and the chief operating decision maker view the Company's operations and manage its business as one operating segment. Geographically, the Company operates out of the U.S. and Italy. The corporate headquarters including the core functions of sales and marketing, medical affairs, research and development and general and administrative are located in the U.S., while substantially all of the Company's manufacturing facilities and operations physically reside in Italy.

Recently Adopted Accounting Pronouncements

Credit Losses

In June 2016, the FASB issued ASU No. 2016-13, Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments (ASU 2016-13). The FASB has subsequently issued amendments to ASU 2016-13, which have the same effective and transition date of fiscal years beginning after December 15, 2019 for SEC filers other than small reporting companies, and fiscal years beginning after December 15, 2022 for all other entities. These standards require that credit losses be reported using an expected losses model rather than the incurred losses model that is currently used, and establish additional disclosures related to credit risks. For available-for-sale debt securities with unrealized losses, these standards now require allowances to be recorded instead of reducing the amortized cost of the investment.

The Company has adopted ASU No. 2016-13 as of January 1, 2021 and the impact of this standard was not material to the Company's consolidated financial statements or related disclosures.

3. Fair Value Measurements

Liabilities that are measured at fair value on a recurring basis, and the level of the fair value hierarchy utilized to determine such fair values, consisted of the following at December 31, 2021 (in thousands):

		Fair Value Measurements		
	Fair Value	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Liabilities:				
Convertible promissory notes (see Note 12)	$ 27,128	$ —	$ —	$ 27,128
Preferred stock warrants	15,821	—	—	15,821
One Srl call option (see Note 11)	2,416	—	—	2,416
Total liabilities measured at fair value	$ 45,365	$ —	$ —	$ 45,365

Assets and liabilities that are measured at fair value on a recurring basis, and the level of the fair value hierarchy utilized to determine such fair values, consisted of the following at December 31, 2020 (in thousands):

		Fair Value Measurements		
	Fair Value	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Assets:				
Marketable securities	$ 23,998	$ 23,998	$ —	$ —
Total assets measured at fair value	$ 23,998	$ 23,998	$ —	$ —
Liabilities:				
Preferred stock warrants	$ 12,099	$ —	$ —	$ 12,099
One Srl call option (see Note 11)	1,545	—	—	1,545
Total liabilities measured at fair value	$ 13,644	$ —	$ —	$ 13,644

There were no transfers into or out of level 3 instruments and/or between level 1 and level 2 instruments during the years ended December 31, 2021 and 2020. The fair value of the tranche right liability, preferred stock warrant liability, and call option liability includes inputs not observable in the market and thus represents a Level 3 measurement. The Company estimates the fair value of the underlying stock by estimating the probability of various change of control events occurring and then estimates the present value of the amount the holders would receive upon the change in control.

The significant assumption used in the model is the probability of the following scenarios occurring:

	At December 31,	
	2021	2020
IPO scenario	2.5%	75.0%
Market adjusted equity value method	2.5%	25.0%
Special purpose acquisition company ("SPAC") scenario	95.0%	0.0%

Tranche right liability

Tranche rights are initially recorded at fair value, are subsequently adjusted for settlement of the tranche rights upon issuance of the tranche shares and are remeasured at each subsequent reporting date. The Company initially measures the fair value of the tranche rights at the issuance date, and subsequently at each reporting date, using a Black-Scholes option pricing model. The significant inputs

used in estimating the fair value of tranche rights include the estimated fair value of the underlying stock, expected term of the tranche right, risk free interest rate, and expected volatility.

The following represents a summary of the changes to Company's tranche right liability during the year ended December 31, 2020 (in thousands):

	Tranche rights liability
Balance at December 31, 2019	$ 310
Change in fair value of tranche rights liability immediately prior to tranche settlement in April 2020	(256)
Settlement of Series 3 Growth tranche rights liability in April 2020	(54)
Balance at December 31, 2020	$ —

The change in the fair value of the Tranche Rights is influenced primarily by the price of the underlying Redeemable Convertible Preferred Stock and the remaining term of the Tranche Right. During the year ended December 31, 2020, the Company recognized a loss of $0.3 million in the consolidated statements of operations related to changes in the fair value of tranche rights. The tranche rights liability was settled in April 2020 and there was no outstanding liability at December 31, 2020.

Preferred stock warrant liability

Preferred stock warrants are recorded at estimated fair value at the date of issuance and are remeasured at each subsequent reporting date. Fair value is determined using a Black-Scholes option pricing model. The significant inputs used in estimating the fair value of warrants include the estimated fair value of the underlying stock, expected term, risk free interest rate, and expected volatility. The Company estimates the fair value of the underlying stock by estimating the probability of various change of control events occurring and then estimates the present value of the amount the holders would receive upon the change in control.

The following represents a summary of the changes to Company's warrant liability for the years ended December 31, 2021 and 2020 (in thousands):

	Series A-1 Warrants	Series A-3 Warrants	Series A-4 Warrants	Series 3 Growth Warrants	Series 4 Growth Options	Total
Balance at December 31, 2019	485	2,541	7,686	4,631	653	15,996
Issuance of Series 4 Growth option liability	-	-	-	-	745	745
Extinguishment of Series 3 Growth warrant	-	-	-	(5,973)	-	(5,973)
Exercise of Series A-4 warrants	-	-	(135)	-	-	(135)
Change in fair value of warrant liability	96	355	1,071	1,342	(1,398)	1,466
Balance at December 31, 2020	$ 581	$ 2,896	$ 8,622	$ —	$ —	$ 12,099
Exercise of warrants	(937)	(2,987)	-	-	-	(3,924)
Change in fair value of warrant liability	356	91	7,199	-	-	7,646
Balance at December 31, 2021	$ —	$ —	$ 15,821	$ —	$ —	$ 15,821

Warrants with an expected term of less than one year from the date of the consolidated balance sheets are recorded under current liabilities on the consolidated balance sheets. At December 31, 2021, the Company reported a warrant liability in the amount of $15.8

million under current liabilities. At December 31, 2020, the Company reported a warrant liability in the amount of $0.6 million and $11.5 million under current and noncurrent liabilities, respectively.

The following weighted average assumptions were used to determine the fair value of the warrant liability at December 31, 2021:

	Series A-4 Warrants
Expected term	0.1 years
Expected volatility	48.0%
Expected dividend yield	0.0%
Risk free interest rate	0.6%
Estimated fair value of the redeemable convertible preferred stock	$ 22.36
Exercise price of warrants	$ 0.04

The following weighted average assumptions were used to determine the fair value of the warrant liability at December 31, 2020:

	Series A-1 Warrants	Series A-3 Warrants	Series A-4 Warrants
Expected term	0.3 years	1.5 years	2.6 years
Expected volatility	48.0%	68.0%	59.0%
Expected dividend yield	0.0%	0.0%	0.0%
Risk free interest rate	0.1%	0.1%	0.2%
Estimated fair value of the redeemable convertible preferred stock	$ 12.24	$ 12.21	$ 12.22
Exercise price of warrants	$ 4.44	$ 0.04	$ 0.04

The Company issued equity-classified common stock warrants during the year ended December 31, 2020 (see Note 13). While the fair value of the common stock warrants represents a Level 3 measurement, equity-classified warrants are recorded at their initial fair value and not subsequently remeasured. As such, the common stock warrants and its unobservable inputs are not included in the above tables.

One Srl call option liability

The One Srl call option liability was recorded at estimated fair value at the date of issuance and is remeasured at each subsequent reporting date with changes in fair value recorded in other income (expense) in the accompanying consolidated statements of operations. Fair value is determined using a Black-Scholes option pricing model. The significant inputs used in estimating the fair value of call option liability include the estimated fair value of the underlying stock price, expected term, risk free interest rate, and expected volatility.

The following represents a summary of the changes to Company's One Srl call option liability for the years ended December 31, 2021 and 2020 (in thousands):

Fair value of One Srl call option	$ 1,494
Foreign currency translation loss	51
Balance at December 31, 2020	$ 1,545
Change in fair value	1,024
Foreign currency translation gain	(153)
Balance at December 31, 2021	$ 2,416

Changes in the unobservable inputs noted above would impact the amount of the respective liability. For the respective liability, increases (decreases) in the estimates of the Company's annual volatility would increase (decrease) the liability and an increase (decrease) in the annual risk-free rate would increase (decrease) the liability.

The following weighted average assumptions were used to determine the fair value of the One Srl call option liability at December 31, 2021 and 2020:

	At December 31,	
	2021	2020
Expected term	2.0 years	1.8 years
Expected volatility	62.0%	61.0%
Expected dividend yield	0.0%	0.0%
Risk free interest rate	0.7%	0.1%
Estimated fair value of ownership interest	$ 6,922	$ 6,066
Exercise price of call option	$ 6,806	$ 7,358

Convertible promissory notes

The convertible promissory notes issued in conjunction with the bridge financing arrangement were recognized at fair value at issuance and subsequent changes in fair value were recorded in the accompanying consolidated statements of operations (see Note 12). Fair value is determined using a multiple scenario-based valuation method. The fair value of the hybrid instrument was determined by calculating the value of the instrument in each scenario "with" the respective conversion feature and "without". The significant inputs used in estimating the fair value of the convertible promissory notes include the estimated discount rate, expected term, and the outcome probability with respect to each scenario.

The following assumptions were used to determine the fair value of the convertible promissory notes at December 31, 2021:

	Convertible Promissory Notes
Expected term	0.1 years
Discount rate	36.3%
Probability of repayment after close of business combination	95.0%
Probability of holder electing conversion option	5.0%

4. Marketable Securities

The following table summarizes the marketable securities held at December 31, 2020 (in thousands):

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Marketable securities:				
Commercial paper	$ 15,999	$ 1	$ (2)	$ 15,998
United States Treasury securities	8,000	—	—	8,000
Total marketable securities	$ 23,999	$ 1	$ (2)	$ 23,998

All marketable securities held at December 31, 2020 reached their respective maturity date during year ended December 31, 2021. No marketable securities remained outstanding at December 31, 2021.

5. Product Revenue Reserve and Allowance

The Company sells the Product principally to a limited number of customers consisting of telemedicine and online pharmacies, that in turn resell the Product to end-user patients and healthcare providers. Patients are required to have a prescription in order to purchase the Product in the US.

Roman Health Pharmacy LLC

In August 2019, the Company entered into a two-year exclusive supply and distribution agreement with Roman Health Pharmacy LLC ("Ro"), giving Ro exclusive distributor rights to sell the Product via telehealth platforms in the United States. Ro submits purchase orders as needed to Cardinal Health, the Company's third-party logistics distribution agent for commercial sales of the Product, and Cardinal Health ships to Ro. Pursuant to the terms of the 2019 agreement, the Company retained control of the Product until Ro received an end-user purchase order and prepared the Product for shipment to Ro patients, at which time control passes to Ro. The Company began shipping products to Ro in May 2020. The Company recognized revenue based on units shipped by Ro to end-users.

In January 2021, the Company and Ro amended and restated its customer agreement. Pursuant to the amended and restated agreement, the Company received $10.0 million of cash as a pre-buy commitment for Product which was recorded to current deferred income in the accompanying consolidated balance sheets. Additionally, the amended and restated agreement ended the consignment arrangement with Ro and the Company no longer retains control of any units shipped to Ro under the amended terms. Henceforth, all products shipped to Ro are immediately recognized as revenue upon the transfer of physical control.

In July 2021, the Company and Ro entered into a second amended and restatement agreement, under which the Company received $30.0 million of cash as a second pre-buy commitment for the Product, which was recorded to current deferred income in the accompanying consolidated balance sheets. Additionally, the Company extended Ro's exclusive period by approximately one year through July 1, 2023. Upon expiration of the exclusive period as amended, the exclusive right and license under the agreement shall automatically convert to non-exclusive for the remainder of term of the agreement unless further extended. The agreement may be terminated by mutual agreement after the exclusive period expired.

During the years ended December 31, 2021 and 2020, the Company recognized $9.7 million and $2.5 million, respectively, of product revenue, net, in the accompanying consolidated statements of operations with respect to Ro. The Company recorded a deferred income balance of $31.0 million at December 31, 2021 and an accounts receivable balance of $0.6 million at December 31, 2020 with respect to Ro in the accompanying consolidated balance sheets.

GoGoMeds

In February 2020, the Company entered into a two-year exclusive distribution agreement with GoGoMeds ("GGM"), giving GGM exclusive distributor rights to all online and mail orders generated in the United States, except those via telehealth. GGM submits purchase orders as needed to Cardinal Health and Cardinal Health ships to GGM. Once GGM has accepted the delivered Product, GGM takes control of the Product and the Company is entitled to payment. The Company began shipping products to GGM in May 2020. The Company recognizes revenue based on units shipped to GGM and upon transfer of physical control. During the years ended December 31, 2021 and 2020, the Company recognized $1.5 million and $0.1 million, respectively, of product revenue, net, in the accompanying consolidated statements of operations with respect to GGM. At December 31, 2021 and December 31, 2020, the Company recorded an accounts receivable balance of $0.8 million and $0.1 million, respectively, prior to reserves and allowances, in the accompanying consolidated balance sheets with respect to GGM.

CMS Bridging DMCC

In June 2020, the Company and CMS Bridging DMCC ("CMS") entered into a set of licensing, collaboration, and investing agreements ("CMS Agreements") involving the license of the Company's intellectual property ("IP") to CMS in Singapore and Greater China (the "CMS Territory") and governing the supply of product from the Company to CMS for sale in the CMS Territory, together with an agreement for CMS to invest in the Company's Series Growth 3 & 4 Preferred Shares.

Under the terms of the CMS Agreement, the Company granted CMS an exclusive, transferable, sub-licensable, and royalty-bearing license of the Company's IP to develop, import, register, manufacture, and commercialize the Product, whether through online sales channels or offline sales channels during the term of the agreement. The agreement can be terminated earlier by mutual agreement of the parties. In accordance with the CMS Agreement, all legal and beneficial ownership of (i) all IP rights relating to the Products (including any data generated from the use of the Products and other improvements) and (ii) all of the information provided or

generated under the agreement or otherwise related to the Products shall both ultimately belong to and remain vested with the Company. CMS must purchase the Product from the Company at a markup of the Company's cost of goods sold.

As consideration for the rights and licenses granted by the Company to CMS under the agreement, CMS paid the Company a one-time, non-refundable and non-creditable upfront fee of $15.0 million and is required to pay a one-time, non-refundable, and non-creditable milestone payment of $5.0 million within thirty days after the earlier of (i) the approval of marketing authorization as a prescription product by the Product by National Medical Products Administration, and (ii) the fifth anniversary of the agreement's effective date. The CMS Agreement also contains commercial milestones due to the Company based on the achievement of annual net product revenue thresholds in the CMS Territory. Additionally, CMS shall pay the Company royalties on net sales of all products in the CMS Territory commencing January 1, 2022 through the expiration date of the agreement.

The Company determined the only performance obligation that exists is the licensing of the Product in the CMS Territory. The transactions price consisted of the $15.0 million upfront payment and the discounted time-based milestone of $3.7 million with the difference of $1.3 million accreted as interest income over five years with the remaining balance being accreted in full upon the approval of the marketing authorization as a prescription product if achieved prior to the end of the five years. The IP license granted to CMS represents a right to use the IP and therefore is recognized at a point in time, which was determined to be the effective date of the agreements. As such, the Company recognized revenue in the amount of $18.7 million during the year ended December 31, 2020, which is included under license and collaboration revenue in the accompanying consolidated statements of operations. At December 31, 2021 and December 31, 2020, the discounted time-based milestone had a balance of $4.1 million and $3.9 million, respectively, included in other assets in the accompanying consolidated balance sheets. The royalties and other commercial milestones will only be recognized in the periods in which the applicable subsequent sales occur.

Total Product Revenue, net and Reserves

During the years ended December 31, 2021 and 2020, the Company recognized $11.2 million and $2.7 million, respectively, of product revenue, net in the accompanying consolidated statements of operations. At December 31, 2021 and December 31, 2020, the Company had accounts receivable of $0.7 million and $0.8 million, respectively, prior to reserves and allowances. The following table summarizes the activity in the product revenue reserve and allowance for the years ended December 31, 2021 and 2020 (in thousands):

	Product Revenue Reserves
Balance at December 31, 2019	$ —
Provision related to product sales	980
Credits and payments made	(966)
Balance at December 31, 2020	14
Provision related to product sales	522
Credits and payments made	(454)
Balance at December 31, 2021	$ 82

At December 31, 2021 and 2020, product related reserve and allowances comprised solely contractual adjustments owed to the Company's telehealth and online pharmacy partners, which were netted to accounts receivable in the Company's consolidated balance sheets for the year. Through December 31, 2021, there had been no product related reserves or allowances owed to other parties, including the federal and state governments or their agencies.

6. Inventories

Inventories consisted of the following (in thousands):

	At December 31,	
	2021	2020
Raw materials	$ 8,074	$ 1,213
Work in process	2,643	913
Finished goods	2,786	2,433
Consignment inventories	—	563
Total inventories	$ 13,503	$ 5,122

7. Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consist of the following (in thousands):

	At December 31,	
	2021	2020
Prepaid expenses	$ 3,874	$ 1,024
Prepaid contract research costs	262	169
Research and development tax credit	579	1,131
Value added tax receivable	5,633	4,315
Deferred financing costs	3,855	38
Prepaid expenses and other current assets	$ 14,203	$ 6,677

8. Property and Equipment, Net

Property and equipment, net, consists of the following (in thousands):

	At December 31,	
	2021	2020
Laboratory and manufacturing equipment	$ 28,101	$ 8,176
Land and buildings	10,404	4,334
Leasehold improvements	1,614	1,742
Computer equipment and software	463	176
Capitalized software	228	17
Construction in process	22,097	35,551
Property and equipment – at cost	62,907	49,996
Less accumulated depreciation	(4,392)	(3,101)
Property and equipment – net	$ 58,515	$ 46,895

The Company owns and operates commercial manufacturing and research and development facilities in Italy, including a 51,000 square foot facility, which the Company expects to further expand to a 88,600 square foot facility, as well as approximately 12 acres of land, where the Company initiated construction of an additional 207,000 square foot facility. Both facilities are near the Town of Lecce in the Puglia region of Italy. Property and equipment classified as construction in process at December 31, 2021 and 2020 are related to the development of manufacturing lines that have not yet been placed into service at December 31, 2021.

Depreciation expense was approximately $1.5 million and $0.5 million and for the years ended December 31, 2021 and 2020, respectively.

9. Accrued Expenses

Accrued expenses and other current liabilities consist of the following (in thousands):

	At December 31,	
	2021	2020
Accrued payroll and related benefits	$ 1,384	$ 3,009
Accrued professional fees and outside contractors (including due to related party of $60 and $109, respectively)	4,359	3,494
Accrued property, plant and equipment additions	1,257	768
Accrued inventory and manufacturing expense	128	-
Unpaid portion of acquisition of intangible asset and investment in related party (see Note 11)	5,604	-
Income taxes payable	145	-
Deferred IPO Fees	738	-
Accrued interest	45	49
Total accrued expenses	$ 13,660	$ 7,320

10. Other Long-Term Liabilities

Other long-term liabilities consist of the following (in thousands):

	At December 31,	
	2021	2020
Deferred IPO fees	$ -	$ 738
Long-term tax liabilities	182	301
Contingent loss for research and development tax credits	2,990	3,233
Unpaid portion of acquisition of intangible asset and investment in related party (see Note 11)	-	5,912
One Srl call option (see Note 11)	2,416	1,545
Total other long-term liabilities	$ 5,588	$ 11,729

11. Significant Agreements

Puglia 1 Grant

In May 2020, the Company was awarded a grant by the Puglia region of Italy as an incentive to manufacture and carry out research and development activities in Italy ("PIA 1 Grant"), with the key underlying activity being the development of the commercial facility to expand production capacity for the Product. The PIA 1 Grant provides funding of up to €5.3 million (approximately $6.0 million at December 31, 2021) as reimbursement for certain facility and equipment investments in the Company's manufacturing facility in Calimera, Italy, and up to €3.9 million (approximately $4.4 million at December 31, 2021) as reimbursement for certain research and development expenditures over a three-year period. The Company is required to adhere to standard workplace safety regulations and local laws in Italy and is not permitted to physically move the reimbursed assets from the Puglia region for five years from the project completion date of May 2023. The Company has concluded that income recognition is appropriate as it is reasonably assured that it will comply with all the conditions of the grant and the proceeds from the grant for costs incurred to date will be received.

The Company recognized grant income of $0.5 million and $3.5 million in other income, net, on the accompanying consolidated statements of operations during the years ended December 31, 2021 and 2020, respectively, related to the PIA 1 Grant, of which $0.2 million and $0.2 million was attributable to research and development expenses and investments in facilities and equipment, respectively, during the year ended December 31, 2021 and $3.4 million and $0.1 million was attributable to research and development expenses and investments in facilities and equipment, respectively, during the year ended December 31, 2020. The Company recorded $6.4 million and $5.8 million of deferred income in the accompanying consolidated balance sheets at December 31, 2021 and 2020, respectively, of which $0.9 million and $0.6 million was recorded as a current liability, respectively, as it is

expected to be recognized within one year of the date of the accompanying consolidated balance sheets. The Company collected zero proceeds and $4.9 million from the PIA 1 grant during the years ended December 31, 2021 and 2020, respectively, and recorded a grant receivable of $5.4 million and $4.3 million in the accompanying consolidated balance sheets at December 31, 2021 and 2020, respectively.

Puglia 2 Grant

In November 2020, the Company was awarded a second grant by the Puglia region of Italy as an incentive to manufacture and carry out research and development activities in Italy ("PIA 2 Grant"), with the key underlying activity being the development of a second manufacturing line at the commercial facility to expand production capacity for the Product, and research and development activities targeting new gastrointestinal health indications. The PIA 2 Grant provides funding of up to €3.3 million (approximately $3.7 million at December 31, 2021) as reimbursement for certain facility and equipment investments in the Company's manufacturing facility in Calimera, Italy, and up to €8.3 million (approximately $9.4 million at December 31, 2021) as reimbursement for certain research and development expenditures over a three-year period. The Company is required to adhere to standard workplace safety regulations and local laws in Italy and is not permitted to physically move the reimbursed assets from the Puglia region for five years from the project completion date of November 2023. The Company has concluded that income recognition is appropriate as it is reasonably assured that it will comply with all the conditions of the grant and the proceeds from the grant for costs incurred to date will be received.

The Company recognized grant income of $1.1 million and $0.8 million in other income, net, on the accompanying consolidated statements of operations during the years ended December 31, 2021, and 2020, respectively, related to the PIA 2 Grant, which was entirely attributable to research and development expenses. The Company has recorded $3.7 million and $3.0 million of deferred income in the accompanying consolidated balance sheets at December 31, 2021 and 2020, respectively, of which $0.4 million and zero was recorded as a current liability, respectively, as it is expected to be recognized within one year of the date of the accompanying consolidated balance sheets. The Company collected $1.9 million and zero proceeds from the PIA 2 grant during the years ended December 31, 2021 and 2020, respectively, and has recorded a grant receivable of $3.6 million and $3.9 in the accompanying consolidated balance sheets at December 31, 2021 and 2020, respectively.

One S.r.l. ("One") Amended Patent License and Assignment Agreement

In October 2008 and December 2008, the Company entered into a patent license and assignment agreement and master agreement with One, the original inventor and owner of the Company's core patents and a related party to the Company (see Notes 19 and 20), to license and subsequently purchase certain intellectual property to develop hydrogel-based product candidates. In December 2014, the Company amended and restated the patent license agreement and the master agreement into a single agreement, referred to as the amended and restated master agreement. The amended and restated master agreement will remain in effect until the expiration of the last patents covered by the agreement or until all obligations under the amended and restated master agreement with respect to payments have terminated or expired.

In June 2019, the Company entered into a transaction with One that further amended the terms of the amended and restated master agreement and resulted in the Company owning 10% equity interest in One (the "2019 One Amendment"). Under the amended and restated master agreement following this transaction, €5.5 million (approximately $6.2 million at December 31, 2021) the Company would be required to pay upon the achievement of future commercial milestones from weight loss medical indications were eliminated, and the percentage of royalties the Company is required to pay on future net revenues was reduced. In return, One received additional consideration consisting of new future milestones of up to €11.0 million (approximately $12.5 million at December 31, 2021) upon the commercial success of new medical indications, and the Company was required to issue to One a warrant for redeemable convertible preferred stock equivalent to 2.7% of the shares of capital stock outstanding on an as converted basis within 30 days of the completion of a future qualifying equity financing that results in at least $50.0 million in gross proceeds. The warrant would have an exercise price equivalent to the issuance price of a future qualifying equity financing (see Note 13). As an additional component to this transaction, the Company acquired a 10% equity interest in One in exchange for cash consideration of €11.5 million (approximately $13.0 million at December 31, 2021) with a net present value of €11.1 million (approximately $12.7 million at the transaction date). During the year ended December 31, 2021 the Company did not make any payments of the agreed upon cash consideration. During the year ended December 31, 2020, the Company paid €2.6 million (approximately $3.1 million at the transaction date) of the agreed upon cash consideration. The unpaid cash consideration to One, after adjusting for a foreign currency translation gain and interest expense was $5.6 million and $5.9 million at December 31, 2021 and 2020, respectively. At December 31, 2021, all $5.6 million was included in accrued expenses in the accompanying consolidated balance sheets as it was expected to be settled within the next twelve months. At December 31, 2020, all $5.9 million was included in other long-term liabilities in the accompanying consolidated balance sheets. None of the future milestones under the master agreement, as amended, have been met, or are deemed to be probable of being met, at the transaction date or at December 31, 2021 and 2020, respectively.

The Company accounted for the reduction in royalties the Company is required to pay on future net revenues that resulted from the 2019 One Amendment as an intangible asset under ASC 350, *Intangibles – Goodwill and Other*, which shall be amortized over its useful life, which was determined to be the earliest expiration of patents related to the underlying intellectual property in November 2028. The Company accounted for the acquisition of the 10% equity interest in One under ASC 323, *Investments – Equity Method and Joint Ventures*. The Company initially allocated consideration in the June 2019 transaction on a relative fair value basis in the following manner (in thousands):

Consideration	
Cash	$ 12,668
Warrants for redeemable convertible preferred stock	4,706
Fair value of total consideration	$ 17,374
Assets acquired at relative fair value	
Intangible asset related to reduction in royalty	$ 15,564
Equity-method investment	1,810
Total assets acquired	$ 17,374

The Company accounted for tax impact of the acquisition of the intangible asset under ASC 740, Income Taxes, which resulted in the recognition of a deferred tax liability of $5.8 million, to account for the book-to-tax basis difference, that was applied to the initial carrying value of the intangible asset acquired.

A summary of the intangible asset activity that resulted from this transaction during the years ended December 31, 2021 and 2020 is as follows (in thousands):

	Intangible Assets
Intangible asset at relative fair value	$ 15,564
Adjustment to record deferred tax liability	5,783
Carrying value of intangible asset at June 2019 acquisition date	$ 21,347
Amortization expense	(1,133)
Balance at December 31, 2019	$ 20,214
Amortization expense	(2,267)
Balance at December 31, 2020	$ 17,947
Amortization expense	(2,267)
Balance at December 31, 2021	$ 15,680

In conjunction with acquiring the investment in One, the Company recognized a deferred tax asset of approximately $3.1 million which represents the excess tax basis over carrying value. The Company recorded this deferred tax asset with a corresponding decrease to the amounts initially allocated to the investment. As the deferred tax asset exceeds the initially allocated balances and results in a reduction of the initial carrying value of the $1.8 million investment balance to zero, the remaining $1.2 million excess was recorded as a deferred credit. In May 2020, the Company transferred the equity-method investment in One from the Gelesis entity in Italy to a Gelesis entity in the US. In connection with the transfer of the equity-method investment, the Company wrote-off the deferred tax asset of $3.0 million generated by the book-to-tax difference and the deferred credit of $1.2 million, resulting in an expense of $1.8 million recorded within provision for income taxes in the accompanying consolidated statements of operations during the year ended December 31, 2020.

In October 2020, the Company further amended the terms of the amended and restated master agreement with One to cancel its obligation to issue to One the warrant for redeemable convertible preferred stock agreed to in the 2019 One Amendment (the "2020 One Amendment"). In return for cancelling the warrant, One received additional consideration consisting of a commercial milestone of €6.5 million (approximately $7.4 million at December 31, 2021) upon a weight loss product reaching €2.0 billion in cumulative net sales, and certain shareholders of One were granted warrants to purchase 522,009 shares of the Company's common stock. The warrant for redeemable convertible preferred stock was remeasured prior to settlement. Additionally, the Company granted One a contingent call option to buy back the 10% ownership that the Company acquired in the 2019 One Amendment at an exercise price of €6.0 million (approximately $6.8 million at December 31, 2021). The call option is only exercisable upon (1) a change of control or a

deemed liquidation event by the Company, as defined, in the Company's Restated Certification of Incorporation (2) the date in which the Company's current Chief Executive Officer is no longer affiliated with the Company in his capacity as either an executive officer or a member of the board of directors.

The Company accounted for the 2020 One Amendment by derecognizing the carrying value of the warrant liability for redeemable convertible preferred stock on the date of the 2020 One Amendment, which had a fair value of approximately $6.0 million, and recognizing the consideration provided in the amendment, which had an aggregate fair value of approximately $5.8 million. The difference between the consideration provided by the Company and the warrant liability derecognized, approximately $0.2 million, represents a gain on settlement of the warrant liability and was recognized in other income (expense), net, on the accompanying consolidated statements of operations during the year ended December 31, 2020.

As the contingent call option granted to One shareholders to buy back the 10% investment in One did not meet the definition of a derivate under ASC 815, Derivatives and Hedging, the Company recorded the grant date fair value of the call option, approximately $1.5 million, to other long-term liabilities on the consolidated balance sheets. Increases or decreases in fair value of the contingent call option are recorded in the consolidated statements of operations. The Company accounted for the common stock warrants under ASC 815, Derivatives and Hedging, which resulted in recording the grant date fair value of the common stock warrants, approximately $4.3 million, to additional paid in capital in the accompanying consolidated balance sheets. As the common stock warrants are equity-classified, the warrants are recorded at their initial fair value and not subsequently remeasured.

The commercial milestone added as part of the 2020 One Amendment constitutes contingent consideration and was provided as additional consideration for a license or asset acquisition, representing one component of the consideration replacing the warrant liability previously provided as part of the consideration for the license. Under asset acquisition accounting, contingent consideration is not recognized until the contingency is resolved. As such, no amount was recognized for the contingent milestone on the date of the amendment.

A summary of the gain on the warrant liability settlement that resulted from the 2020 One Amendment during the year ended December 31, 2020 is as follows (in thousands):

Carrying value of warrants for redeemable convertible preferred stock	$ 5,973
Fair value of common stock warrants, net of cash consideration paid of $10	(4,312)
Fair value of contingent call option granted to One shareholders	(1,494)
Gain on warrant liability extinguishment	$ 167

Research Innovation Fund ("RIF") Financing

In August 2020, the Gelesis S.r.l. entered into a loan and equity agreement with RIF, an investment fund out of the EU, whereby Gelesis S.r.l. received €10.0 million (approximately $11.3 million at December 31, 2021) from RIF as an equity investment and €15.0 million (approximately $17.0 million at December 31, 2021) as a loan with a fixed interest rate of 6.35% per annum (see Note 12). The equity investment can be called by Gelesis, Inc., beginning in December 2023 and ending in December 2026, by paying the investment plus 15% percent annual interest. If the Company does not exercise this call option, beginning in January 2027 and ending in December 2027, RIF may put the investment to the Company at a cost of the investment amount plus 3.175% percent annual interest. The loan has a termination date of December 31, 2030 and is repayable over 8 years starting 24 months subsequent to its issuance. Any unpaid principal and interest must be repaid upon exercise of the call option by the Company, or subsequent exercise of a put option by RIF. At December 31, 2021, RIF holds approximately 20% of the equity of Gelesis S.r.l.

The Company concluded that Gelesis Inc. is the only equity investment at risk as RIF's investment is not considered equity due to the call and put options. The Company further evaluated the sufficiency of the equity at risk and concluded that given the fact that Gelesis S.r.l. had to receive the RIF investment, which represents subordinated financial support but not equity, the fair value of Gelesis Inc. equity is not sufficient to absorb its expected losses resulting from its research and development operations and business plan, rather some of its expected losses will have to be absorbed by the RIF investment.

The RIF investment is equity held by a noncontrolling interest. Since the put option does not make the equity mandatorily redeemable, and the call option is held by the Company, the noncontrolling interest is not considered mandatorily redeemable and as such, is not presented as a liability. The noncontrolling interest is therefore classified as temporary equity – noncontrolling interest, and is accounted for in accordance with ASC 810, *Consolidation*.

The noncontrolling interest is initially recorded at €10.0 million (approximately $11.3 million at transaction date, net of issuance costs of $0.4 million), the consideration allocated to the shareholder investment based on its fair value. The Company has applied ASC 810 to subsequently remeasure the noncontrolling interest, which results in no losses being attributed to the noncontrolling interest, rather,

only earnings of the Gelesis S.r.l. entity based on the shareholder rights as a whole instrument. However, the noncontrolling interest shall not be reduced below the current redemption value of the put option, which represents the initial investment plus the accrued rate of return of 3.175% per annum. Adjustments to the noncontrolling interest that result from accreting the put option to its redemption value are recorded to accumulated deficit in the accompanying consolidated balance sheets. The Company recorded accretion of $0.6 million and foreign currency translation loss of $0.5 million to the noncontrolling interest during the year ended December 31, 2020. The Company recorded accretion of $0.4 million and foreign currency translation gain of $1.0 million to the noncontrolling interest during the year ended December 31, 2021. The noncontrolling interest balance was $11.9 million and $12.4 million at December 31, 2021 and 2020, respectively, in the accompanying consolidated balance sheets.

12. Debt

Italian Economic Development Agency Loan

In May 2014, the Company entered into a loan agreement with an Italian economic development agency in connection with a grant. In February 2016, the Company received a second tranche of financing under this loan agreement. Borrowings under the loan totaled €1.2 million (approximately $1.4 million at December 31, 2021), and the loan bears interest at 0.332% per annum. The Company is required to make annual principal and interest payments from January 2017 through January 2024.

Intesa Sanpaolo Loan

In November 2019, the Company entered into a loan agreement with Intesa Sanpaolo. Initial borrowings under the loan totaled €2.4 million (approximately $2.8 million at December 31, 2021), net of transaction costs of €0.1 million (approximately $0.1 million at December 31, 2021), and the loan bears interest at base rate of 2.3% plus the 3-month Euribor rate per annum. The Company is required to make payments of interest only on borrowings under the loan agreement on a quarterly basis through and including October 31, 2021 (the interest only termination date), after which payments of principal in equal quarterly installments and accrued interest will be due until the loan matures on October 31, 2029. The Company pledged certain manufacturing facilities, excluding equipment, as collateral under this loan agreement.

During the year ended December 31, 2020, the Company borrowed an additional €5.0 million (approximately $5.7 million at December 31, 2021), net of transaction costs of approximately €13,000 (approximately $14,000 at December 31, 2021). The additional borrowings under the loan had the same terms and repayment schedule as the November 2019 loan.

In March 2021, the Company entered into another loan agreement with Intesa Sanpaolo for aggregate borrowing of up to €5.0 million. Borrowings under the second loan agreement upon closing and at December 31, 2021, totaled €4.8 million (approximately $5.4 million at December 31, 2021), net of transaction costs of €0.2 million (approximately $0.2 million at December 31, 2021), and the loan bears interest at base rate of 0.701%. The Company is required to make payments of interest only on borrowings under the loan agreement on a monthly basis through March 2023 (the interest only termination date), after which payments of principal in equal monthly installments and accrued interest will be due until the loan matures on March 26, 2024.

Horizon 2020 Loan

In December 2019, as part of the Horizon 2020 Grant (see Note 11), the Company entered into a loan agreement with the Italian Finance Ministry. Borrowings under the loan totaled €0.3 million (approximately $0.3 million at December 31, 2021), net of transaction costs and discounts of approximately €21,000 (approximately $24,000 at December 31, 2021), and the loan bears interest at 0.171% per annum. The Company is required to make payments of interest only on borrowings under the loan agreement on a semiannual basis through and including June 30, 2020 (the interest only termination date), after which payments of principal in equal semiannual installments and accrued interest will be due until the loan matures on June 30, 2028.

In October 2020, the Company borrowed an additional €0.2 million (approximately $0.2 million at December 31, 2021), net of transaction costs of approximately €19,000 (approximately $22,000 at December 31, 2021). The additional borrowings under the loan had the same terms and repayment schedule as the December 2019 loan.

RIF Shareholders Loan

In August 2020, as part of the RIF financing transaction (see Note 11), the Company entered into a loan agreement with the shareholders of RIF. Borrowings under the loan totaled €14.5 million (approximately $16.4 million at December 31, 2021), net of transaction costs of €0.5 million (approximately $0.6 million at December 31, 2021), and the loan bears interest at 6.35% per annum. The Company is required to make payments of interest only on borrowings under the loan agreement on an annual basis starting December 31, 2020 and through and including December 30, 2022 (the interest only termination date), after which payments of principal in equal annual installments and accrued interest will be due until the loan matures on December 31, 2030. If either party

exercises its call option or put option on the equity investment as part of the RIF Transaction, the unpaid principal and accrued interest as of that date must be paid by the Company.

UniCredit Loan

In November 2020, the Company entered into a loan agreement with UniCredit. Borrowings under the loan totaled €4.9 million (approximately $5.7 million at December 31, 2021), net of transaction costs and discounts of €0.1 million (approximately $0.1 million at December 31, 2021), and the loan bears interest at 2.12% per annum. The Company is required to make payments of principal and accrued interest on a semiannual basis starting December 10, 2021 until the loan matures on December 10, 2027.

PPP Loan

On March 27, 2020, the Coronavirus Aid, Relief, and Economic Security Act (the "CARES Act") was enacted to, amongst other provisions, provide emergency assistance for individuals, families and businesses affected by the COVID-19 pandemic. The CARES Act includes a Paycheck Protection Program ("PPP") administered through the Small Business Association ("SBA"). Under the PPP, beginning April 3, 2020, small businesses and other entities and individuals could apply for loans from existing SBA lenders and other approved regulated lenders that enroll in the program, subject to numerous limitations and eligibility criteria.

In April 2020, the Company issued a promissory note to Silicon Valley Bank, pursuant to which it received loan proceeds of $0.3 million (the "PPP Loan") provided under the PPP established under the CARES Act and guaranteed by the U.S. Small Business Administration. In November 2020, the Company was notified by Silicon Valley Bank that the PPP Loan had been fully forgiven by the SBA and there is no remaining balance on its account. The Company recognized income of $0.3 million in other income on the consolidated statements of operations during the year ended December 31, 2020, for debt extinguishment pursuant to ASC 470, *Debt*.

2021 Bridge Financing

On December 13, 2021, the Company entered into a bridge financing arrangement, executing convertible promissory note agreements for $12.0 million with SSD2 an existing investor and related party (see Note 20) and $15.0 million with PureTech, an existing investor and related party (see Note 20). These promissory notes bear interest at 10% and shall be settled in cash for principal plus accrued interest by the third (3rd) business day following the closing of the Business Combination Agreement with CPSR, or thirty (30) days following the termination of the Business Combination Agreement. In the event the Business Combination Agreement is terminated, the majority holders of the promissory notes may elect to convert outstanding principal and interest into the securities being issued and sold to investors in a subsequent qualified financing at a discounted conversion price equal to 75% of the price per share paid by other investors in the financing. The Company elected to recognize the hybrid instrument at fair value at issuance and record subsequent changes in fair value in the accompanying consolidated statements of operations (see Note 3). At issuance the Company determined the aggregate fair value of the convertibles promissory notes was $27.0 million. At December 31, 2021, the fair value was determined to be $27.1 million. During the year ended December 31, 2021, the Company recognized a loss of $0.1 million with respect to the change in fair value of the convertible promissory notes on the accompanying consolidated statements of operations.

Future maturities with respect to non-convertible debt outstanding at December 31, 2021 are as follows (in thousands):

	At December 31, 2021
2022	2,183
2023	8,585
2024	5,771
2025	4,199
2026	4,221
More than 5 years	12,877
Unamortized loan discount and issuance costs	(754)
Total obligation	$ 37,081

13. Warrants

Summary of Outstanding Warrants

The following represents a summary of the warrants outstanding at December 31, 2021:

Issued	Classification	Exercisable for	Number of Shares Issuable
August 2013	Liability	Series A-4 redeemable convertible preferred stock ("Series A-4")	708,493
October 2020	Equity	Common stock	522,009

The following represents a summary of the warrants outstanding at December 31, 2020:

Issued	Classification	Exercisable for	Number of Shares Issuable
April 2011	Liability	Series A-1 redeemable convertible preferred stock ("Series A-1")	74,784
June 2012	Liability	Series A-3 redeemable convertible preferred stock ("Series A-3")	238,189
August 2013	Liability	Series A-4 redeemable convertible preferred stock ("Series A-4")	708,493
October 2020	Equity	Common stock	522,009

Warrants Issued in Connection with 2008 Loan Agreement

In April 2011, in connection with an amendment to the 2008 Loan, the Company issued a warrant to purchase shares of Series A-1 at an exercise price equal to the lower of $4.44 per share or the price per share received in the first sale of shares of the Company's stock resulting in at least $5.0 million gross proceeds to the Company. The warrant is exercisable for the number of shares of Series A-1 equal to the quotient of $0.3 million divided by the exercise price of the warrant. Following the issuance of Series A-5 redeemable convertible preferred stock ("Series A-5") in March 2015 (see Note 14) the warrant became exercisable for 74,784 shares of Series A-1 at an exercise price of $4.44. The warrant terminates upon the earlier of (i) April 27, 2021, (ii) three years after the effective date of an initial public offering or (iii) a sale of the Company. The warrant liability is remeasured at each reporting date with increases or decreases in the fair value being recorded in the consolidated statements of operations. The fair value of the warrants was $0.6 million at December 31, 2020. In April 2021, the Company issued 52,222 shares of Series A-1 upon the net exercise of the remaining outstanding warrants. The warrants exercised had an aggregate fair value of $0.9 million on the date of exercise. No Series A-1 warrants remained outstanding at December 31, 2021.

Series A-3 Warrants

In June 2012, in connection with an amendment to the Master Agreement and Patent and License Assignment Agreement with One (see Note 11), in exchange for the right to expand the field use of the intellectual property purchased, the Company issued fully vested warrants to purchase 238,189 shares of Series A-3 at an exercise price of $0.04 per share. The warrant is subject to automatic exercise upon a deemed liquidation event, as defined, in the Company's Restated Certification of Incorporation. The warrants expire in June 2022.

The fair value of the warrants was $0.7 million at the date of issuance and was recorded as a research and development expense, and a corresponding warrant liability was recorded as a component of other non-current liabilities. The warrant liability is remeasured at each reporting date with increases or decreases in the fair value being recorded in the consolidated statements of operations. The fair value of the warrants was $2.9 million at December 31, 2020. In March 2021, the Company issued 238,189 shares of Series A-3 upon the exercise of the remaining outstanding warrants. The warrants exercised had an aggregate fair value of $3.0 million on the date of exercise. No Series A-3 warrants remained outstanding at December 31, 2021.

Series A-4 Warrants

In August 2013, in connection with the issuance of Series A-4, the Company issued contingent warrants to purchase 719,670 shares of Series A-4 at an exercise price of $0.04 per share. Such warrants were issuable if the Company did not sell shares of its common stock in a firm commitment underwritten public offering on or before February 15, 2015 or if the Company was liquidated, dissolved,

wound up or closes a deemed liquidation event prior to an IPO. The warrants were issued in February 2015 when the contingencies were not met. The warrants expire in February 2025.

The fair value of the warrants was $1.7 million at the date of issuance and was recorded as a research and development expense, and a corresponding warrant liability was recorded as a component of other non-current liabilities. The warrant liability is remeasured at each reporting date with increases or decreases in the fair value being recorded in the consolidated statements of operations. In October 2020, the Company issued 11,177 shares of Series A-4 upon the exercise of the associated warrants. The warrants exercised had an aggregate fair value of $0.1 million on the date of exercise. At December 31, 2021 and 2020, 708,493 warrants remained outstanding with an aggregate fair value of $15.8 million and $8.6 million, respectively.

Series 3 Growth Warrants

In June 2019, in connection with the terms of the amended and restated master agreement between the Company and One, the Company agreed to issue to One a warrant for redeemable convertible preferred stock equivalent to 2.7% of the shares of capital stock outstanding on an as converted basis within 30 days of the completion of a future equity financing that results in at least $50.0 million in gross proceeds with an exercise price equal to the issuance price of the future equity financing (see Note 11).

Due to the fact that the settlement value was dependent on something other than the fair value of the issuer's equity shares, ASC 480 – *Distinguishing Liabilities from Equity* required that the warrants be accounted for as liabilities, until such time that the warrants truly became 'fixed for fixed' and no longer had any potential changes in the settlement value due to the underlying contingent events. The Company determined its obligation to issue such warrants was a component of the consideration issued to One in the June 2019 transaction. The Company determined such future warrants had a fair value of $4.7 million as of the transaction date based on the terms of the warrant per the amended and restated master agreement and its capital structure. The warrant liability is remeasured at each reporting date with increases or decreases in the fair value being recorded in the consolidated statements of operations. The warrant liability had a fair value of $4.6 million at December 31, 2019.

In December 2019, the Company entered into the Series 3 & 4 Growth Preferred Stock Purchase Agreement (the "Series 3 & 4 Growth Agreement"), under which, it closed a $50.0 million equity financing round for Series 3 Growth (see Note 11) and the warrant became issuable for 478,828 shares of Series 3 Growth.

In October 2020, the Company and One amended the terms of the amended and restated master agreement which resulted in the Company being relieved from its obligation to issue the warrants for Series 3 Growth in exchange for the delivery of warrants to common stock, a contingent call option and contingent consideration of the commercial milestone (see Note 11). The warrant liability relating to the obligation to issue Series 3 Growth warrants was adjusted to its extinguishment date fair value of $6.0 million prior to being derecognized. The difference between the consideration provided by the Company and the warrant liability derecognized resulted in a gain on warrant liability extinguishment of $0.2 million and was recognized in other income on the accompanying consolidated statements of operations during the year ended December 31, 2020. No Series 3 Growth warrants remained outstanding at December 31, 2020.

Series 4 Growth Options

Pursuant to the Series 3 & 4 Growth Agreement, Series 3 Growth shareholders were given the right, but not the obligation, to purchase shares of Series 4 Growth at a purchase price of $20.72, within one year of the Series 3 Growth initial closing in December 2019 (the "Series 4 Growth Options").

In conjunction with the 2,973,270 shares of Series 3 Growth issued during the Series 3 Growth initial closing, the Company issued 2,419,573 Series 4 Growth Options. During the year ended December 31, 2020, the Company issued an additional 2,845,625 shares of Series 3 Growth to current and new investors, resulting in the issuance of an additional 2,371,812 Series 4 Growth Options.

The Series 4 Growth Options were evaluated under ASC 480 – *Distinguishing Liabilities from Equity* and it was determined that they met the requirements for separate accounting as freestanding financial instruments and should be classified as liabilities, as they relate to an obligation to issue shares that are potentially redeemable. From an accounting perspective, the Company determined that the Series 4 Growth Options should be accounted for as a warrant for redeemable convertible preferred shares. Accordingly, the Company recorded a warrant liability for Series 4 Growth Options upon issuance at fair value with the corresponding offset recorded as a discount to the Series 3 Growth. The Series 4 Growth Options liability is remeasured at each reporting date up to the exercise or expiration of the options with increases or decreases in fair value being recorded in the consolidated statements of operations. At the date of issuance, the fair value of the Series 4 Growth Options was recorded at $0.7 million as a current liability in the accompanying consolidated balance sheets, as it was set to expire in December 2020 if unexercised. In connection with the subsequent issuances of Series 3 Growth in 2020 (see Note 14), the Company recorded an additional $0.7 million as a Series 4 Growth Option liability. In

December 2020, the Series 4 Growth Options expired, resulting in a gain on the change in fair value of $1.4 million during the year ended December 31, 2020.

Common Stock Warrants

In October 2020, in connection with the 2020 One Amendment (see Note 11), the Company granted certain shareholders of One warrants to purchase 522,009 shares of the Company's common stock. The Company accounted for the common stock warrants under ASC 815, *Derivatives and Hedging*, which resulted in recording the grant date fair value of the common stock warrants, approximately $4.3 million, to additional paid in capital on the consolidated balance sheets. As the common stock warrants are equity-classified, the warrants are recorded at their initial fair value and are not subsequently remeasured.

14. Redeemable Convertible Preferred Stock

Redeemable convertible preferred stock consisted of the following at December 31, 2021 (in thousands, except for share data):

	Preferred Stock Authorized	Issued and Outstanding	Liquidation Preference	Carrying Value	Common Stock Issuable Upon Conversion
Series A-1	1,711,755	1,689,193	$ 7,505	$ 7,113	1,689,193
Series A-2	1,161,254	1,161,254	3,030	3,033	1,161,254
Series A-3	1,730,874	1,730,874	5,188	7,460	1,730,874
Series A-4	2,159,022	1,450,529	5,473	2,602	1,450,529
Series A-5	1,977,114	1,977,114	24,536	44,307	1,977,114
Series Growth	2,538,274	2,538,274	31,500	56,959	2,538,274
Series 2 Growth	2,370,803	2,370,803	30,370	53,201	2,370,803
Series 3 Growth	6,308,529	5,818,895	150,768	136,919	5,818,895
Total	19,957,625	18,736,936	$ 258,370	$ 311,594	18,736,936

Redeemable convertible preferred stock consisted of the following at December 31, 2020 (in thousands, except for share data):

	Preferred Stock Authorized	Issued and Outstanding	Liquidation Preference	Carrying Value	Common Stock Issuable Upon Conversion
Series A-1	1,711,755	1,636,971	$ 7,273	$ 6,176	1,636,971
Series A-2	1,161,254	1,161,254	3,030	3,033	1,161,254
Series A-3	1,730,874	1,492,685	4,474	4,463	1,492,685
Series A-4	2,159,022	1,450,529	5,473	2,602	1,450,529
Series A-5	1,977,114	1,977,114	24,536	24,991	1,977,114
Series Growth	2,538,274	2,538,274	31,500	32,763	2,538,274
Series 2 Growth	2,370,803	2,370,803	30,370	30,684	2,370,803
Series 3 Growth	6,308,529	5,818,895	150,768	108,813	5,818,895
Total	19,957,625	18,446,525	$ 257,424	$ 213,525	18,446,525

Series A-1

In April 2011, the Company issued units comprised of 1,636,971 shares of Series A-1 and 1,636,971 shares of common stock upon the conversion of $3.2 million of outstanding principal and accrued interest related to convertible notes issued in 2009 and 2010 and $0.4 million of deferred interest related to the 2008 Loan. The conversion was based on an issuance price of $4.44 per unit, whereby each unit is comprised of one share of Series A-1 and one share of common stock.

In April 2021, the Company issued 52,222 shares of Series A-1 upon the net exercise of the Series A-1 warrants. The warrants exercised had an aggregate fair value of $0.9 million on the date of exercise.

Series A-2

In May 2011, the Company issued:

- 409,440 shares of Series A-2 at an issuance price of $2.61 per share, resulting in gross proceeds of $1.1 million.
- 284,249 shares of Series A-2 upon conversion of $0.6 million outstanding principal and accrued interest on convertible notes issued in 2011 at a conversion price of $1.96 per share, recorded at the fair value of Series A-2 issued of $0.7 million.

- 191,625 shares of Series A-2 upon conversion of $0.5 million of deferred interest related to the 2008 Loan, based on an issuance price of $2.61 per share.

In addition, in May 2011, the Company entered into an agreement with PureTech Health LLC ("PureTech") to issue a total of 275,940 shares of Series A-2 in exchange for management and consulting services (see Note 20). The fair value of the services was not readily determinable and, accordingly, the initial carrying value of Series A-2 issued in exchange for services was equal to the then-current fair value of the Series A-2 of $0.7 million, based on the Series A-2 issuance price of $2.61 per share.

Series A-3

In June 2012, the Company issued 1,017,648 shares of Series A-3 at an issuance price of $3.00 per share resulting in gross proceeds of $3.1 million and the Company incurred issuance costs of approximately $10,000. In June 2012, the Company issued 219,792 shares of Series A-3 upon conversion of $0.7 million of outstanding principal and accrued interest related to a promissory note issued in 2012 at an issuance price of $3.00 per share and 255,245 shares of Series A-3 upon the conversion of $0.7 million of outstanding principal and accrued interest related to a bridge loan issued in 2012 at $2.85 per share.

In March 2021, the Company issued 238,189 shares of Series A-3 upon the exercise of the Series A-3 warrants. The warrants exercised had an aggregate fair value of $3.0 million on the date of exercise.

Series A-4

In August 2013, the Company issued 1,439,352 equity units, each consisting of (i) one share of Series A-4 with a contingently issuable warrant to purchase 50% of one share of Series A-4 and (ii) one share of common stock of the LLC with a contingently issuable warrant to purchase 50% of one share of common stock of the LLC, for $3.00 per unit, resulting in proceeds of $4.3 million, net of issuance costs of approximately $11,000. The Company determined that the warrants to purchase shares of Series A-4 met the criteria for classification as a liability and were to be accounted for at fair value (see Note 13). Accordingly, the proceeds from the sale of the equity units were first allocated to the Series A-4 warrants at their fair value at issuance of $1.7 million, with the residual proceeds allocated to the Series A-4, the LLC common stock and the LLC common warrants based on their relative fair values of $2.5 million, $0.1 million and $0.1 million, respectively.

In October 2020, the Company issued 11,177 shares of Series A-4 upon the exercise of the Series A-4 warrants. The warrants exercised had an aggregate fair value of $0.1 million on the date of exercise.

Series A-5

In March 2015, the Company issued 1,450,265 shares of Series A-5 at an issuance price of $12.41 per share resulting in gross proceeds of $18.0 million and the Company incurred issuance costs of $0.1 million. In conjunction with the financing, approximately $4.3 million of outstanding principal and accrued interest on the 2014 Bridge Notes converted to 492,900 shares of Series A-5 at a conversion price of $8.69. In a subsequent and final closing in April 2015, the Company issued 33,949 shares of Series A-5 at an issuance price of $12.41 per share resulting in gross proceeds of $0.4 million.

Series Growth

In December 2015, the Company issued 2,538,274 shares of Series Growth to current and new investors at an issuance price of $12.41 per share resulting in gross proceeds of $31.5 million and the Company incurred issuance costs of $0.1 million.

Series 2 Growth

In February 2018, the Company entered into the Series 2 Growth Preferred Stock Purchase Agreement with current investors (the "Series 2 Growth Initial Purchasers"). In the February 2018 closing, the Series 2 Growth Initial Purchasers purchased 780,640 shares of Series 2 Growth at an issuance price of $12.81 resulting in gross proceeds of $10.0 million and the Company incurred issuance costs of $0.2 million. The Series 2 Growth Initial Purchasers also agreed to purchase up to 1,561,280 additional Series 2 Growth shares for aggregate proceeds of $20.0 million in subsequent closings.

In the June 2018 closing, the Company issued 9,269 shares of Series 2 Growth resulting in gross proceeds of $0.1 million and the Company incurred issuance costs of approximately $6,000. In September 2018, under the Series 2 Growth Tranche Rights, the Company issued 390,320 shares of Series 2 Growth resulting in gross proceeds of $5.0 million and incurring issuance costs of approximately $7,000. In December 2018, the Company issued 390,320 shares of Series 2 Growth resulting in gross proceeds of $5.0 million. No issuance costs were incurred in conjunction with this issuance.

In April 2019, the Company issued 390,320 shares of Series 2 Growth resulting in gross proceeds of $5.0 million. No issuance costs were incurred in conjunction with this issuance. Subsequently in April 2019, the Company issued 409,574 shares of Series 2 Growth resulting in gross proceeds of $5.2 million. No issuance costs were incurred in conjunction with this issuance.

Series 3 Growth

In December 2019, the Company entered into the Series 3 Growth Preferred Stock Purchase Agreement with current and new investors (the "Series 3 Growth Initial Purchasers"). In the December 2019 closing, the Series 3 Growth Initial Purchasers purchased 2,269,831 shares of Series 3 at an issuance price of $17.27 per share, resulting in gross proceeds of $39.2 million and incurred issuance costs of $0.3 million. As part of the Series 3 & 4 Growth Agreement certain Series 3 Growth Initial Purchasers agreed to purchase, 775,911 additional Series 3 Growth shares at $17.27 per share for aggregate proceeds of $13.4 million in subsequent closings (the "Series 3 Growth Tranche Rights") (see Note 3). The fair value of the Series 3 Growth on the date of issuance was determined by the Company to be $17.09 per share with the assistance of a third-party valuation specialist.

In April 2020, the Company issued 818,990 shares of Series 3 Growth resulting in gross proceeds of $14.1 million and incurring issuance costs of approximately $26,000. The issuance included 775,911 shares under the Series 3 Growth Tranche Rights. The Series 3 Growth Tranche Rights liability was remeasured to its estimated fair value immediately prior to settlement, resulting in $0.3 million of income being recorded in the consolidated statements of operations. The tranche issuance was the final Series 3 Growth tranche closing and resulted in the settlement of the remaining $0.1 million of Series 3 Growth Tranche Rights.

In June 2020, the Company issued 1,158,077 shares of Series 3 Growth to CMS in conjunction with the CMS Bridging DMCC Licensing, Collaboration, and Investing Agreements (see Note 5) resulting in gross proceeds of $20.0 million and incurring issuance costs of $0.2 million. In August 2020, the Company issued 868,558 shares of Series 3 Growth resulting in gross proceeds of $15.0 million and incurring issuance costs of $0.1 million.

Redeemable Convertible Preferred Stock Rights and Preferences

On December 2, 2019, the Company filed its Twelfth Amended and Restated Certificate of Incorporation which amended the terms of the Company's redeemable convertible preferred stock to designate Series A-1, Series A-2, Series A-3 and Series A-4 as Junior Preferred Stock, collectively, and Series A-5, Series Growth, Series 2 Growth, Series 3 Growth and Series 4 Growth as Senior Preferred, collectively, and together with the Junior Preferred, the Series Preferred.

In addition, the Twelfth Amended and Restated Certificate of Incorporation designated Series Growth and Series 2 Growth as Junior Growth Preferred, collectively, and Series 3 Growth and Series 4 Growth as Senior Growth Preferred, collectively.

Voting

The holders of Series Preferred have full voting rights and powers equal to the rights and powers of holders of shares of common stock, with respect to any matters upon which holders of shares of common stock have the right to vote. Holders of Series Preferred are entitled to the number of votes equal to the number of whole shares of common stock into which such share of Series Preferred could be converted at the record date for determination of the stockholders entitled to vote on such matters. Holders of record of the shares of common stock and preferred stock, voting together as a single class, are entitled to elect the directors of the Company.

Dividends

Liquidation Preference Prepayment Dividends

On June 27, 2012, the terms of the Series Preferred were amended. An 8% non-cumulative dividend payable when and if declared by the Board was replaced with a liquidation preference prepayment dividend ("Liquidation Preference Prepayment Dividend"). The Senior Growth Preferred Stock rank senior to the Junior Growth Preferred Stock, which rank senior to the Series A-5, which rank senior to the Junior Series Preferred Stock in the event of a Liquidation Preference Prepayment Dividend. The Board of Directors, which is controlled by Series 3 Growth holders at December 31, 2021, may elect to declare of the above designations of Series Preferred, one or more dividends equal to the liquidation preference of such shares, or any portion thereof, to the holders of such shares. If a liquidation preference prepayment dividend is paid, it would reduce the liquidation preference payable to the respective Series Preferred holders upon liquidation or deemed liquidation.

Dividends subsequent to Liquidation Preference Prepayment Dividend

After Liquidation Preference Prepayment Dividends have been paid in full and after the holders of common stock have received aggregate dividends per share equal to the lowest per share Liquidation Preference Prepayment Dividend, then the holders of Series Preferred will participate in any dividends declared on a pro rata basis with common stock.

Liquidation Preference

The Senior Growth Preferred Stock rank senior to the Junior Growth Preferred Stock, which rank senior to the Series A-5, which rank senior to the Junior Series Preferred Stock, which rank senior to Company's common stock in the event of liquidation dissolution or winding-up of the Company.

In the event of any liquidation, dissolution or winding-up of the Company, the holders of Senior Growth Preferred shall be entitled to receive, prior to any distributions being made to Junior Growth Preferred, Series A-5, Junior Preferred and common stock, an amount per share equal to one and one-half times (1.5x) the original issuance price ($17.27 and $20.72 per share for Series 3 Growth and Series 4 Growth, respectively) less any Liquidation Preference Prepayment Dividend paid for such shares of Senior Growth Preferred, plus any dividends declared but unpaid. If upon liquidation, dissolution or winding up of the Company, the assets available for distribution are insufficient to pay the Senior Growth Preferred the full amount to which they are entitled, the holders of Senior Growth Preferred share ratably in any distribution of the assets.

After payment to holders of the Senior Growth Preferred, the Junior Growth Preferred, Series A-5, and Junior Series Preferred, each shall be entitled to receive, prior and in preference to any distribution of any of the assets of the Company to the holders of a lower ranking designation of stock an amount per share equal to the greater of (i) the applicable original issue price ($12.81, $12.41, $12.41, $3.77, $3.00, $2.61, and $4.44 per share for Series 2 Growth, Series Growth, Series A-5, Series A-4, Series A-3, Series A-2, and Series A-1, respectively), less any Liquidation Preference Prepayment Dividend paid for such shares of the respective designation of stock, plus any dividends declared but unpaid, or (ii) such amount per share as would have been payable had all shares of Series Preferred been converted into common stock immediately prior to such liquidation, dissolution or winding up, less any Liquidation Preference Prepayment Dividend paid for such shares of the respective designation of stock and after giving effect to any other applicable Liquidation Preference Prepayment Dividend. If upon liquidation, dissolution or winding up of the Company, the assets available for distribution are insufficient to pay the holders of a particular designation of stock the full amount to which they are entitled, the holders of the particular designation of stock share ratably in any distribution of the assets.

In the event of any liquidation, dissolution or winding-up of the Company, after the Series Preferred liquidation payments have been made, the remaining assets for distribution shall be distributed among the holders of the Senior Growth Preferred and common stock pro rata based on the number of shares held by each Senior Growth Preferred and common stockholder, treating for this purpose all such securities as if they had converted to common stock.

Redemption

Modification of Senior Preferred Stock terms

On February 28, 2018, the terms of the Senior Series Preferred were amended to add a redemption feature provided to holders of the Senior Preferred Stock. Shares of Senior Preferred Stock shall be redeemed by the Company, upon an elective redemption request by the investors on or after February 28, 2025, at a price equal to the greater of i) the conversion price per share, plus all declared but unpaid dividends thereon, and ii) the fair market value of a single share of each applicable series of Senior Preferred. Outstanding shares of Senior Preferred Stock shall be accreted to the redemption value at each reporting period, with the offset recorded to additional paid-in capital in the accompanying consolidated balance sheets.

On December 2, 2019, the redemption date was amended to December 2, 2026.

Conversion

Each share of Series Preferred is convertible at the option of the holder at any time after issuance into the number of fully paid and nonassessable shares of common stock as determined by dividing the original issue price of each series of preferred stock by the conversion price of each series in effect at time of the conversion. The initial conversion price is the respective original issue price, subject to adjustment in accordance with the antidilution provisions of each series. Each Series Preferred will subject to automatic conversion into common stock in the event of either (i) a qualified initial public offering that results in minimum gross proceeds to the Company of $50.0 million and a price of at least $17.27 per share, or (ii) at the election of the holders of a majority of the then outstanding Series Preferred. Each share of Series Preferred will be automatically converted into one share of common stock at the then effective conversion rate, provided however that in the event of a qualified initial public offering, the holders of the Senior Growth Preferred Stock will be entitled to receive additional shares of common stock equal to one and one-half times (1.5x) the original issue price of the Senior Growth Preferred divided by the price per share of common stock offered in such initial public offering. Series A-3 may only be converted at the election of the holders of a majority of the then outstanding Series A-3 and the Board of Directors in its sole discretion if the conversion occurs following the payment in full of the Series Preferred Liquidation Preference Payment. At December 31, 2021, none of the outstanding shares of Series Preferred were converted into common stock.

15. Common Stock

The holders of the common stock are entitled to one vote for each share of common stock. Subject to the payment in full of all preferential dividends to which the holders of the preferred stock are entitled, the holders of common stock shall be entitled to receive dividends out of funds legally available. In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company, after the payment or provision for payment of all debts and liabilities of the Company and all preferential amounts to which

the holders of preferred stock are entitled with respect to the distribution of assets in liquidation, the holders of common stock shall be entitled to share ratably in the remaining assets of the Company available for distribution.

At December 31, 2021 and 2020 common stock reserved for future issuance was as follows:

	At December 31,	
	2021	2020
Common stock options and RSUs outstanding	5,203,174	5,034,858
Conversion of all classes of redeemable convertible preferred stock	18,736,936	18,446,525
Issuances upon exercise of warrants to purchase Series A-1, upon conversion to common warrants	—	74,784
Issuances upon exercise of warrants to purchase Series A-3, upon conversion to common warrants	—	238,189
Issuances upon exercise of warrants to purchase Series A-4, upon conversion to common warrants	708,493	708,493
Issuances upon exercise of common stock warrants	522,009	522,009
Total common stock reserved for future issuance	25,170,612	25,024,858

16. Stock-Based Compensation

2016 Stock Option Plan

In September 2016, the Company's Board of Directors approved the 2016 Stock Option and Grant Plan (the "2016 Plan"), which supersedes the 2006 Stock Incentive Plan, and provides for the grant of incentive stock options, nonqualified stock options, and restricted stock to employees, directors, and nonemployees of the Company. The 2016 Plan was authorized to issue up to 4,018,185 shares on common stock at January 1, 2019. In June 2020, the 2016 Plan was amended to increase the number of authorized shares of common stock to 5,634,251. Under the 2016 Plan, 73,164 and 496,542 shares remained available for issuance at December 31, 2021 and 2020, respectively.

Options and restricted stock awards generally vest based on the grantee's continued service with the Company during a specified period following a grant as determined by the Board of Directors and expire ten years from the grant date. In general, awards typically vest in three years, but vesting conditions can vary based on the discretion of the Company's Board of Directors.

The fair value of the options is estimated at the grant date using Black-Scholes and recognized over the vesting period, taking into account the terms and conditions upon which options are granted. The fair value of restricted stock awards is the fair value at the date of grant reduced by the exercise price of the award, if any. The fair value of both options and restricted stock awards are amortized on a straight-line basis over the requisite service period of the awards.

Stock Option Activity

The following table summarizes the Company's stock option activity for the year ended December 31, 2021:

	Number of Options	Weighted-Average Exercise Price per Share	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2020	5,034,858	$ 9.26	6.12	$ 14,742
Granted	518,684	18.52		
Exercised	(255,062)	0.57		5,304
Forfeited	(68,090)	10.98		
Expired	(340,570)	1.49		
Outstanding at December 31, 2021	4,889,820	$ 10.39	6.17	$ 54,449
Exercisable at December 31, 2021	3,704,417	$ 9.21	5.28	$ 45,211
Nonvested at December 31, 2021	1,185,403	$ 14.10	8.95	$ 9,238

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the common stock. The total fair value of options vested during the years ended December 31, 2021 and 2020 was $5.5 million and $3.1 million, respectively.

Stock-based compensation expense is classified in the consolidated statements of operations as follows (in thousands):

	Year ended December 31,	
	2021	2020
Research and development	$ 1,565	$ 1,960
General and administrative	3,967	2,848
Total	$ 5,532	$ 4,808

The fair value of each option issued was estimated at the date of grant using Black-Scholes with the following weighted-average assumptions:

	Year ended December 31,	
	2021	2020
Fair value of common stock	$ 20.02	$ 11.18
Expected volatility	60.1%	63.6%
Expected term (in years)	5.8	5.8
Risk-free interest rate	1.1%	0.2%
Expected dividend yield	0.0%	0.0%

The weighted-average grant date fair value of stock options granted during the years ended December 31, 2021 and 2020 was $11.25 and $6.31 per share, respectively. At December 31, 2021 and 2020, there was $8.7 million and $8.7 million, respectively, of unrecognized compensation cost related to unvested stock option grants under the 2016 Plan, which is expected to be recognized over a weighted-average period of 1.7 and 2.2 years, respectively.

Restricted Stock Unit ("RSU") Activity

During the year ended December 31, 2021, the Company issued 313,354 RSUs at a weighted-average fair value of $21.41 per unit.

Each RSU entitles the holder to one share of common stock on vesting and the RSU awards are based on a cliff vesting schedule over requisite service periods in which the Company recognizes compensation expense for the RSUs. Vesting of the RSUs is subject to the satisfaction of certain performance conditions. The Company recognizes the estimated grant date fair value of these performance-based awards as stock-based compensation expense over the performance period based upon its determination of whether it is probable that the performance conditions will be achieved. The Company assesses the probability of achieving the performance conditions at each reporting period. Cumulative adjustments, if any, are recorded to reflect subsequent changes in the estimated or actual outcome of performance-related conditions.

During the year ended December 31, 2021, as the Company deemed the outcome of the performance condition probable, the Company recognized $36,000 with respect to certain RSUs within general and administrative expense on the accompanying consolidated statements of operations. At December 31, 2021, unrecognized compensation cost for RSU awards granted totaled $6.7 million..

17. Income Taxes

Consolidated (loss) income before income taxes on a geographic basis during the years ended December 31, 2021 and 2020 are as follows (in thousands):

	Year Ended December 31	
	2021	2020
United States	$ (86,693)	$ (19,658)
Non-U.S.	(6,637)	(4,208)
Total	$ (93,330)	$ (23,866)

The provision for income taxes consists of the following components during the years ended December 31, 2021 and 2020 (in thousands):

	Year Ended December 31,	
	2021	2020
Current tax expense (benefit):		
U.S. federal	$ —	$ —
Foreign	17	(24)
Total current tax expense (benefit)	17	(24)
Deferred tax expense:		
U.S. federal	—	—
State	—	—
Foreign	—	2,063
Total deferred tax benefit	—	2,063
Total provision for income taxes	$ 17	$ 2,039

A reconciliation setting forth the differences between the effective tax rates of the Company for the years ended December 31, 2021 and 2020 and the U.S. federal statutory tax rate is as follows:

	Year Ended December 31,	
	2021	2020
U.S. Federal income tax provision expense at statutory rate	21.0%	21.0%
Effect of nondeductible stock-based compensation	0.8%	(1.9)%
Foreign rate differential	0.2%	2.2%
Mark to market of warrant liabilities	(1.7)%	(1.3)%
State taxes net of federal benefit	4.3%	4.5%
Non-deductible financing expenses	(0.3)%	0.4%
Valuation allowance	(24.2)%	(38.3)%
Investment transfer	0.0%	6.8%
Other differences	(0.4)%	(0.4)%
US federal and state research credits	0.4%	1.6%
Uncertain tax positions	(0.1)%	(1.1)%
Foreign earnings includible in US	0.0%	(2.0)%
Effective income tax rate	0.0%	(8.5)%

Significant components of the Company's consolidated deferred tax assets and liabilities at December 31, 2021 and 2020 are as follows at (in thousands):

	At December 31,	
	2021	2020
Deferred tax assets:		
Federal net operating loss carryforwards	$ 40,469	$ 24,730
State net operating loss carryforwards	10,643	7,207
Equity compensation	5,620	4,353
Accruals and reserves	-	26
Uncollected grants	998	712
Investment in subsidiaries	3,820	3,931
Research credits	1,578	1,298
Other assets	152	46
Deferred income	239	-
Interest	257	-
Deferred rent	547	600
Total deferred tax assets	64,323	42,903
Valuation allowance	(59,841)	(37,427)
Total deferred tax assets net of valuation allowance	4,482	5,476
Deferred tax liabilities:		
Intangible assets and amortization	(3,932)	(4,680)
Right-of-Use asset	(536)	(591)
Other liabilities	(14)	(204)
Total deferred tax liabilities	(4,482)	(5,476)
Net deferred tax assets	$ —	$ —

Deferred income taxes reflect the net tax effect of temporary differences between the carrying amount of assets and liabilities for financial reporting purposes and the amount used for income tax purposes. At December 31, 2021 and 2020, the Company has federal net operating loss carryforwards totaling $184.6 million and $114.4 million, respectively, of which $63.5 million expire in 2027 through 2037 and $121.1 million do not expire. At December 31, 2021 and 2020, the Company has state net operating loss carryforwards totaling $168.4 million and $114.0 million, respectively, which expire in 2030 through 2041, as well as other temporary differences and attributes that will be available to offset regular taxable income during the carryforward period. At December 31, 2021, the Company has foreign net operating loss carryforwards of $7.1 million which do not expire.

Under the provisions of the Internal Revenue Code, the net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating loss and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has not completed a change in control analysis, as defined under Sections 382 and 383 of the Internal Revenue Code, through December 31, 2021 and has not determined whether the future utilization of net operating loss carryforwards may be materially limited based upon past financings. In addition, the Company may complete future financings that could result in an ownership change, which may limit the Company's ability to utilize its tax attributes.

The Company files income tax returns in Italy, the United States and in various state jurisdictions with varying statutes of limitations. Due to net operating losses incurred, the Company's tax returns from inception to date are subject to examination by taxing authorities.

The Company has evaluated the positive and negative evidence bearing upon the realizability of its net deferred tax assets and determined that it is not more likely than not that the Company will recognize the benefits of the net deferred tax assets. Therefore, a

full valuation allowance has been recorded against the balance of net deferred tax assets in the United States. Additionally, the Company has determined that it is not more likely than not that the Company will recognize the benefits of the net deferred tax assets in Italy, primarily due to uncertainty regarding continued funding of the operations of Italy and from the restructuring of the intercompany services agreement between Gelesis, Inc., and Gelesis S.r.l., in connection with the RIF financing (see Note 11). As a result, the Company recorded a deferred tax provision of approximately $2.0 million in Italy during the year ended December 31, 2020 to establish a full valuation allowance against the balance of net deferred tax assets in Italy and maintains a full valuation allowance against the balance of net deferred tax assets in Italy as of December 31, 2021. The Company will continue to evaluate all positive and negative evidence each period.

The change in the valuation allowance during the years ended December 31, 2021 and 2020 was an increase of $22.4 million and $9.1 million, respectively. The increase in the valuation allowance during the year ended December 31, 2021 and 2020 primarily relates to an increase in net operating losses in both years as well as the establishment of a full valuation allowance in the Italian subsidiary during the year ended December 31, 2020.

The Company generally considers all earnings generated in Italy to be indefinitely reinvested. Therefore, the Company does not accrue U.S. taxes on the repatriation of the foreign earnings it considers to be indefinitely reinvested outside of the U.S. At December 31, 2021, the Company had not provided for federal income tax on $7.5 million of accumulated undistributed earnings of its foreign subsidiaries. In the event the Company were to repatriate the foreign earnings, the Company does not estimate the repatriation being subject to taxation.

The Company follows the provisions of ASC 740-10, Accounting for Uncertainty in Income Taxes, which specifies how tax benefits for uncertain tax positions are to be recognized, measured, and recorded in financial statements; requires certain disclosures of uncertain tax matters; specifies how reserves for uncertain tax positions should be classified on the balance sheet; and provides transition and interim period guidance, among other provisions. At December 31, 2021 and 2020, the Company has not recorded any liability for uncertain tax positions which relate primarily to certain federal and state research tax credits. The Company presents the uncertain tax positions as a reduction to the gross deferred tax assets with respect to research credits. The Company's policy is to recognize interest and penalties accrued on any uncertain tax positions as a component of income tax expense, if any, in its consolidated statements of operations. For the years ended December 31, 2021 and 2020, no estimated interest or penalties were recognized on uncertain tax positions. The Company does not expect that the amounts of uncertain tax positions will change significantly within the next twelve months. A reconciliation of the beginning and ending amount of uncertain tax positions is as follows (in thousands):

	Year Ended December 31,	
	2021	2020
Unrecognized tax benefits at the beginning of year	$ (281)	$ —
Increase for current year positions	(71)	(82)
Increase for prior year positions	—	(199)
Expiration of statute of limitations	—	-
Unrecognized tax benefits at the end of year	(352)	(281)
Gross research credit tax assets	1,930	1,579
Net research credit tax assets	$ 1,578	$ 1,298

18 Earnings (Loss) per Share

Basic and diluted loss per share attributable to common stockholders were calculated as follows:

	December 31,	
	2021	2020
Numerator:		
Net loss	$ (93,347)	$ (25,905)
Accretion of redeemable convertible preferred stock to redemption value	(94,134)	(11,372)
Accretion of noncontrolling interest put option to redemption value	(376)	(567)
Net loss attributable to common stockholders	$ (187,857)	$ (37,844)
Denominator:		
Weighted average common shares outstanding, basic and diluted	2,204,486	2,149,182
Net loss per share, basic and diluted	$ (85.22)	$ (17.61)

The Company's potential dilutive securities, which include stock options, redeemable convertible preferred stock and warrants have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted-average number of common stock outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same for all periods presented. The Company excluded the following potential common stock, presented based on amounts outstanding at December 31, 2021 and 2020 from the computation of diluted net loss per share attributable to common stockholders because including them would have had an anti-dilutive effect.

	December 31,	
	2021	2020
Convertible preferred stock	18,736,936	18,446,525
Warrants on convertible preferred stock	708,493	1,021,466
Options and RSUs to acquire common stock	5,203,174	5,074,547
Warrants on common stock	522,009	522,009
Total	25,170,612	25,064,547

19. Commitments and Contingencies

Operating Leases

The Company has operating leases for office, laboratory and manufacturing space with remaining terms between four and six years. Leases with initial terms of less than twelve months are not recorded as operating leases. The Company recognizes expenses for leases on a straight-line basis over the lease period and has accrued for lease expense incurred but not yet paid. While certain leases contain renewal options, the Company does not include renewal options in determining the term of the lease, used for calculating the associated lease liabilities, unless it is reasonably certain it will execute the renewal option. None of the Company's leases include variable payments, residual value guarantees or restrictive covenants.

In June 2019, the Company entered into an operating lease agreement with PureTech for office space located in Boston, Massachusetts. The lease expires in August 2025, with total lease payments of $3.2 million over the term.

At December 31, 2021, the Company's operating lease right of use assets was $2.0 million, of which $0.5 million and $1.5 million were short-term and long-term lease liabilities, respectively. At December 31, 2020, the Company's operating lease right of use assets was $2.2 million, of which $0.4 million and $1.8 million were short-term and long-term lease liabilities, respectively. Operating lease expense was $0.5 million during the years ended December 31, 2021 and 2020, respectively. The remaining noncancelable term of the Company's operating leases was 3.7 years at December 31, 2021, and the weighted average discount rate was 5.9%.

Future maturities of the lease liability under the Company's noncancelable operating leases at December 31, 2021 are as follows (in thousands):

	At December 31, 2021
2022	$ 634
2023	639
2024	555
2025	385
2026	33
More than 5 years	16
Total undiscounted lease maturities	$ 2,262
Imputed interest	(202)
Total lease liability	$ 2,060

Royalty Agreements

Expenses from royalty agreements on net product sales and sublicense income is recognized as a cost of goods sold in the accompanying consolidated statements of operations during the period in which the associated revenues are recognized.

PureTech

In December 2009, the Company entered into a royalty and sublicense income agreement with PureTech, a significant stockholder in the Company, whereby the Company is required to pay PureTech a 2.0% royalty on net product sales received as a result of developing products and technology using the intellectual property purchased from One.

One S.r.l

Under the amended and restated master agreement with One, the Company is required to pay a 2.0% royalty on net product sales and €17.5 million (approximately $19.9 million at December 31, 2021) upon the achievement of certain milestones and pay royalties on future sales and/or a percentage of sublicense income. At December 31, 2021, none of the milestones have been met.

Grant Agreements

The Company has been awarded grants from governmental agencies, which are recognized as income as the qualifying expenses are incurred (see Note 11). The grant agreements contain certain provisions, including, among others, maintaining a physical presence in the region for defined periods. Failure to comply with these covenants would require either a full or partial refund of the grant to the granting authority.

Research and Development Tax Credits

The Company's wholly owned subsidiary, Gelesis S.r.l., which conducts core research and development activities on behalf of the Company, is eligible to receive a non-income based and non-refundable tax credits for qualified research and development activities. The Company has earned research and development tax credits in Italy for qualifying expenses incurred by performing certain research and development activities. For the years ended December 31, 2021 and 2020, less than $0.1 million and $0.6 million, respectively, were recorded as other income (expense), net in the accompanying consolidated statements of operations.

In December 2018, the Italian government passed a new budget law, effective January 1, 2019, that amended the eligibility criteria for recognizing qualifying research and development tax credits ("2019 Budget Law). The 2019 Budget Law requires retroactive application for research and development tax credits earned during the year ended December 31, 2019. Under the 2019 Budget Law, research and development tax credits claimed in prior periods under previous interpretations of the research and development tax credit law may potentially be repaid by the Company.

The Company evaluated the potential loss under ASC 450, *Contingencies*. The Company concluded that the likelihood of a potential loss arising from this matter is probable.

The Company has recorded $3.0 million and $3.1 million as a component of other long-term liabilities in the accompanying consolidated balance sheets at December 31, 2021 and 2020, respectively. In October 2021, the Italian federal tax authority initiated an audit of the research and development tax credits for the calendar years 2017 through 2019. The Company expects that this tax audit will continue into 2022.

20. Related Party Transactions

The Company had the following transactions with related parties:

PureTech

In June 2019, PureTech executed a sublease agreement with Gelesis (see Note 19). With respect to the sublease, the Company incurred lease expense of $0.5 million during each of the years ended December 31, 2021 and 2020, respectively, recorded in general and administrative expenses in the accompanying consolidated statements of operations. The Company incurred royalty expense of $0.2 million and less than $0.1 million in connection with the PureTech royalty agreement (see Note 19) during the years ended December 31, 2021 and 2020, respectively, recorded in cost of goods sold in the accompanying consolidated statements of operations. The Company had an accounts payable balance to PureTech of $0.1 million and less than $0.1 million at December 31, 2021 and 2020, respectively, in the accompanying consolidated balance sheets.

On December 13, 2021, the Company issued a convertible promissory note to PureTech Health LLC in the principal amount of $15.0 million (see Note 12). At December 31, 2021, the outstanding balance was $15.1 million, recorded in notes payable in the accompanying consolidated balance sheets. The Company recorded a loss of less than $0.1 million within the consolidated statements of operations with respect to the change in fair value of the instrument.

SSD2

On December 13, 2021, the Company issued a convertible promissory note to SSD2, LLC in the principal amount of $12.0 million (see Note 12). At December 31, 2021, the outstanding balance was $12.1 million, recorded in notes payable in the accompanying consolidated balance sheets. The Company recorded a loss of less than $0.1 million within the consolidated statements of operations with respect to the change in fair value of the instrument.

One S.r.l

Consulting Agreement with Founder of One

In 2008, in connection with entering into a patent license and assignment agreement with One, the Company and one of the founders of One, who is also a stockholder of the Company, executed a consulting agreement for the development of the underlying intellectual property. The Company incurred costs for consulting services received from the founder totaling $0.3 million and $0.3 million during the years ended December 31, 2021 and 2020, respectively, recorded in research and development expense in the accompanying consolidated statements of operations. The Company recorded accrued expenses to the founder of less than $0.1 million at December 31, 2021 and 2020, respectively, in the accompanying consolidated balance sheets.

Acquisition of One

In connection with the amended and restated master agreement with One (see Note 11), Gelesis S.r.l., a VIE of the Company, acquired a 10.0% equity interest in One. During the year ended December 31, 2021 the Company made no payments to One shareholders with respect to the acquisition. During the year ended December 31, 2020, the Company made payments to One shareholders totaling $3.1 million with respect to the acquisition. The Company had remaining undiscounted payments of €5.0 million due to one at December 31, 2021 and December 31, 2020, respectively (approximately $5.7 million and $6.1 million due to One at December 31, 2021 and 2020, respectively). The balance at December 31, 2021 was recorded in accrued expenses in the accompanying consolidated balance sheets as it is expected to be settled within the next twelve months.

Additionally, the Company incurred royalty expense of $0.2 million and less than $0.1 million in connection with the One royalty agreement (see Note 19) during the years ended December 31, 2021 and December 31, 2020, respectively, recorded in cost of goods sold in the accompanying consolidated statements of operations Company had recorded accrued expenses to One Srl of $0.1 million and $3.0 million at December 31, 2021 and 2020, respectively, in the accompanying consolidated balance sheets.

RIF Transaction

In connection with the RIF transaction entered into in August 2020, the Company received $12.3 million from RIF as an equity investment that can be called by the Company beginning in December 2023 and ending in December 2026 by paying the investment plus 15.0% percent annual interest or put by RIF starting in January 2027 and ending in December 2027 for the investment amount plus 3.175% percent annual interest. RIF holds approximately 20% of the equity of Gelesis S.r.l. at December 31, 2021 (see Note 11). In addition, the shareholders of RIF provided the Company with a loan for $18.4 million with a fixed interest rate of 6.35% per annum (see Note 12).

21. Employee Benefit Plan

The Company has a 401(k) retirement plan in which substantially all U.S. employees are eligible to participate. Eligible employees may elect to contribute up to the maximum limits, as set by the Internal Revenue Service, of their eligible compensation. The Company made discretionary plan contributions of $0.2 million and $0.2 million during the years ended December 31, 2021 and 2020, respectively.

22. Subsequent Event(s)

The Company has evaluated subsequent events which may require adjustment to or disclosure in the consolidated financial statements through the date of issuance of these consolidated financial statements.

Business Combination

On January 13, 2022, CPSR, a Delaware corporation and the predecessor company consummated the previously announced business combination, pursuant to the terms of the business combination agreement, dated as of July 19, 2021 (as amended on November 8, 2021 and December 30, 2021). The business combination, together with the PIPE financing and the sale of the backstop purchase shares, generated approximately $105 million in gross proceeds. In connection with the business combination, all outstanding shares of Legacy Gelesis' Redeemable Convertible Preferred Stock and Legacy Gelesis' Warrants Exercisable for Redeemable Convertible Preferred Stock converted into Gelesis Holdings Common Stock and Gelesis Holdings Common Warrants, respectively, pursuant to an exchange ratio of 2.59. On January 14, 2022, certain of the Gelesis Holdings' securities began trading on the New York Stock Exchange under the symbols "GLS" and "GLS.W".

2021 Bridge Financing Settlement

On January 19, 2022, pursuant to the terms of the bridge financing arrangements with two existing investors, the Company settled the convertible promissory notes in cash for principal plus accrued interest in the aggregate amount of $27.3 million.