UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington D.C. 20549

FORM 20-F

☐ **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 _____

☐ **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 .....

Commission file number 001-40106

4D PHARMA PLC
(Exact Name of Registrant as specified in its charter
and translation of Registrant's name into English)

England and Wales
(Jurisdiction of incorporation or organization)

5th Floor, 9 Bond Court
Leeds
LS1 2JZ
United Kingdom
(Address of principal executive offices)

Duncan Peyton
Chief Executive Officer
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(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	Name of each exchange on which registered
American Depositary Receipts, each representing eight ordinary shares	**The Nasdaq Global Market**
Ordinary Shares, nominal value £0.0025 per share*	**The Nasdaq Global Market***
Warrants	**The Nasdaq Global Market**

* Not for trading, but in connection with the registration of American Depositary Shares, pursuant to the requirements of the Securities and Exchange Commission.

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:

Title of each class	Number of shares outstanding as of December 31, 2021
Ordinary Shares, nominal value £0.0025 per Share	180,300,967

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 definition 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. ☐

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 ☒

† 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.

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INTRODUCTION

In this Annual Report on Form 20-F the terms the "Company," "4D Pharma," "4D" and the "Group" refer to the parent company 4D pharma plc together with its consolidated subsidiaries, except where it is clear from the context that such term means only the parent company and excludes subsidiaries.

CERTAIN DEFINITIONS

Unless otherwise indicated and except where the context otherwise requires, references in this Annual Report on Form 20-F to:

- "**ADR**" are to American Depository Receipt.
- "**ADS**" are to American Depositary Shares.
- "**CMS**" are to Centers for Medicare & Medicaid Services.
- "**CNS**" are to the central nervous system.
- "**CROs**" are to contract research organizations.
- "**DSMB**" are to the data safety monitoring board.
- "**EMA**" are to the European Medicines Agency.
- "**FDA**" are to the U.S. Food and Drug Administration.
- "**HHS**" are to U.S. Department of Health and Human Services.
- "**HNSCC**" are to head and neck squamous cell carcinoma.
- "**IBD**" are to inflammatory bowel disease.
- "**IBS**" are to irritable bowel syndrome.
- "**ICI**" are to immune checkpoint inhibitor.
- "**Keytruda**" are to ICI Keytruda (pembrolizumab) made by MSD.
- "**LBPs**" are to live biotherapeutic products.
- "**MCBs**" are to master cell banks.
- "**Merck**" are to Merck Sharp & Dohme Corp.
- "**MHRA**" are to the United Kingdom's Medicines and Healthcare Products Regulatory Agency.
- "**MS**" are to multiple sclerosis.
- "**MSD**" are to Merck Sharp & Dohme Corp.
- "**MSI-H**" are to microsatellite instable.
- "**NSCLC**" are to non-small cell lung cancer.
- "**RCC**" are to renal cell carcinoma.
- "**TNBC**" are to triple negative breast cancer.
- "**UC**" are to urothelial carcinoma.
- "**USPTO**" are to the United States Patent and Trademark Office.

TRADEMARKS, TRADE NAMES AND SERVICE MARKS

4D Pharma owns or has rights to trademarks, trade names and service marks that it uses in connection with the operation of its business. In addition, 4D Pharma's names, logos and website names and addresses are its trademarks or service marks. Other trademarks, trade names and service marks appearing in this Annual Report on Form 20-F are the property of their respective owners. Solely for convenience, in some cases, the trademarks, trade names and service marks referred to in this Annual Report on Form 20-F are listed without the applicable ®, ™ and SM symbols, but they will assert, to the fullest extent under applicable law, their rights to these trademarks, trade names and service marks.

PRESENTATION OF FINANCIAL AND OTHER INFORMATION

Financial Statements

This Annual Report on Form 20-F contains our audited consolidated financial statements as of December 31, 2021 and 2020 and for the years ended December 31, 2021, 2020 and 2019 (our "**audited consolidated financial statements**"), prepared in accordance with the generally accepted accounting principles in the United States ("**GAAP**"). Our financial information is presented in U.S. dollars.

Currencies and Exchange Rates

References in this Annual Report on Form 20-F to "**USD**," "**U.S. dollars**," "**dollars**," "**$**" or "**cents**" are to the currency of the United States and references to "**GBP**," "**pounds sterling**," "**pounds**," "**£**," "**pence**" or "**p**" are to the currency of the United Kingdom. There are 100 pence to each pound.

In this Annual Report on Form 20-F, unless otherwise stated, pounds sterling have been translated into U.S. dollars at the noon buying rate in New York City for cable transfers in pounds sterling as certified for custom purposes by the Federal Reserve Bank of New York, on the date indicated. On March 25, 2022, the noon buying rate in New York City for cable transfers in pounds sterling as certified for customs purposes by the Federal Reserve Bank of New York was $1.3193 per £1.00. These translations should not be construed as a representation that the U.S. dollar amounts actually represent, or could be converted into, pounds sterling at the rates indicated.

Rounding

We have made rounding adjustments to reach some of the figures included in this Annual Report on Form 20-F. As a result, numerical figures shown as totals in some tables may not be an arithmetic aggregation of the figures that precede them.

Industry and Market Data

The industry and market data relating to our business included in this Annual Report on Form 20-F on our internal estimates and research, as well as publications, research, surveys and studies conducted by independent third parties not affiliated to us. We include data obtained from Globaldata Service (found at https://www.globaldata.com/).

Industry publications, studies and surveys generally state that they were prepared based on sources believed to be reliable, although there is no guarantee of accuracy. While we believe that each of these studies and publications is reliable, we have not independently verified the market and industry data provided by third-party sources. In addition, while we believe our internal research is reliable, such research has not been verified by any independent source. We believe that all market data in this Annual Report on Form 20-F is reliable, accurate and complete. We note that assumptions underlying industry and market data are subject to risks and uncertainties, including those discussed under "Special Note Regarding Forward-Looking Statements" and "Item 3. Key Information—D. Risk Factors" of this annual report.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 20-F contains or may contain "forward-looking statements" within the meaning of the Securities Exchange Act of 1933, as amended (the "**Securities Act**") and Section 21E of the Exchange Act. These forward-looking statements are management's beliefs and assumptions. In addition, other written or oral statements that constitute forward-looking statements are based on current expectations, estimates and projections about the industry and markets in which we operate and statements may be made by or on our behalf or included in other materials released to the public. Words such as "may," "will," "could," "should," "would," "plan," "potential," "intend," "anticipate," "project," "target," "believe," "seek," "estimate" or "expect" and other words, terms and phrases of similar nature are often intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Forward-looking statements are statements which are not historical fact and involve estimates, expectations, projections, goals, forecasts, assumptions, risks and uncertainties, and include, but are not limited to, statements regarding intent, belief or current expectations. These statements are not guarantees of future performance and involve certain risks, uncertainties and assumptions that are difficult to predict. There are a number of important factors that could cause our actual results to differ materially from those indicated by such forward-looking statements. .

Forward-looking statements are based on the current beliefs and assumptions of our management and on information currently available to our management. While our management believes that these forward-looking statements are reasonable as and when made, there can be no assurance that future developments will be as anticipated. Such statements are subject to risks and uncertainties, and actual results may differ materially from those expressed or implied in the forward-looking statements due to of various factors, including, but not limited to, those identified under the section "Item 3. Key Information—D. Risk Factors" in this annual report. These risks and uncertainties include factors relating to:

- the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics and operating as an early clinical stage company;
- our ability to develop, initiate or complete preclinical studies and clinical trials for, obtain approvals for and commercialize any of our therapeutic candidates;
- the timing, progress and results of preclinical studies and clinical trials for MRx0518, MRx-4DP0004, MRx0029, MRx0005, Blautix, Thetanix or any other of our therapeutic candidates, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work and the period during which the results of the trials will become available;
- changes in our plans to develop and commercialize our therapeutic candidates;
- the potential for clinical trials of MRx0518, MRx-4DP0004, MRx0029, MRx0005, Blautix, Thetanix or any other of our therapeutic candidates to differ from preclinical, preliminary or expected results;
- our ability to enroll patients and volunteers in clinical trials, timely and successfully completion of those trials and receipt of necessary regulatory approvals;
- our ability to continue to manufacture sufficient quantity of our therapeutic candidates and to scale manufacturing to clinical-scale and small-to-mid-scale commercial supply;
- negative impacts arising from pandemics, such as COVID-19, on our operations, including the impact on clinical trials;
- the risk of the occurrence of any event, change or other circumstance that could give rise to the termination of the strategic collaboration agreement with the University of Texas MD Anderson Cancer Center ("**MD Anderson**") or the research collaboration and option to license agreement with Merck Sharp & Dohme Corp.;
- our ability to obtain funding for our operations, including funding necessary to complete the clinical trials of any of our therapeutic candidates, and the terms on which we are able to raise additional capital;
- the risk of the occurrence of any event, change or other circumstance that could give rise to the triggering the security agreement with Oxford Finance Luxembourg S.À R.L., which is secured by our assets;
- regulatory developments in the United Kingdom, the United States and other countries;
- our reliance on third parties, including contract research organizations;
- our ability to claim UK Research and Development tax credits;
- our estimates regarding future expenses, revenues and needs for additional financing and the accuracy thereof, including the risk that values on financial instruments, such as warrants and share options, create unforeseen fluctuations in profits and tax liability;
- our ability to obtain and maintain intellectual property protection for our therapeutic candidates;
- the future composition of our management team and directors and those of our subsidiaries;
- competition in the industry in which we operate;
- matters relating to Brexit; and
- other risk factors discussed under "Item 3. Key Information—D. Risk Factors."

The foregoing list is not intended to be exhaustive, and there may be other key risks that are not listed above that are not presently known to us or that we currently deem immaterial. Should one or more of these or other risks or uncertainties materialize, or should any of the underlying assumptions prove incorrect, actual results may vary in material respects from those expressed or implied by the forward-looking statements made by us contained in this Annual Report on Form 20-F. As a result of the foregoing, readers should not place undue reliance on the forward-looking statements contained in this Annual Report on Form 20-F. The forward-looking statements contained in this Annual Report on Form 20-F are expressly qualified in their entirety by the foregoing cautionary statements.

Forward looking statements speak only as of the date on which they are made, and we undertake no obligation to update any forward-looking statements or other information contained in this report, whether as a result of new information, future events or otherwise. You are advised, however, to consult any additional disclosures we make in our reports on Form 6-K filed with the U.S. Securities and Exchange Commission (the "**SEC**"). Please also see the cautionary discussion of risks and uncertainties under "Item 3. Key Information—D. Risk Factors."

ENFORCEABILITY OF CIVIL LIABILITIES

We are a corporation organized under the laws of England and Wales. A substantial portion of our assets and most of our directors and executive officers are located and reside, respectively, outside the United States. Because of the location of our assets and board members, it may not be possible for investors to serve process within the United States upon us or such persons with respect to matters arising under the United States federal securities laws or to enforce against us or persons located outside the United States judgments of United States courts asserted under the civil liability provisions of the United States federal securities laws.

We understand that there is doubt as to the enforceability in the United Kingdom, in original actions or in actions for enforcement of judgments of United States courts, of civil liabilities predicated solely upon the federal securities laws of the United States insofar as they are fines or penalties. In addition, awards of punitive damages in actions brought in the United States or elsewhere may be unenforceable in the United Kingdom by reason of being a penalty.

We have appointed Cogency Global Inc. as its agent to receive service of process in any action against it in any state or federal court in the State of New York.

PART I

ITEM 1. IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISERS

Not applicable.

ITEM 2. OFFER STATISTICS AND TIMETABLE

Not applicable.

ITEM 3. KEY INFORMATION

A. Selected Financial Data

[Reserved]

B. Capitalization and Indebtedness

Not applicable.

C. Reasons for the Offer and Use of Proceeds

Not applicable.

D. Risk Factors

SUMMARY RISK FACTORS

The below summary risks provide an overview of the material risks we are exposed to in the normal course of our business activities. The below summary risks do not contain all of the information that may be important to you, and you should read the summary risks below together with the more detailed discussion of risks set forth following this section under the heading "Risk Factors," as well as elsewhere in this annual report. The summary risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not currently known to us or that we currently deem less significant may also affect our business operations or financial results. Consistent with the foregoing, we are exposed to a variety of risks, including those associated with the following:

- We are a development-stage company and have incurred significant losses since our inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.
- We will require substantial additional capital to finance our operations. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and/or eliminate one or more of our research and drug development programs or future commercialization efforts. Such capital raises may cause dilution to our holders, including holders of our shares and ADSs.
- We are very early in our development efforts and may not be successful in our efforts to use our platform to build a pipeline of therapeutic candidates and develop marketable drugs. We may encounter substantial delays in the design, manufacture, regulatory approval, and launch of any of our therapeutic candidates, which could prevent us from commercializing any products we develop on a timely basis, if at all.
- We have a limited operating history, have not initiated or completed any pivotal clinical trials, and have no products approved for commercial sale, which may make it difficult for you to evaluate our current business and likelihood of success and current and future viability.
- We have limited experience manufacturing our therapeutic candidates at commercial scale, and if we decide to expand our own manufacturing facility, we cannot assure you that we can manufacture our therapeutic candidates in compliance with regulations at a cost or in quantities necessary to make them commercially viable.
- Our therapeutic candidates are single-strain LBPs, which are an unproven approach to therapeutic intervention.
- There may be adverse events, such as immunotoxicity associated with the fundamental pharmacology of our therapeutic candidates or our therapeutic candidates may cause undesirable side effects, toxicities or other undesirable side effects when used alone or in combination with other approved products or investigational new drugs.
- Companies with differing microbiome or microbial products may produce negative clinical data which could adversely affect public perception of microbiome-derived therapies, and may negatively impact regulatory approval of, or demand for, our potential products.
- The clinical trials of our therapeutic candidates may not demonstrate safety and efficacy to the satisfaction of the MHRA, FDA, EMA or other comparable foreign regulatory authorities or otherwise produce positive results and the outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and the results of our clinical trials may not satisfy the requirements of the MHRA, FDA, EMA or other comparable foreign regulatory authorities.
- If we experience delays or difficulties in the enrolment of patients in clinical trials or data from our clinical trials may changes as more patient data become available, our regulatory submissions or receipt of necessary regulatory approvals could be delayed or prevented.
- We have begun developing and expect to continue to develop MRx0005, MRx0029, MRx0518 and potentially other therapeutic candidates in combination with other therapies, which exposes us to additional risks.
- We face significant competition, and if our competitors develop and market technologies or products more rapidly than we do or that are more effective, safer or less expensive than the products we develop, our commercial opportunities will be negatively impacted.
- We expect to depend on collaborations with third parties for the research, development, and commercialization of certain of the therapeutic candidates we may develop. If any such collaborations are not successful, we may not be able to realize the market potential of those therapeutic candidates.

- If we are unable to obtain and maintain patent and other intellectual property protection for any therapeutic candidates we develop, or if the scope of the patent and other intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully commercialize any therapeutic candidates we may develop may be adversely affected.
- We may need to defend ourselves against intellectual property infringement claims, which may be time-consuming and could cause us to incur substantial costs.
- Our operations and financial results could be adversely impacted by a variety of events outside our control, including, outbreaks of infectious diseases such as the COVID-19 pandemic in the United Kingdom, United States and the rest of the world and political instability such as the recent conflict in Ukraine.
- The withdrawal of the United Kingdom from the EU, commonly referred to as "Brexit," may adversely impact our ability to obtain regulatory approvals of our therapeutic candidates in the EU, result in restrictions or imposition of taxes and duties for importing our therapeutic candidates into the EU, and may require us to incur additional expenses in order to develop, manufacture and commercialize our therapeutic candidates in the EU.
- Our ability to claim UK Research and Development tax credits would impact our cash requirements and the amount of additional capital required.

Risks Related to Our Financial Position and Need for Additional Capital

We are a development-stage company and have incurred significant losses since our inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses, have not generated any revenue from product sales to date and have financed our operations principally from proceeds from sales of our ordinary shares on Alternative Investment Market of the London Stock Exchange (the "**AIM**") and NASDAQ with further capital raised from our acquisition of Longevity and certain loans. Our net loss was $31.9 million for the year ended December 31, 2021, $30.5 million for the year ended December 31, 2020, $30.3 million for the year ended December 31, 2019. As of December 31, 2021, we had an accumulated deficit of $180.2 million. We have devoted substantially all of our financial resources and efforts to developing our MicroRx LBP discovery platform, identifying potential therapeutic candidates and conducting preclinical and clinical studies of our therapeutic candidates. We are in the early stages of developing our therapeutic candidates, and we have not completed the development of any microbiome therapies or other drugs or biologics. As a result, we expect that it could be several years, if ever, before we have a commercialized product and generate revenue from product sales. Even if we succeed in receiving marketing approval for and commercialize one or more of our therapeutic candidates, we expect that we will continue to incur substantial research and development costs and other expenses in order to discover, develop and market additional potential products.

As of December 31, 2021, the Company's cash and cash equivalents were $21.0 million. The Company expects that its existing cash and cash equivalents, will be sufficient to satisfy its working capital needs, capital asset purchases, outstanding commitments and other liquidity requirements associated with our existing operations into the fourth quarter of 2022, which raises substantial doubt regarding the Company's ability to continue as a going concern for a period of one year after the date that the financial statements are issued. Certain elements of the Company's operating plan to alleviate the conditions that raise substantial doubt are outside of the Company's control and cannot be included in management's evaluation under the requirements of Accounting Standards Codification (ASC) 205-40, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern. Accordingly, the Company has concluded that substantial doubt exists about the Company's ability to continue as a going concern for a period of at least twelve months from the date of the issuance of these consolidated financial statements.

We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate that our expenses will increase substantially as we

- continue and expand clinical trials to investigate the efficacy of our current therapeutic candidates;
- seek to enhance our discovery platform and discover and develop additional therapeutic candidates;
- seek regulatory approvals for any therapeutic candidates that successfully complete clinical trials;
- seek to establish a sales, marketing and distribution infrastructure and scale-up manufacturing capabilities to commercialize any products for which we may obtain regulatory approval;
- maintain, expand and protect our intellectual property portfolio; and
- add clinical, scientific, operational, financial and management information systems and personnel, including personnel to support our product development and potential future commercialization efforts and to support our operations as a public company.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. In addition, we anticipate that our expenses will increase substantially if we experience any delays or encounter any issues with any of the above, including but not limited to failed studies, complex results, safety issues or other regulatory challenges. The net losses we incur may fluctuate significantly from quarter to quarter such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our working capital, our ability to fund the development of our therapeutic candidates and our ability to achieve and maintain profitability and the performance of our shares and ADSs.

We will require substantial additional capital to finance our operations. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and/or eliminate one or more of our research and drug development programs or future commercialization efforts.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. Our operations have consumed substantial amounts of cash since inception, and we expect our expenses to increase in connection with our ongoing activities, particularly as we conduct clinical trials of, and seek marketing approval for MRx0518, MRx-4DP0004, MRx0029, Blautix and Thetanix and our other programs. Even if one or more of the therapeutic candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with sales, marketing, manufacturing and distribution activities. Our expenses could increase beyond expectations if we are required by the MHRA, FDA, the EMA or other regulatory agencies to perform clinical trials or preclinical studies in addition to those that we currently anticipate. Other unanticipated costs may also arise. Because the design and outcome of our planned and anticipated clinical trials are highly uncertain, we cannot reasonably estimate the actual amount of resources and funding that will be necessary to successfully complete the development and commercialization of any product candidate we develop. While we have met with the MHRA, FDA and EMA to discuss the clinical development of our candidates, we have not discussed commercialization of any of programs, and we are not permitted to market or promote MRx0518, MRx-4DP0004, MRx0029, Blautix and Thetanix, or any other product candidate, before we receive marketing approval from the MHRA, FDA or EMA. Accordingly, we will need to obtain substantial additional funding in order to continue our operations.

As of December 31, 2021, we had $21.0 million in cash and cash equivalents. We expect our current cash and cash equivalents, including the €1 million ($1.1 million) overdraft facility and a $12.5 million loan from Oxford Finance, will be sufficient to fund our current operating plan to the fourth quarter of 2022. Our estimate as to how long we expect our existing cash and cash equivalents, to be able to continue to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned.

We could be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources, which may dilute our stockholders or restrict our operating activities. We do not have any committed external source of funds. Adequate additional financing may not be available to us on acceptable terms, or at all.

To the extent that we 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 stockholder. Debt financing may result in imposition of debt covenants, increased fixed payment obligations or other restrictions that may affect our business. If we raise additional funds through upfront payments or milestone payments pursuant to strategic collaborations with third parties, we may have to relinquish valuable rights to our therapeutic candidates, or grant licenses on terms that are not favorable to us. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

Our failure to raise capital as and when needed or on acceptable terms would have a negative impact on our financial condition and our ability to pursue our business strategy, and we may have to delay, reduce the scope of, suspend or eliminate one or more of our research-stage programs, clinical trials or future commercialization efforts.

Our ability to generate revenue and achieve profitability depends significantly on our ability to achieve several objectives relating to the discovery, development and commercialization of our therapeutic candidates.

Our business depends entirely on the successful discovery, development and commercialization of therapeutic candidates. We have no products approved for commercial sale and do not anticipate generating any revenue from product sales in the short to medium term, if ever. To become and remain profitable, we, and any future collaborators, must succeed in developing and eventually commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our therapeutic candidates, discovering additional therapeutic candidates, obtaining regulatory approval for these therapeutic candidates and manufacturing, marketing and selling any products for which we may obtain regulatory approval. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenue that is significant enough to achieve profitability.

Because of the numerous risks and uncertainties associated with pharmaceutical product and biological product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. If we are required by the MHRA, FDA or EMA or other regulatory authorities to perform preclinical or clinical studies in addition to those currently expected, or if there are any delays in completing our preclinical studies or clinical trials or the development of any of our therapeutic candidates, our expenses could increase and revenue could be further delayed.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress our value and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our therapeutic offerings or even continue our operations.

We have a limited operating history, have not initiated or completed any pivotal clinical trials, and have no products approved for commercial sale, which may make it difficult for you to evaluate our current business and likelihood of success and current and future viability.

We are a clinical-stage biopharmaceutical company with a limited operating history upon which you can evaluate our business and prospects. Since our inception in 2014, we have devoted substantially all of our resources to identifying and developing our therapeutic candidates, building our intellectual property portfolio, process development and manufacturing function, taking candidates through preclinical and clinical development, planning our business, raising capital and providing general and administrative support for these operations. All of our therapeutic candidates are in clinical or preclinical development.

Drug development is a highly uncertain undertaking and involves a substantial degree of risk. While we have now completed three clinical trials and have five more clinical trials ongoing, we do not have any products approved for sale. For instance, MRx0518, our lead immuno-oncology therapeutic candidate is being assessed in three separate clinical trials: in combination with Keytruda in patients with advanced or metastatic NSCLC, RCC, UC, TNBC, HNSCC and MSI-H tumors that are refractory to prior anti-PD-1/PD-L1 therapy, as a monotherapy in the neoadjuvant setting in patients undergoing surgical resection of solid tumors, and in combination with hypofractionated radiotherapy in the neoadjuvant setting in patients with potentially resectable pancreatic cancer. In our respiratory program, our therapeutic candidate, MRx-4DP0004, is being assessed in patients with partly controlled asthma. We also have other therapeutic candidates in discovery and preclinical trials that are being assessed in a variety of disease types including, MRx1299 in solid tumors in various types of cancer, MRx0029 and MRx0005 in Parkinson's disease, MRx0006 in rheumatoid arthritis and MRx0002 in multiple sclerosis. We have also investigated the efficacy of two therapeutic candidates in our gastrointestinal program in clinical trials, Blautix and Thetanix for patients with IBS and pediatric Crohn's disease, respectively. To date, however, we have not obtained marketing approval for and successfully commercialized a therapeutic candidate. We have devoted substantially all of our resources to research and development activities, including with respect to MRx0518, MRx-4DP0004, MRx0005, MRx0029,Blautix and Thetanix therapeutic candidates, MicroRx and other preclinical programs, business planning, establishing and maintaining our intellectual property portfolio, hiring personnel, raising capital and providing general and administrative support for these operations.

We have not yet demonstrated our ability to successfully initiate and complete a pivotal clinical trial, obtain marketing approvals, obtain regulatory approvals to commercialize a product, manufacture a commercial-scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. As a result, it may be more difficult for you to accurately predict our likelihood of success and viability than it could be if we had a longer operating history. In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors and risks frequently experienced by clinical-stage biopharmaceutical companies in rapidly evolving fields. We also may need to transition from a company with a research and development focus to a company capable of supporting commercial activities.

Additionally, we expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history.

Raising additional capital may cause dilution to our holders, including holders of our ADSs, restrict our operations or require us to relinquish rights to our technologies or therapeutic candidates.

We expect that significant additional capital will be needed in the future to continue our planned operations, including expanded research and development activities and potential commercialization efforts. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through any or a combination of securities offerings, debt financings, license and collaboration agreements and research grants and tax credits.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a shareholder. Debt financing and preferred equity financing, if available, could result in fixed payment obligations, and we may be required to accept terms that restrict our ability to incur additional indebtedness, force us to maintain specified liquidity or other ratios or restrict our ability to pay dividends or make acquisitions. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, future revenue streams, research programs or therapeutic candidates or to grant licenses on terms that may not be favorable to us. In addition, we could also be required to seek funds through arrangements with collaborators or others at an earlier stage than otherwise would be desirable.

If we raise funds through research grants or take advantage of research and development tax credits, we may be subject to certain requirements, which may limit our ability to use the funds or require us to share information from our research and development. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to a third party to develop and market therapeutic candidates that we would otherwise prefer to develop and market ourselves. Raising additional capital through any of these or other means could adversely affect our business and the holdings or rights of our shareholders and may cause the market price of our ADSs to decline.

The terms of our loan and security agreement require us to meet certain operating and financial covenants and place restrictions on our operating and financial flexibility. If we raise additional capital through debt financing, the terms of any new debt could further restrict our ability to operate our business.

As of December 31, 2021, we had $12.5 million outstanding in the form of a term loan under our loan and security agreement with Oxford Finance Luxembourg S.À R.L., as lender and collateral agent, which was entered into as of July 29, 2021. The loan is secured by substantially all of our assets, including all of the capital stock held by us, if any. The loan and security agreement contains a number of restrictive covenants, and the terms may restrict our current and future operations, particularly our ability to respond to certain changes in our business or industry, or take future actions. See “Item 5—Operating and Financial Review and Prospects—Liquidity and Capital Resources.”

The loan and security agreement contains customary representations and warranties and affirmative covenants and also contains certain restrictive covenants, including, among others, limitations on: the incurrence of additional debt, liens or other encumbrances on property, acquisitions and investments, loans and guarantees, mergers, consolidations, liquidations and dissolutions, asset sales, assets held at certain subsidiaries, dividends and other payments in respect of our capital stock, prepayments of certain debt, transactions with affiliates and changes to our type of business, management of the business, control of the business or business locations. The loan and security agreement also includes a financial covenant that requires the Company to maintain a minimum amount of cash in bank accounts and is subject to a control agreement if the Company does not achieve a certain equity raise threshold. The loan and security agreement also contains customary events of default. If we fail to comply with all such covenants, payments or other terms of the agreement, our lender could declare an event of default, which would give it the right to declare all borrowings outstanding, together with accrued and unpaid interest and fees, to be immediately due and payable. In addition, our lender would have the right to proceed against the assets we provided as collateral pursuant to the loan and security agreement. If the debt under the loan and security agreement were accelerated, we may not have sufficient cash or be able to sell sufficient assets to repay this debt, which would harm our business and financial condition.

Risks Related to the Discovery, Development, Regulatory Approval and Potential Commercialization of Our Therapeutic Candidates

We are very early in our development efforts and may not be successful in our efforts to use our platform to build a pipeline of therapeutic candidates and develop marketable drugs.

We are using our MicroRx platform, with an initial focus on developing therapies in immuno-oncology, inflammatory and CNS conditions, to discover and develop a pipeline of therapeutic candidates. While we believe our preclinical and clinical studies to date have validated our platform to a degree, we are at an early stage of development and our platform has not yet, and may never lead to, approvable or marketable products. We are developing these therapeutic candidates and additional therapeutic candidates that we intend to use to treat additional immunological diseases, respiratory diseases, neuroinflammation and neurodegeneration, behavioral, and other therapeutic areas. We may have problems applying our technologies to these other areas, and our new therapeutic candidates may not demonstrate a comparable ability in treating disease as our initial or our competitors' therapeutic candidates. Even if we are successful in identifying additional therapeutic candidates, they may not be suitable for clinical development as a result of our inability to manufacture products comprising bacteria which are challenging to produce on a large scale, or which have limited efficacy, unacceptable safety profiles or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance, or will be unacceptably challenging to manufacture. The success of our therapeutic candidates will depend on several factors, including the following:

- completion of preclinical studies and clinical trials with positive results;
- receipt of marketing approvals from applicable regulatory authorities;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our therapeutic candidates;
- making arrangements with third-party manufacturers, or the success of our existing commercial manufacturing capabilities;
- launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- entering into new collaborations throughout the development process as appropriate, from preclinical studies through to commercialization;
- acceptance of our products, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- obtaining and maintaining coverage and adequate reimbursement by third-party payors, including government payors, for our products, if approved;
- protecting our rights in our intellectual property portfolio;
- operating without infringing or violating the valid and enforceable patents or other intellectual property of third parties;
- maintaining an acceptable safety profile of the products following approval; and
- maintaining and growing an organization of scientists and business people who can develop and commercialize our products and technology.

If we do not successfully develop and commercialize therapeutic candidates based upon our technological approach, we will not be able to obtain product revenue in future periods, which likely would result in significant harm to our financial position and adversely affect our stock price.

Certain of our therapeutic candidates are intended to act on cells in the small intestine to produce therapeutic effects in tissues remote from the gut with limited side effects. This biological interaction between the small intestine and the rest of the body may not function in humans the way we have observed in mice and our drugs may not reproduce the systemic effects we have seen in preclinical data.

We believe certain of our therapeutic candidates, including MRx0518, MRx-4DP0004, MRx0005, MRx0029, Blautix and Thetanix, work by modulating systemic responses via interactions with cells in the small intestine. This requires our therapeutics be dosed to achieve sufficient exposure to the small intestine, requiring them to firstly pass safely through the gut. Dosing to achieve sufficient exposure may require an inconvenient dosing regimen. Even with successful formulation and delivery to achieve proper exposure of our LBPs to the small intestine, we may not get sufficient or even any activity at the site of disease. This may be because our understanding of the mechanisms of the small intestine do not work in humans the way we believe they do. Despite the positive early results observed in our clinical studies and the strong justification in the academic literature to support the concept, these principles and the ability to use microbiome derived therapies to modulate the immune system and other systems has not yet been proven in large scale studies in humans.

Our therapeutic candidates are Live Biotherapeutics Products, which are an unproven approach to therapeutic intervention.

All of our LBP candidates are based on single strains of commensal bacteria. We have not, nor to our knowledge has any other company, received regulatory approval for an oral therapeutic based on this approach. Because we use the same approach or novel platform for all of our LBP candidates, any failure with one LBP product candidate will increase the actual or perceived likelihood that our other LBP candidates will experience similar failures, which could have a material adverse effect on our business and prospects. We cannot be certain that our approach will lead to the development of approvable or marketable products. In addition, our LBPs may have different safety profiles and efficacy in various indications. Finally, regulatory agencies may lack experience in evaluating the safety and efficacy of products based on live bacteria, which could result in a longer than expected regulatory review process, increase our expected development costs and delay or prevent commercialization of our therapeutic candidates.

Even if our therapeutic candidates do not cause off target adverse events, there may be adverse events such as immunotoxicity associated with the fundamental pharmacology of our therapeutic candidates.

Our therapeutic candidates, including MRx0518, MRx-4DP0004 and Thetanix, work by modulating the immune system. While we have observed in preclinical studies that our LBPs have favorable side effect profiles, the pharmacological immune effects we induce are often remote from the gut. Although not observed in any of the clinical studies we have run to date, systemic immunomodulation from taking our LBPs could lead to immunotoxicity in patients, which may cause us or regulatory authorities to delay, limit or suspend clinical development. Other immunomodulatory agents have shown immunotoxicity. In the case of immune activating agents, such as pembrolizumab and nivolumab, induction of adverse auto-immune events has been observed in some patients. Immunotoxicity in one program could cause regulators to view these adverse events as a class effect of our LBPs, which may impact the timing of the development of our pipeline of potential therapeutic candidates. Even if the adverse events are manageable, the profile of the drug may be such that it limits or diminishes the possible number of patients who could receive our therapy.

Our therapeutic candidates may cause undesirable side effects, toxicities or other undesirable side effects when used alone or in combination with other approved products or investigational new drugs, or have other properties that may result in a safety profile that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, prevent market acceptance, or result in significant negative consequences following marketing approval, if any.

If our therapeutic candidates are associated with undesirable side effects or have unexpected characteristics in preclinical studies or clinical trials when used alone or in combination with other approved products or investigational new drugs we may need to interrupt, delay or abandon their development or limit 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. Treatment-related side effects could also affect patient recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. Any of these occurrences may prevent us from achieving or maintaining market acceptance of the affected product candidate and may harm our business, financial condition and prospects significantly.

For example, our current therapeutic candidates consist of lyophilized live biological material that remains viable in the gastrointestinal tract of humans. If these bacteria exert a pathogenic effect, despite this not having been observed in any preclinical studies or clinical trials to date, the bacteria carry a risk of causing infections in patients. Some infections may require treatment with antibiotics to eliminate the pathogenic bacteria. All our therapeutic candidates are screened for antibiotic sensitivity but it is possible that if antibiotic therapy does not eliminate the live biological material, a resistant version of our strain could emerge. These events, while unlikely, could cause a delay in our clinical development and/or could increase the regulatory standards for the entire class of microbiome derived therapies. In an instance where the infection risk of taking our therapeutic candidates is high, this may cause the benefit risk profile of therapy to be non-competitive in the market and may lead to discontinuation of development of the product.

In addition, it is possible that infections from our therapeutic candidates could be rare and not frequently observed in our clinical trials. In larger post marketing authorization trials, however, data could show that the infection risk, while small, does exist. If unacceptable side effects arise in the development of our therapeutic candidates, we, the MHRA, FDA, EMA or comparable foreign regulatory authorities, the IRBs at the institutions in which our studies are conducted, or ethics committees, or the DSMB could suspend or terminate our clinical trials or the MHRA, FDA, EMA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of our therapeutic candidates for any or all targeted indications. Although none have been observed in any of our clinical studies to date, treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We expect to have to train medical personnel using our therapeutic candidates to understand the side effect profiles for the LBPs we are studying in our clinical trials and upon any commercialization of any of our therapeutic candidates. Inadequate training in recognizing or managing the potential side effects of our therapeutic candidates could result in patient injury or death. Any of these occurrences may harm our business, financial condition and prospects significantly.

If any of our therapeutic candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the product;
- we may be required to recall a product or change the way such product is administered to patients;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof;
- we may be required to conduct post-marketing studies or clinical trials;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- we may be required to implement a risk evaluation and mitigation strategy or create a medication guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

Any of the foregoing events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and result in the loss of significant revenues to us, which would materially and adversely affect our results of operations and business.

Companies with differing microbiome or microbial products may produce negative clinical data which will adversely affect public perception of microbiome-derived therapies, and may negatively impact regulatory approval of, or demand for, our potential products.

Our LBP therapeutic candidates are pharmaceutical compositions of commensal bacteria. While we believe our approach is distinct from other types of microbiome therapy, negative data from clinical trials using microbiome-based therapies and other types of microbiome therapy could negatively impact the perception of the therapeutic use of microbiome-based products. This could negatively impact our ability to enroll patients in clinical trials. The clinical and commercial success of our potential products will depend in part on the public and clinical communities' acceptance of the use of LBPs. Moreover, our success depends upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of therapeutic candidates we may develop in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available.

Adverse events in our preclinical studies or clinical trials or those of our competitors or of academic researchers utilizing microbiome technologies, even if not attributable to our therapeutic candidates, and the resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our potential therapeutic candidates, stricter labeling requirements for our therapeutic candidates that are approved, if any, and a decrease in demand for any such products.

We have limited experience manufacturing our therapeutic candidates at commercial scale, and if we decide to expand our own manufacturing facility, we cannot assure you that we can manufacture our therapeutic candidates in compliance with regulations at a cost or in quantities necessary to make them commercially viable.

We have significantly invested in our in-house manufacturing facility for our therapeutic candidates for production at a commercial scale. Although we have taken nine strains through process development and scale-up to be able to manufacture clinic-ready product, and our in-house facility has the ability to produce over 30 million capsules of current good manufacturing practice (cGMP) drug product per year, with capacity to support our ongoing trials and potentially small-scale commercial supply, we have limited experience in commercial-scale manufacturing of our therapeutic candidates. We are investigating external manufacturing capability as we scale our therapeutic candidates and prepare for commercialization of one or more of our therapeutic candidates. Currently, we are dependent on the manufacturing of product for each of our therapeutic candidates at our internal manufacturing facility. Developing our in-house manufacturing facility, required and continues to require substantial additional funds and hiring and training a significant number of qualified employees to staff this facility. We may not be able to develop commercial-scale manufacturing facilities that are able to produce an adequate supply of materials in the event of significant commercial uptake of one of LBP therapeutics.

Although having in-house control of production has been a significant advantage in a field that has experienced significant hurdles relating to manufacturing, the equipment and facilities employed in the manufacture of pharmaceuticals are subject to stringent qualification requirements by regulatory agencies, including validation of facility, equipment, systems, processes and analytics. Our in-house manufacturing facility is currently compliant with cGMP regulations. However, if we are found to no longer comply with cGMP regulations or similar regulatory requirements outside of the United States or if we cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA, EMA or others, we will not be able to secure and/or maintain marketing approval for our manufacturing facility or any future facilities.

Catastrophic events at our manufacturing facility or loss of our master cell banks could significantly impair our ability to manufacture our therapeutic candidates.

We currently manufacture all of the material for our therapeutic candidates out of our sole manufacturing facility in Leòn, Spain. We have not undertaken a systematic analysis of the potential consequences to our business and financial results if our manufacturing facility is impacted by flood, fire, earthquake, power loss, terrorist activity or other disasters, including the ongoing geopolitical tensions related to Russia's actions in the Ukraine, and do not have a recovery plan or alternative manufacturing facility. In addition, we do not carry sufficient insurance to compensate us for actual losses from interruption of our business that may occur, and any losses or damages incurred by us could harm our business. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

In addition, our LBP therapeutic candidates require that we manufacture from MCBs of strains from our library of single strain bacteria. There is a possibility of a catastrophic failure or destruction of our MCBs. This could make it impossible for us to continue to manufacture a specific product. Recreating and recertifying our MCBs is possible, as we have back-up stocks of our clinical candidates stored remotely from the MCBs, but not certain and could put at risk the supply of our therapeutic candidates for preclinical studies or clinical trials or any products, if approved, to our customers.

Material modifications in the methods of product candidate manufacturing may result in additional costs or delay.

As product candidates progress from preclinical studies to late-stage clinical trials to marketing approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods, materials and processes, are altered along the way in an effort to optimize yield, manufacturing batch size, minimize costs and achieve consistent purity, identity, potency, quality and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and could affect planned or other clinical trials conducted with product candidates produced using the modified manufacturing methods, materials, and processes. This could delay completion of clinical trials and could require non-clinical or clinical bridging and comparability studies, which could increase costs, delay approval of our product candidates and jeopardize our ability to commercialize our product candidates, if approved.

The regulatory approval processes of the MHRA, FDA, EMA and other comparable foreign regulatory authorities are lengthy, time consuming and their outcome is inherently unpredictable. If we are ultimately unable to obtain regulatory approval of our therapeutic candidates, we will be unable to generate product revenue and our business will be substantially harmed.

Obtaining approval by the MHRA, FDA, EMA and other comparable foreign regulatory authorities is unpredictable, typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the type, complexity and novelty of the therapeutic candidates involved. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other data. Even if we eventually complete clinical testing and receive approval for our therapeutic candidates, the MHRA, FDA, EMA and other comparable foreign regulatory authorities may approve our therapeutic candidates for a more limited indication or a narrower patient population than we originally requested or may impose other prescribing limitations or warnings that limit the product's commercial potential. We have not submitted for, or obtained, regulatory approval for any product candidate, and it is possible that none of our therapeutic candidates will ever obtain regulatory approval. Further, development of our therapeutic candidates and/or regulatory approval may be delayed for reasons beyond our control.

Applications for our therapeutic candidates could fail to receive regulatory approval for many reasons, including the following:

- the MHRA, FDA, EMA or other comparable foreign regulatory authorities may disagree with the design, implementation or results of our clinical trials;
- the MHRA, FDA, EMA or other comparable foreign regulatory authorities may determine that our therapeutic candidates are not safe and effective, are only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use;
- the population studied in the clinical trial may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- the MHRA, FDA, EMA or other comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- we may be unable to demonstrate to the MHRA, FDA, EMA or other comparable foreign regulatory authorities that our product candidate's risk-benefit ratio for its proposed indication is acceptable;
- the MHRA, FDA, EMA or other comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications or facilities of third-party manufacturers with which we contract for clinical and commercial supplies;
- the MHRA, FDA, EMA or other comparable regulatory authorities may fail to approve companion diagnostic tests required for our therapeutic candidates; and
- the approval policies or regulations of the MHRA, FDA, EMA or other comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market any of our therapeutic candidates, which would significantly harm our business, results of operations and prospects.

The clinical trials of our therapeutic candidates may not demonstrate safety and efficacy to the satisfaction of the MHRA, FDA, EMA or other comparable foreign regulatory authorities or otherwise produce positive results.

Before obtaining marketing approval from the MHRA, FDA, EMA or other comparable foreign regulatory authorities for the sale of our therapeutic candidates, we must complete preclinical development and extensive clinical trials to demonstrate with substantial evidence the safety and efficacy of such therapeutic candidates. Clinical testing is expensive, difficult to design and implement, can take many years to complete and its ultimate outcome is uncertain. A failure of one or more clinical trials can occur at any stage of the process. The outcome of preclinical studies and early-stage clinical trials may not be predictive of the success of later clinical trials. Moreover, preclinical and clinical data are often susceptible to varying 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 of their drugs.

- We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent receipt of marketing approval or our ability to commercialize our therapeutic candidates, including:
- receipt of feedback from regulatory authorities that requires us to modify the design of our clinical trials;
- negative or inconclusive clinical trial results that may require us to conduct additional clinical trials or abandon certain drug development programs;
- the number of patients required for clinical trials being larger than anticipated, enrollment in these clinical trials being slower than anticipated or participants dropping out of these clinical trials at a higher rate than anticipated;
- third-party contractors failing to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- the suspension or termination of our clinical trials for various reasons, including non-compliance with regulatory requirements or a finding that our therapeutic candidates have undesirable side effects or other unexpected characteristics or risks;
- the cost of clinical trials of our therapeutic candidates being greater than anticipated;
- the supply or quality of our therapeutic candidates or other materials necessary to conduct clinical trials of our therapeutic candidates being insufficient or inadequate; and
- regulators revising the requirements for approving our therapeutic candidates.

If we are required to conduct additional clinical trials or other testing of our therapeutic candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our therapeutic candidates or other testing in a timely manner, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may incur unplanned costs, be delayed in seeking and obtaining marketing approval, if we receive such approval at all, receive more limited or restrictive marketing approval, be subject to additional post-marketing testing requirements or have the drug removed from the market after obtaining marketing approval.

The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and the results of our clinical trials may not satisfy the requirements of the MHRA, FDA, EMA or other comparable foreign regulatory authorities.

We will be required to demonstrate with substantial evidence through well-controlled clinical trials that our therapeutic candidates are safe and effective for use in a diverse population before we can seek marketing approvals for their commercial sale. Success in preclinical studies and early-stage clinical trials does not mean that future clinical trials will be successful. For example, we have not yet completed a clinical trial of MRx-4DP0004. While we have received positive results from the preclinical trials of MRx-4DP0004 and Part A of the clinical trial of MRx-4DP0004 in patients with partly controlled asthma taking long term medication, we do not know how it will perform in current or future clinical trials as it has in prior preclinical and clinical studies. Therapeutic candidates in later-stage clinical trials may fail to demonstrate sufficient safety and efficacy to the satisfaction of the MHRA, FDA, EMA and other comparable foreign regulatory authorities despite having progressed through preclinical studies and early-stage clinical trials.

Additionally, while we are aware of several other clinical-stage companies developing new therapeutics, to our knowledge, there are no therapeutics approved for the treatment of patients with solid tumors that are refractory to ICI therapy. However, the development of MRx0518 and our share price may be impacted by inferences, whether correct or not, that are drawn between the success of our therapeutic candidates and those of other companies. Regulatory authorities may also limit the scope of later-stage trials until we have demonstrated satisfactory safety, which could delay regulatory approval, limit the size of the patient population to which we may market our therapeutic candidates, or prevent regulatory approval.

In some instances, there can be significant variability in safety and efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, differences in and adherence to the dose and dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. Patients treated with our therapeutic candidates may also be undergoing surgical, and other treatments and may be using other approved products or investigational new drugs, which can cause side effects or adverse events that are unrelated to our therapeutic candidates. As a result, assessments of efficacy can vary widely for a particular patient, and from patient to patient and site to site within a clinical trial. This subjectivity can increase the uncertainty of, and adversely impact, our clinical trial outcomes.

We do not know whether any clinical trials we may conduct will demonstrate consistent or adequate efficacy and safety sufficient to obtain approval to market any of our therapeutic candidates.

We may apply for one or more accelerated or expedited programs instituted by the FDA for eligible product candidates, such as Fast Track or priority review designation. Even if one or more of our product candidates are reviewed under an expedited program, we may be unable to obtain and maintain the benefits associated with such designations. These designations may not lead to a faster development or regulatory review or approval process, and will not increase the likelihood that such product candidates will receive marketing approval.

For example, Fast Track designation is designed to facilitate the development and expedite the review of therapies for serious conditions with an unmet medical need. Programs with Fast Track designation may benefit from early and frequent communications with the FDA, potential priority review and the ability to submit a rolling application for regulatory review. Fast Track designation applies to both the product candidate and the specific indication for which it is being studied. However, if we do not continue to meet the criteria of the Fast Track designation, or if our clinical trials are delayed, suspended or terminated, or put on clinical hold due to unexpected adverse events or issues with clinical supply, we will not receive the benefits associated with the Fast Track program. Furthermore, Fast Track designation does not change the standards for approval. Fast Track designation alone does not guarantee qualification for the FDA's priority review procedures. Fast track designation also does not guarantee our product candidate will be approved in a timely manner, if at all.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. 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 a product that has orphan drug designation from the FDA subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug product for the same indication, for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan product exclusivity or if FDA finds that the holder of the orphan exclusivity has not shown that it can ensure the availability of sufficient quantities of the orphan product to meet the needs of patients with the disease or condition for which the product was designated. Even if we or our collaborators obtain orphan designation to a product candidate, we may not be the first to obtain marketing approval for any particular orphan indication due to uncertainties associated with developing pharmaceutical products. The scope of exclusivity is limited to the scope of any approved indication, even if the scope of the orphan designation is broader than the approved indication. Additionally, exclusive marketing rights may be limited if we or our collaborators seek approval for an indication broader than the orphan designated indication and may be lost if the FDA later determines that the request for 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. Further, even if a product obtains orphan drug exclusivity, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve a product with the same active moiety for the same condition if the FDA concludes that the later product is safer, more effective, or makes a major contribution to patient care. Furthermore, the FDA can waive orphan exclusivity if we or our collaborators are unable to manufacture sufficient supply of the product. If we or our collaborators do not receive or maintain orphan drug designation to product candidates for which we seek such designation, it could limit our ability to realize revenues from such product candidates.

We may pursue Breakthrough Therapy designation for one or more of our eligible product candidates in the future. Even if granted by the FDA, such designation may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that the product candidate will receive marketing approval. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA are also eligible for priority review if supported by clinical data at the time of the submission of a BLA or NDA.

Although Fast Track or Breakthrough Therapy Designation or access to any other expedited program may expedite the development or approval process, it does not change the standards for approval. We may not experience faster development timelines or achieve faster review or approval compared

to conventional FDA procedures. For example, the time required to identify and resolve issues relating to manufacturing and controls, the acquisition of a sufficient supply of our product for clinical trial purposes or the need to conduct additional nonclinical or clinical studies may delay approval by the FDA, even if the product qualifies for Fast Track or Breakthrough designation or access to any other expedited program. Access to an expedited program may also be withdrawn by the FDA if the Agency believes that the designation is no longer supported by data from our clinical development program. Additionally, qualification for any expedited review procedure does not ensure that we will ultimately obtain regulatory approval for such product candidate.

If we experience delays or difficulties in the enrolment of patients in clinical trials, our regulatory submissions or receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our therapeutic candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the MHRA, FDA, EMA or other comparable foreign regulatory authorities. We are developing our therapeutic candidates, MRx0518, to treat multiple types of cancer, MRx-4DP0004 to treat asthma and MRx0005 and MRx0029 to treat central nervous system disorders. There are a limited number of patients from which to draw for clinical studies for many of our therapeutic candidates.

Enrollment of patients in our clinical trials and maintaining patients in our ongoing clinical trials may be delayed or limited as our clinical trial sites limit their onsite staff or temporarily close as a result of the COVID-19 pandemic. In addition, patients may not be able to visit clinical trial sites for dosing or data collection purposes due to limitations on travel and physical distancing imposed or recommended by federal or state governments or patients' reluctance to visit the clinical trial sites during the pandemic. These factors resulting from the COVID-19 pandemic could delay the anticipated readouts from our clinical trials and our regulatory submissions. For example, enrolment for our Phase I/II clinical trial of MRx-4DP0004 in patients with partly controlled asthma was impacted due to factors associated with the COVID-19 pandemic, which delayed expected preliminary data for this clinical trial.

Patient enrolment is also affected by other factors including:

- the severity of the disease under investigation;
- the patient eligibility criteria for the study in question;
- the existence of competing clinical trials with the same patient population;
- the perceived risks and benefits of the product candidate under study;
- the availability of other treatments for the disease under investigation;
- the efforts to facilitate timely enrollment in clinical trials;
- our payments for conducting clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll a sufficient number of patients or volunteers for our clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our therapeutic candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

Interim, "topline" and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary or topline data from our preclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline 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, topline data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our preclinical studies and clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrolment continues and more patient data become available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our shares and ADSs.

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 product candidate or product 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 material or otherwise appropriate information to include in our disclosure.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on therapeutic candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we intend to focus on developing therapeutic candidates that we identify as most likely to succeed, in terms of both regulatory approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other therapeutic candidates or for other indications that may prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and product development programs and therapeutic candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product 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 product candidate.

We have begun developing and expect to continue to develop MRx0518 and potentially other therapeutic candidates in combination with other therapies, which exposes us to additional risks.

We have begun developing and intend to continue to develop MRx0518 and potentially other programs, in combination with one or more currently approved therapies. In 2019, we initiated a Phase I/II study evaluating our LBP MRx0518 in combination with Keytruda in heavily pre-treated patients with secondary resistant tumors refractory to ICIs. Although we have dosed patients with MRx0518 and Keytruda without any observed drug related serious adverse events, as we move into larger study populations, we cannot exclude the possibility of observing that some patients may not be able to tolerate MRx0518 or any of our other therapeutic candidates in combination with other therapies, like Bavencio (avelumab), or dosing of MRx0518 in combination with other therapies may have unexpected consequences. Even if any of our therapeutic candidates were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the MHRA, FDA, EMA or other comparable foreign regulatory authorities could revoke approval of the therapy used in combination with any of our therapeutic candidates, or safety, efficacy, manufacturing or supply issues could arise with these existing therapies. In addition, it is possible that existing therapies with which our therapeutic candidates are approved for use could themselves fall out of favor or be relegated to later lines of treatment. This could result in the need to identify other combination therapies for our therapeutic candidates or our own products being removed from the market or being less successful commercially.

Additionally, if the third-party providers of therapies or therapies in development used in combination with our therapeutic candidates are unable to produce sufficient quantities for clinical trials or for commercialization of our therapeutic candidates, or if the cost of combination therapies are prohibitive, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects. For example, for our Phase I/II trial of MRx0518 in combination with the ICI Keytruda, we entered into a clinical trial collaboration and supply agreement with MSD. Under the terms of the clinical trial collaboration and supply agreement, MSD supply us with Keytruda to use in combination with MRx0518. If this agreement terminates and we are unable to obtain Keytruda on the current terms, the cost to us to conduct this trial may significantly increase.

Even if any of our therapeutic candidates receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, hospitals, third-party payors and others in the medical community necessary for commercial success.

Even if our therapeutic candidates pass scrutiny by regulatory authorities, since LBPs are a new therapeutic modality, the degree of market acceptance by physicians, patients, hospitals, third-party payors and others in the medical community of any of our approved therapeutic candidates will depend on a number of factors, including:

- the efficacy and safety profile as demonstrated in clinical trials compared to alternative treatments;
- the timing of market introduction of the product candidate as well as competitive products;
- the clinical indications for which a product candidate is approved;
- restrictions on the use of therapeutic candidates in the labelling approved by regulatory authorities, such as boxed warnings or contraindications in labelling, or a risk evaluation and mitigation strategy, if any, which may not be required of alternative treatments and competitor products;
- the potential and perceived advantages of our therapeutic candidates over alternative treatments;
- the cost of treatment in relation to alternative treatments;
- the availability of coverage and adequate reimbursement by third-party payors, including government authorities;
- the availability of an approved product candidate for use as a combination therapy;
- relative convenience and ease of administration;
- the willingness of the target patient population to try new therapies and undergo required diagnostic screening to determine treatment eligibility and of physicians to prescribe these therapies and diagnostic tests;
- the effectiveness of sales and marketing efforts;
- unfavorable publicity relating to our therapeutic candidates; and
- the approval of other new therapies for the same indications.

If any of our therapeutic candidates are approved but do not achieve an adequate level of acceptance by physicians, hospitals, healthcare payors and patients, we may not generate or derive sufficient revenue from that product candidate and our financial results could be negatively impacted.

Even if we receive regulatory approval of our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates.

Any regulatory approvals that we receive for our product candidates will require surveillance to monitor the safety of the product candidate. The FDA may also require REMS as a condition of approving our product candidates, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or foreign health authorities approve our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and GCPs for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- Restrictions on the marketing or manufacturing of our product candidates, withdrawal of the product from the market or voluntary or mandatory product recalls;
- Fines, warning letters or holds on clinical trials;
- Refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of license approvals;
- Withdrawal of the drug from the market or voluntary or mandatory product recalls;
- Adverse publicity, fines, warning letters or holds on clinical trials;
- Product seizure or detention, or refusal to permit the import or export of our product candidates; and
- Injunctions or the imposition of civil or criminal penalties.

The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We 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 we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

The FDA strictly regulates manufacturers' promotional claims of drug products. In particular, a drug product may not be promoted by manufacturers for uses that are not approved by the FDA, as reflected in the FDA-approved labeling, although healthcare professionals are permitted to use drug products for off-label uses. The FDA, the Department of Justice, the Inspector General of the Department of Health and Human Services, among other government agencies, actively enforce the laws and regulations prohibiting manufacturers' 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 large civil and criminal fines, penalties, and enforcement actions. The FDA has also imposed consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed for companies that engaged in such prohibited activities. If we cannot successfully manage the promotion of our approved product candidates, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

If we are unable to establish sales or marketing capabilities or enter into agreements with third parties to sell or market our therapeutic candidates, we may not be able to successfully sell or market our therapeutic candidates that obtain regulatory approval.

We currently do not have and have never had a marketing or sales team. In order to commercialize any therapeutic candidates, if approved, we must build marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services for each of the territories in which we may have approval to sell or market our therapeutic candidates. We may not be successful in accomplishing these required tasks.

Establishing an internal sales or marketing team with technical expertise and supporting distribution capabilities to commercialize our therapeutic candidates will be expensive and time-consuming, and will require significant attention of our executive officers to manage. Any failure or delay in the development of our internal sales, marketing and distribution capabilities could adversely impact the commercialization of any of our therapeutic candidates that we obtain approval to market, if we do not have arrangements in place with third parties to provide such services on our behalf. Alternatively, if we choose to collaborate, either globally or on a territory-by-territory basis, with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems, we will be required to negotiate and enter into arrangements with such third parties relating to the proposed collaboration and such arrangements may prove to be less profitable than commercializing the product on our own. If we are unable to enter into such arrangements when needed, on acceptable terms, or at all, we may not be able to successfully commercialize any of our therapeutic candidates that receive regulatory approval, or any such commercialization may experience delays or limitations. If we are unable to successfully commercialize our approved therapeutic candidates, either on our own or through collaborations with one or more third parties, our future product revenue will suffer, and we may incur significant additional losses.

We face significant competition, and if our competitors develop and market technologies or products more rapidly than we do or that are more effective, safer or less expensive than the products we develop, our commercial opportunities will be negatively impacted.

The development and commercialization of new drug and biologic products is highly competitive and is characterized by rapid and substantial technological development and product innovations. We face competition with respect to our current therapeutic candidates and will face competition with respect to therapeutic candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. We are aware of a number of large pharmaceutical and biotechnology companies, including AbbVie Inc., Amgen Inc., AstraZeneca plc, Biogen Inc., Bristol-Myers Squibb, F. Hoffmann-La Roche A.G., Novartis, Janssen, GlaxoSmithKline plc, Johnson & Johnson, MSD, Novartis International A.G., Pfizer Inc., Regeneron Pharmaceuticals, Inc., Sanofi S.A. and Teva Pharmaceutical Industries Ltd., as well as smaller, early-stage companies, that are pursuing the development of products, including microbiome-based therapeutics in some instances, for disease indications we are targeting. Some of these competitive products and therapies are based on scientific approaches that are similar to our approach, and others may be based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources, established presence in the market and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and reimbursement and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors.

These third parties compete with us in recruiting and retaining qualified scientific, sales and marketing and management personnel, 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 products that are more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain MHRA, FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could delay us from obtaining MHRA, FDA approval to market our therapeutic candidates and result in our competitors establishing a strong market position before we are able to enter the market, especially for any competitor developing a microbiome-based therapeutic which will likely share our same regulatory approval requirements. For more information, please see “Risk Factors — Our therapeutic candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated, which may delay us from marketing our therapeutic candidates.” In addition, our ability to compete may in future be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic or biosimilar products.

Product liability lawsuits against us could cause us to incur substantial liabilities and limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our therapeutic candidates in clinical trials and will face an even greater risk if we commercially sell any products that we develop. If we cannot successfully defend ourselves against claims that our therapeutic candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- regulatory investigations, product recalls or withdrawals, or labeling, marketing or promotional restrictions;
- decreased demand for any therapeutic candidates or products 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;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

Our current product liability insurance coverage and any product liability insurance coverage that we acquire in the future may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our therapeutic candidates. Insurance coverage is increasingly expensive. 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.

Our therapeutic candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated, which may delay us from marketing our therapeutic candidates.

Even if we are successful in achieving regulatory approval to commercialize a product candidate faster than our competitors, we may face competition from biosimilars. In the US, the BPCIA created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product 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 product. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our biological products.

We believe that any of our therapeutic candidates approved as a biological product 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 our therapeutic candidates to be reference products for competing products, 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, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

In Europe, the European Commission has granted marketing authorizations for biosimilars pursuant to a set of general and product class-specific guidelines for biosimilar approvals issued over the past few years. Post-Brexit, it is understood that the UK will follow the same regulatory regime. According to this regime, a competitor may reference data supporting approval of an innovative biological product but will not be able to get on the market until 10 years after the time of approval of the innovative product. This 10-year marketing exclusivity period will be extended to 11 years if, during the first eight of those 10 years, the marketing authorization holder obtains an approval for one or more new therapeutic indications that bring significant clinical benefits compared with existing therapies. In addition, companies may be developing biosimilars in other countries that could compete with our products. If competitors are able to obtain marketing approval for biosimilars referencing our products, our products may become subject to competition from such biosimilars, with the attendant competitive pressure and consequences.

Failure to obtain marketing approval in international jurisdictions would prevent our therapeutic candidates from being marketed abroad.

In order to market and sell our therapeutic candidates in the United Kingdom, United States, the European Union and many other jurisdictions, we or our collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval in foreign countries may differ substantially from that required to obtain UK, FDA, EMA or other applicable regulatory approval. Additionally, the Medicines and Healthcare products Regulatory Agency ("**MHRA**") has taken on additional regulatory responsibilities for medical products marketed in the UK, as pan-EU regulatory procedures before EMA no longer apply in the UK. MHRA and the National Institute for Biological Standards and Control ("**NIBSC**") have issued guidance documents to the industry regarding regulation under the UK system. Proposals set forth in the new MHRA guidance will take effect through legislative changes that are subject to parliamentary approval, which may increase the amount of resources and time needed for obtaining regulatory approval in the UK and delay our clinical development and commercialization. The full impact of Brexit on our business remains unclear.

Furthermore, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining MHRA, FDA, EMA or other applicable regulatory approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or our collaborators may not obtain approvals for our therapeutic candidates from regulatory authorities outside the United States on a timely basis, if at all. Approval by the MHRA or FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

Any therapeutic candidates we develop may become subject to unfavorable third-party coverage and reimbursement practices, as well as pricing regulations.

The availability and extent of coverage and adequate reimbursement by third-party payors, including government health administration authorities, private health coverage insurers, managed care organizations and other third-party payors is essential for most patients to be able to afford expensive treatments. Sales of any of our therapeutic candidates that receive marketing approval will depend substantially, both in the United States and internationally, on the extent to which the costs of such therapeutic candidates will be covered and reimbursed by third-party payors. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our 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 an adequate return on our investment. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not successfully commercialize any product candidate for which we obtain marketing approval.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved products. In the United States, for example, principal decisions about reimbursement for new products are typically made by the CMS, an agency within the HHS. CMS decides whether and to what extent a new product will be covered and reimbursed under Medicare, and private third-party payors often follow CMS's decisions regarding coverage and reimbursement to a substantial degree. However, one third-party payor's determination to provide coverage for a product candidate does not assure that other payors will also provide coverage for the product. As a result, the coverage determination process is often time-consuming and costly. This process will require us to provide scientific and clinical support for the use of our products to each third-party payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. The approval process may be more cumbersome for us since our LBP therapeutic candidates have not been previously marketed for the uses we propose.

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. Further, such payors are increasingly challenging the price, examining the medical necessity and reviewing the cost effectiveness of medical therapeutic candidates. There may be especially significant delays in obtaining coverage and reimbursement for newly approved drugs. Third-party payors may limit coverage to specific therapeutic candidates on an approved list, known as a formulary, which might not include all FDA-approved drugs for a particular indication. We may need to conduct expensive pharmaco-economic studies to demonstrate the medical necessity and cost effectiveness of our products. Nonetheless, our therapeutic candidates may not be considered medically necessary or cost effective. We cannot be sure that coverage and reimbursement will be available for any product that we commercialize and, if reimbursement is available, what the level of reimbursement will be.

In addition, companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, will apply to any companion diagnostics we invent and develop with intent to commercialize. Additionally, if any companion diagnostic provider is unable to obtain reimbursement or is inadequately reimbursed, that may limit the availability of such companion diagnostic, which would negatively impact prescriptions for our therapeutic candidates, if approved.

Outside the United States, the commercialization of therapeutics is generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost containment initiatives in Europe, Canada and other countries has and will continue to put pressure on the pricing and usage of therapeutics such as our therapeutic candidates. In many countries, particularly the countries of the European Union, medical product prices are subject to varying price control mechanisms as part of national health systems. In these countries, pricing negotiations with governmental authorities can take considerable time after a product receives marketing approval. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. In general, product prices under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for products 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 our therapeutic candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

If we are unable to establish or sustain coverage and adequate reimbursement for any therapeutic candidates from third-party payors, the adoption of those products and sales revenue will be adversely affected, which, in turn, could adversely affect the ability to market or sell those therapeutic candidates, if approved. 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 we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

We expect to depend on collaborations with third parties for the research, development, and commercialization of certain of the therapeutic candidates we may develop. If any such collaborations are not successful, we may not be able to realize the market potential of those therapeutic candidates.

We currently use and expect to continue to work with third-party collaborators for the research, development, and commercialization of certain of the therapeutic candidates we may develop. For example, we have entered into a research collaboration and option to license agreement with MSD to discover and develop LBPs for vaccines. We also entered into a strategic alliance with MD Anderson. To date, we have initiated two clinical trials as part of this strategic alliance. For additional information on our relationships with MSD and the MD Anderson, see “Item 4. Information about the Company—B. Business Overview— Collaborations.” Our likely collaborators for any other collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies, biotechnology companies and academic institutions. While we generally impose diligence obligations on our collaborators, we often have limited control over the amount and timing of resources that they dedicate to the development or potential commercialization of any therapeutic candidates we may seek to develop with them. Our ability to generate revenue from these arrangements with commercial entities will depend on our collaborators’ abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any collaboration that we enter into.

Collaborations involving any therapeutic candidates we may develop pose the following risks to us:

- despite being subject to contractual diligence obligations, collaborators generally control the efforts and resources that they will apply to these collaborations;
- collaborators may not properly obtain, maintain, enforce, or defend intellectual property or proprietary rights relating to our therapeutic candidates or research programs or may use our proprietary information in such a way as to expose us to potential litigation or other intellectual property related proceedings, including proceedings challenging the scope, ownership, validity, and enforceability of our intellectual property;
- collaborators may own or co-own intellectual property covering our therapeutic candidates or research and development programs that results from our collaboration with them, and in such cases, we may not have the right to commercialize such intellectual property or such therapeutic candidates or research programs;
- we may need the cooperation of our collaborators to enforce or defend any intellectual property we contribute to or that arises out of our collaborations, which may not be provided to us;
- collaborators may decide to not pursue development and commercialization of any therapeutic candidates we develop or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities or collaborators may elect to fund or commercialize a competing product;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials, or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our therapeutic candidates or research programs if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators may restrict us from researching, developing, or commercializing certain products or technologies without their involvement;
- collaborators with marketing and distribution rights to one or more therapeutic candidates may not commit sufficient resources to the marketing and distribution of such therapeutic candidates;
- we may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control;
- collaborators may grant sublicenses to our technology or therapeutic candidates or undergo a change of control, and the sublicensees or new owners may decide to take the collaboration in a direction which is not in our best interest;
- collaborators may become bankrupt, which may significantly delay our research or development programs, or may cause us to lose access to valuable technology, know-how, or intellectual property of the collaborator relating to our products, therapeutic candidates, or research programs;
- key personnel at our collaborators may leave, which could negatively impact our ability to productively work with our collaborators;
- collaborations may require us to incur short and long-term expenditures, issue securities that dilute our stockholders, or disrupt our management and business;
- if our collaborators do not satisfy their obligations under our agreements with them, or if they terminate our collaborations with them, we may not be able to develop or commercialize therapeutic candidates as planned;

- collaborations may require us to share in development and commercialization costs pursuant to budgets that we do not fully control, and our failure to share in such costs could have a detrimental impact on the collaboration or our ability to share in revenue generated under the collaboration;
- collaborations may be terminated in their entirety or with respect to certain therapeutic candidates or technologies and, if so terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable therapeutic candidates or technologies; and
- collaboration agreements may not lead to development or commercialization of therapeutic candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our development or commercialization program under such collaboration could be delayed, diminished, or terminated.

We may face significant competition in seeking appropriate collaborations. Recent business combinations among biotechnology and pharmaceutical companies have resulted in a reduced number of potential collaborators. In addition, the negotiation process is time-consuming and complex, and we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop therapeutic candidates or bring them to market and generate product revenue.

We may not realize the benefit of collaborations if we or our collaborator elects not to exercise the rights granted under the agreement or if we or our collaborator are unable to successfully integrate a product candidate into existing operations and company culture. In addition, if our agreement with any of our collaborators terminates, our access to technology and intellectual property licensed to us by that collaborator may be restricted or terminate entirely, which may delay our continued development of our therapeutic candidates utilizing the collaborator's technology or intellectual property or require us to stop development of those therapeutic candidates completely. We may also find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. Many of the risks relating to product development, regulatory approval, and commercialization described in this "Risk Factors" section also apply to the activities of our collaborators and any negative impact on our collaborators may adversely affect us.

We rely, and expect to continue to rely, on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research and studies.

We rely, and expect to continue to rely, on third parties, such as CROs, clinical data management organizations, medical institutions, clinical investigators and potential pharmaceutical partners, to conduct and manage our clinical trials, including our clinical trials of MRx0518, MRx-4DP0004 and potential future trials with MRx0005, MRx0029, Blautix and Thetanix.

Third parties have a significant role in the conduct of our clinical trials and the subsequent collection and analysis of data. These third parties are not our employees, and except for obligations imposed upon those third parties and remedies available to us under our agreements with such third parties, we have limited ability to control the amount or timing of resources that any such third party will devote to our clinical trials. The third parties we rely on for these services may also have relationships with other entities, some of which may be our competitors. Some of these third parties may be able to terminate their engagements with us at any time. If we need to enter into alternative arrangements with a third party, it would delay our drug development activities.

Our reliance on these third parties for such drug development activities will reduce our control over these activities but will not relieve us of our regulatory responsibilities. For example, we will 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 GCP standards, regulations for conducting, recording and reporting the results of clinical trials to assure that data and reported results are reliable and accurate and that the rights, integrity and confidentiality of trial participants are protected. The MHRA and EMA also require us to comply with similar standards. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, MHRA, EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials substantially comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under current cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the marketing approval process.

If these third parties 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 will not be able to obtain, or may be delayed in obtaining, marketing approvals for our therapeutic candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our therapeutic candidates.

We also rely on third parties to store and distribute drug product required by our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our therapeutic candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent and other intellectual property protection for any therapeutic candidates we develop, or if the scope of the patent and other intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully commercialize any therapeutic candidates we may develop may be adversely affected.

Our commercial success will depend in large part on our ability to obtain and maintain patent, trademark, trade secret and other intellectual property protection of our therapeutic candidates and other technology, methods used to manufacture them and methods of treatment, as well as successfully defending our patent and other intellectual property rights against third-party challenges. It is difficult and costly to protect and enforce intellectual property rights, and we may not be able to ensure the same for every product. Our ability to stop unauthorized third parties from making, using, selling, offering to sell, importing or otherwise commercializing our therapeutic candidates is dependent upon the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities.

We seek to protect our proprietary position by developing a comprehensive intellectual property portfolio including filing patent applications and obtaining granted patents in the United States and abroad related to our therapeutic candidates that are important to our business. If we are unable to obtain or maintain patent protection with respect to a product candidate we may develop, or if the scope of the patent protection secured is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours and our ability to commercialize that product candidate may be adversely affected.

The patent prosecution process is expensive, time-consuming, and complex, and we may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. In addition, we may not pursue or obtain patent protection in all relevant markets. It is also possible that we will fail to identify patentable aspects of our research and development output in time to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. In addition, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our inventions and the prior art allow our inventions to be patentable over the prior art. Furthermore, 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 be certain that 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.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights are uncertain and we may become involved in complex and costly litigation. Our pending and future patent applications may not result in patents being issued which protect therapeutic candidates or effectively prevent others from commercializing competitive technologies and therapeutic candidates.

Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our inventions, obtain, maintain, enforce and defend our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our owned and licensed patent rights. We also cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will be valid and enforceable and provide sufficient protection from competitors. Any patents that we own or in-license may be challenged, narrowed, circumvented, or invalidated by third parties. Consequently, we do not know whether any therapeutic candidates we may develop will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner.

In addition, 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 intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Moreover, some of our owned patents and patent applications may in the future be, co-owned by us with third parties. If we are unable to obtain an exclusive license to such third-party co-owners' interest in such patents or patent applications, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we may need the cooperation of any such co-owners of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Our patents and patent applications contain claims directed to compositions of matter on therapeutic candidates, as well as methods directed to the use of such therapeutic candidates for treatment of specific indications. Method-of-use patents do not prevent a competitor or other third party from developing or marketing an identical product for an indication that is outside the scope of the patented method. Moreover, with respect to method-of-use patents, even if competitors or other third parties do not actively promote their product for our targeted indications or uses for which we may obtain patents, providers may recommend that patients use these products off-label, or patients may do so themselves.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own may fail to result in issued patents with claims that cover our therapeutic candidates or uses thereof in the United States or in other foreign countries. For example, while our patent applications are pending, we may be subject to a third party pre-issuance submission of prior art to the USPTO or become involved in interference or derivation proceedings, or equivalent proceedings in foreign jurisdictions. Even if patents do successfully issue, third parties may challenge their inventorship, validity, enforceability or scope, including through opposition, revocation, reexamination, post-grant and *inter partes* review proceedings. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable certain patent rights, allow third parties to commercialize our technology or therapeutic candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Moreover, we may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge features of patentability with respect to one or more patents and patent applications. Such challenges may result in loss of patent rights, loss of exclusivity, or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and therapeutic candidates. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. If the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our therapeutic candidates. Further, if we encounter delays in development, testing, and regulatory review of new therapeutic candidates, the period of time during which we could market our therapeutic candidates under patent protection would be reduced.

Given that patent applications in the United States and other countries are confidential for a period of time after filing, at any moment in time, we cannot be certain that we were in the past or will be in the future the first to file any patent application related to our therapeutic candidates. In addition, some patent applications in the United States may be maintained in secrecy until the patents are issued. As a result, there may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim, and we may be subject to priority disputes. We may in the future become a party to proceedings or priority disputes in Europe or other foreign jurisdictions. The loss of priority for, or the loss of, these patents could have a material adverse effect on the conduct of our business.

We may be required to disclaim part or all of the term of certain patents or patent applications. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim. There also may be prior art of which we or potential future licensors are aware, but which we or those licensors do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. No assurance can be given that, if challenged, our patents would be declared by a court, patent office or other governmental authority to be valid or enforceable or that even if found valid and enforceable, a competitor's technology or product would be found by a court to infringe our patents. We may analyze patents or patent applications of our competitors that we believe are relevant to our activities, and consider that we are free to operate in relation to our therapeutic candidates or if applicable challenge the validity of any issued patents, but our competitors may achieve issued claims, including in patents we consider to be unrelated, that block our efforts or potentially result in our therapeutic candidates or our activities infringing such claims. It is possible that our competitors may have filed, and may in the future file, patent applications covering our products or technology similar to ours. Those patent applications may have priority over our patent applications or patents, which could require us to obtain rights to issued patents covering such technologies. The possibility also exists that others will develop products that have the same effect as our therapeutic candidates on an independent basis that do not infringe our patents or other intellectual property rights, or will design around the claims of our patent applications or our in-licensed patents or patent applications that cover our therapeutic candidates.

Likewise, our current patents and patent applications directed to our therapeutic candidates are expected to expire from December 2035 through March 2042 (upon issuing as patents), without taking into account any possible patent term adjustments or extensions. Our patents may expire before, or soon after, our first product candidate achieves marketing approval in the United States or foreign jurisdictions. Additionally, no assurance can be given that the USPTO or relevant foreign patent offices will grant any of the pending patent applications we own or in-license currently or in the future. Upon the expiration of our current patents, we may lose the right to exclude others from practicing these inventions. The expiration of these patents could also have a similar material adverse effect on our business, financial condition, results of operations and prospects.

We may also be subject to claims that former employees, collaborators, or other third parties have an interest in our patents or patent applications or other intellectual property as an inventor or co-inventor. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such patent applications, such co-owners may be able to license their rights to other third parties, including our competitors. In addition, we may need the cooperation of any such co-owners to enforce any patents that issue from such patent applications against third parties, and such cooperation may not be provided to us.

If we are unsuccessful in any interference proceedings or other priority, validity (including any patent oppositions), or inventorship disputes to which we may be subject, we may lose valuable intellectual property rights through the loss of one or more of our owned, licensed, or optioned patents, or such patent claims may be narrowed, invalidated, or held unenforceable, or through loss of exclusive ownership of or the exclusive right to use our patents. In the event of loss of patent rights as a result of any of these disputes, we may be required to obtain and maintain licenses from third parties, including parties involved in any such interference proceedings or other priority or inventorship disputes. Such licenses may not be available on commercially reasonable terms or at all, or may be non-exclusive. If we are unable to obtain and maintain such licenses, we may need to cease the development, manufacture, and commercialization of one or more of the therapeutic candidates we may develop. The loss of exclusivity or the narrowing of our patent claims could limit our ability to stop others from using or commercializing similar or identical technology and therapeutic candidates. Even if we are successful in an interference proceeding or other similar priority or inventorship disputes, it could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could result in a material adverse effect on our business, financial condition, results of operations, or prospects.

We have intellectual property coverage for our therapeutic candidates in the United States, Europe, and other territories, but our foreign intellectual property rights are not exhaustive.

We have intellectual property for our therapeutic candidates in many key markets such as the United States and Europe. However, we do not have intellectual property rights in every country throughout the world. Filing, prosecuting, and defending patents on therapeutic candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States, and Europe can be less extensive than those in the United States. In addition, the laws of foreign countries do not protect intellectual property rights to the same extent as federal and state laws of the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but where enforcement is not as strong as that in the United States. These products may compete with our therapeutic candidates 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 products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products against third parties in violation of our intellectual property and proprietary rights generally. Proceedings to enforce our patents and intellectual property rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our 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. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Moreover, the initiation of proceedings by third parties to challenge the scope or validity of our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business and / or the limitation or loss of key patent rights. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many 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 or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected.

Geo-political actions in the United States and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any current or future licensors and the maintenance, enforcement or defense of our issued patents or those of any current or future licensors. For example, the United States, United Kingdom, and other foreign government actions related to Russia's invasion of Ukraine may limit or prevent filing, prosecution and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in Russia. If such an event were to occur, it could have a material adverse effect on our business. In addition, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit inventions owned by patentees that have citizenship or nationality in, are registered in, or have predominately primary place of business or profit-making activities in the United States, United Kingdom, and other countries that Russia has deemed unfriendly without consent or compensation. Consequently, we would not be able to prevent third parties from practicing our inventions in Russia or from selling or importing products made using our inventions in and into Russia. Accordingly, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

We may enter into license agreements for intellectual property rights in the future and if we fail to comply with our obligations in such agreements or otherwise experience disruptions to our business relationships with our licensors or research and development partners, we could lose license rights that are important to our business.

We cannot provide any assurances that third-party patents do not exist which might be enforced against our current technology, resulting in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant. It is possible that our ability to commercialize some therapeutic candidates in the United States and abroad may be adversely affected if we cannot obtain a license to any potentially relevant third-party patents on commercially reasonable terms that would allow us to make an appropriate return on our investment. In addition, the licensing or acquisition of third-party intellectual property rights is a highly competitive area, and other, potentially more established companies may pursue strategies to license or acquire third party intellectual property rights that we may, in the future, consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. Further, even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. Even if we believe third-party intellectual property claims are without merit, there is no assurance that a court would find in our favor on questions of infringement, validity, enforceability, or priority. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. As such, we could be forced, including by court order, to cease developing, manufacturing, and commercializing the infringing technology or therapeutic candidates. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. Thus, we may be required to expend significant time and resources to redesign our technology, therapeutic candidates, or the methods for manufacturing them or to develop or license replacement technology, or we may need to abandon development of the relevant program or product candidate, all of which may not be feasible on a technical or commercial basis and could have a material adverse effect on our business, financial condition, results of operations, and prospects. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar material adverse effect on our business, financial condition, results of operations, and prospects.

The intellectual property landscape pertaining to live biotherapeutics is in constant flux.

The field of Live Biotherapeutics is still in its infancy, and no LBP candidates have reached the market. Due to the intense research and development that is taking place by several companies, including us and our competitors, in this field, the intellectual property landscape is evolving and in flux, and it may remain uncertain for the coming years. There may be significant intellectual property related litigation and proceedings relating to intellectual property and proprietary rights in the future.

Our commercial success depends upon our ability and the ability of future collaborators to develop, manufacture, market, and sell any therapeutic candidates that we may develop and use our proprietary technologies without infringing, misappropriating, or otherwise violating the intellectual property and proprietary rights of third parties. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights as well as administrative proceedings for challenging patents, including interference, derivation, *inter partes* review, post grant review, and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We are, and may in the future be, subject to and may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights including interference proceedings, post-grant review, *inter partes* review, and derivation proceedings before the USPTO and similar proceedings in foreign jurisdictions such as oppositions before the European Patent Office "**EPO**"). Currently three of our European patents have been challenged by third parties in Opposition proceedings before the EPO. One of these patents has been revoked by the EPO at the first instance. We disagree with the EPO's decision and have filed an appeal. Under European law the patent is considered to be in good standing until a final decision from the appeal. Another of our three challenged patents was upheld in amended form. The challenge against the third patent was dismissed without having to be amended. Numerous U.S. and foreign issued patents and pending patent applications that are owned by third parties exist in the fields in which we are developing our therapeutic candidates and they may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit.

As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our therapeutic candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of therapies, products or their methods of use or manufacture. There may be third-party patents or patent application with claims to technologies, methods of manufacture or methods for treatment related to the use or manufacture of our therapeutic candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our therapeutic candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents.

Defense of third-party claims of infringement of misappropriation, or violation of intellectual property rights involves substantial litigation expense and would be a substantial diversion of management and employee time and resources from our business. Some third parties may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, financial condition, results of operations and prospects. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our ordinary shares or ADSs. Any of the foregoing events could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may become involved in lawsuits to protect or enforce our patents, which could be expensive, time consuming, and unsuccessful and could result in a finding that such patents are unenforceable or invalid.

Competitors may infringe our patents, or we may be required to defend against claims of infringement. In addition, our patents also are, and may in the future become, involved in inventorship, priority, validity or enforceability disputes. Countering or defending against such claims can be expensive and time consuming. In future infringement proceedings, a court may decide that a patent owned by us is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our owned or any in-licensed patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly.

In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. These types of mechanisms include re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). These types of proceedings could result in revocation or amendment to our patents such that they no longer cover our therapeutic candidates. The outcome for any particular patent 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, our patent counsel and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, or if we are otherwise unable to adequately protect our rights, we would lose at least part, and perhaps all, of the patent protection on our technology and/or therapeutic candidates. Defense of these types of claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business.

Conversely, we may choose to challenge the patentability of claims in a third party's U.S. patent by requesting that the USPTO review the patent claims in re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). We are currently challenging, and in the future may choose to challenge, third party patents in patent opposition proceedings in the EPO or before another foreign patent office. Even if successful, the costs of these opposition proceedings could be substantial, and may consume our time or other resources. If we fail to obtain a favorable result at the USPTO, EPO or other patent office then we may be exposed to litigation by a third party alleging that the patent may be infringed by our therapeutic candidates or other proprietary technologies.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our personnel from their normal responsibilities. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation in the US and certain other jurisdictions, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our ordinary shares or ADSs. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

No earlier that October 1, 2022, European applications will soon have the option, upon grant of a patent, of becoming a Unitary Patent, which will be subject to the jurisdiction of the Unitary Patent Court ("UPC"). This will be a significant change in European patent practice. As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by government 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 government fees on patents and applications are due to be paid to the USPTO and foreign patent agencies outside of the United States over the lifetime of our patents and applications. The USPTO and foreign patent agencies require compliance with several procedural, documentary, fee payment, and other similar provisions during the patent application process. While an inadvertent lapse can ordinarily be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations, however, in which non-compliance can result a partial or complete loss of patent rights in the relevant jurisdiction. Were a noncompliance event to occur, our competitors might be able to enter the market with similar or identical products or technology, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Changes in patent law in the United States and in non-U.S. jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our therapeutic candidates.

As is the case with other biotech and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain.

Changes in either the patent laws or interpretation of the patent laws could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of our issued patents. For example, in March 2013, under the Leahy-Smith America Invents Act, or the America Invents Act, the United States transitioned from a "first to invent" to a "first-to-file" patent system. Under a "first-to-file" system, assuming that other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on an invention regardless of whether another inventor had made the invention earlier. 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 to be cognizant going forward of the time from invention to filing of a patent application. 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 or our licensors were the first to either file any patent application related to our technology or therapeutic candidates or invent any of the inventions claimed in our or our licensor's patents or patent applications. The America Invents Act also includes a number of other significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted, allowing third party submission of prior art and establish a new post-grant review system 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 United States 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. The effects of these changes are currently unclear as the USPTO continues to promulgate new regulations and procedures in connection with the America Invents Act and many of the substantive changes to patent law, including the "first-to-file" provisions, only became effective in March 2013. In addition, the courts have yet to address many of these provisions and the applicability of the act and new regulations on the specific patents discussed in this filing have not been determined and would need to be reviewed. Thus, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

In addition, recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. These cases include *Association for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 12-398 (2013) or *Myriad*; *Alice Corp. v. CLS Bank International*, 573 U.S. 13-298 (2014); and *Collaborative Services v. Prometheus Laboratories, Inc.*, or *Prometheus*, 566 U.S. 10-1150 (2012). In addition to increasing uncertainty with regard to our ability to obtain patents in the future, 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 weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. For example, in the case, *Assoc. for Molecular Pathology v. Myriad Genetics, Inc.*, the U.S. Supreme Court held that certain claims to DNA molecules are not patentable, but claims to complementary DNA, "**cDNA**," molecules, which are not genomic sequences, may be patent eligible because they are not a natural product. The effect of the decision on patents for other isolated natural products is uncertain. However, on March 4, 2014, the USPTO issued a memorandum to patent examiners providing guidance for examining claims that recite laws of nature, natural phenomena or natural products under the *Myriad* and *Prometheus* decisions. The guidance did not limit the application of *Myriad* to DNA but, rather, applied the decision broadly to other natural products, which may include our therapeutic candidates. The March 4, 2014 memorandum and the USPTO's interpretation of the cases and announced examination rubric received widespread criticism from stakeholders during a public comment period and was superseded by interim guidance published on December 15, 2014. We cannot predict how this and future decisions by the courts, the U.S. Congress or the USPTO may impact the value of our patents. Any similar adverse changes in the patent laws of other jurisdictions could also have a material adverse effect on our business, financial condition, results of operations and prospects.

Patent terms may be inadequate to protect our competitive position on our therapeutic candidates for an adequate amount of time.

Patents have a limited lifespan. The terms of individual patents depends upon the legal term for patents in the countries in which they are granted. In most countries, including the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest non-provisional filing date in the applicable country. However, the actual protection afforded by a patent varies from country to country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent. Various extensions, including Patent Term Extensions ("**PTEs**") and Patent Term Adjustments ("**PTA**s"), may be available, but the life of a patent, and the protection it affords, is limited. For more information regarding PTA and PTE, please see "Business — Intellectual Property." Even if patents covering our therapeutic candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics and / or biosimilars. Given the amount of time required for the development, testing and regulatory review of new therapeutic candidates, patents protecting our therapeutic candidates might expire before or shortly after we or our partners commercialize those candidates. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If we do not obtain PTEs for any therapeutic candidates we may develop, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any therapeutic candidates we may develop, one or more of our U.S. patents may be eligible for limited PTE under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Amendments. Analogous extensions of patent term may be available upon marketing approval in other jurisdictions. The Hatch-Waxman Amendments PTE term of up to five years as compensation for patent term lost during the FDA regulatory review process. A PTE cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent per product may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, even if we were to seek a PTE or corresponding extension of patent term in other jurisdictions, it may not be granted because of, for example, the failure to exercise due diligence during the testing phase or regulatory review process, the failure to apply within applicable deadlines, the failure to apply prior to expiration of relevant patents, or any other failure to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain PTE or a corresponding extension of patent term in other jurisdictions, or the term of any such extension is less than we request, our competitors may be able to launch competing products earlier than anticipated following our patent expiration, and our business, financial condition, results of operations, and prospects could be materially harmed.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for our technology and therapeutic candidates, we also rely on know-how and trade secret protection, as well as confidentiality agreements, non-disclosure agreements and invention assignment agreements with our employees, consultants and third parties, to protect our confidential and proprietary information, especially where we do not believe patent protection is appropriate or obtainable.

It is our policy to require our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors, and other third parties to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed by or made known to the individual or entity during the course of the party's relationship with us is to be kept confidential and not disclosed to third parties, except in certain specified circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and that are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. In the case of consultants and other third parties, the agreements provide that all inventions conceived in connection with the services provided are our exclusive property. However, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. Additionally, the assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time-consuming, and the outcome is unpredictable.

In addition to contractual measures, we try to protect the confidential nature of our proprietary information through other appropriate precautions, such as physical and technological security measures. However, trade secrets and know-how can be difficult to protect. These measures may not, for example, in the case of misappropriation of a trade secret by an employee or third party with authorized access, provide adequate protection for our proprietary information. Our security measures may not prevent an employee or consultant from misappropriating our trade secrets and providing them to a competitor, and any recourse we might take against this type of misconduct may not provide an adequate remedy to protect our interests fully. In addition, trade secrets may be independently developed by others in a manner that could prevent us from receiving legal recourse. If any of our confidential or proprietary information, such as our trade secrets, were to be disclosed or misappropriated, or if any of that information was independently developed by a competitor, our competitive position could be harmed.

In addition, some courts inside and outside the United States are sometimes less willing or unwilling to protect trade secrets. If we choose to go to court to stop a third party from using any of our trade secrets, we may incur substantial costs. Even if we are successful, these types of lawsuits may consume our time and other resources. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

Third parties may assert that our employees, consultants, or advisors have wrongfully used or disclosed confidential information or misappropriated trade secrets.

As is common in the biotechnology and pharmaceutical industries, we employ individuals that are currently or were previously employed at universities, research institutions or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants, and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Also, we have in the past and may in the future be subject to claims that these individuals are violating non-compete agreements with their former employers. We may then have to pursue litigation to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, that perception could have a substantial adverse effect on the price of our ordinary shares or ADSs. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development activities, and we may not have sufficient financial or other resources to adequately conduct this type of litigation or proceedings. For example, some of our competitors may be able to sustain the costs of this type of litigation or proceedings more effectively than we can because of their substantially greater financial resources. In any case, uncertainties resulting from the initiation and continuation of intellectual property litigation or other intellectual property related proceedings could adversely affect our ability to compete in the marketplace.

If our 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 registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors or other third parties 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 registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we 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. Our efforts to enforce or protect our proprietary rights related to trademarks, 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 business, financial condition, results of operations and growth prospects.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- any therapeutic candidates we may develop will likely eventually become commercially available in generic or biosimilar product forms;
- others may be able to make live biotherapeutic products that are similar to any therapeutic candidates we may develop but that are not covered by the claims of the patents that we own or may own in the future;
- we, or our current or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or may own in the future;
- we, or our current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- we, or our current or future collaborators, may fail to meet our obligations to the U.S. government regarding any patents and patent applications funded by U.S. government grants, leading to the loss or unenforceability of patent rights;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications or those that we may own in the future will not lead to issued patents;
- it is possible that there are prior public disclosures that could invalidate our patents, or parts of our patents;
- it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our therapeutic candidates or technology similar to ours
- it is possible that our patents or patent applications omit individual(s) that should be listed as inventor(s) or include individual(s) that should not be listed as inventor(s), which may cause these patents or patents issuing from these patent applications to be held invalid or unenforceable;
- issued patents that we hold rights to may be held invalid, unenforceable, or narrowed in scope, including as a result of legal challenges by our competitors;
- the claims of our issued patents or patent applications, if and when issued, may not cover our therapeutic candidates;
- the laws of foreign countries may not protect our proprietary rights or the proprietary rights of current or future collaborators to the same extent as the laws of the United States;
- the inventors of our patents or patent applications may become involved with competitors, develop products or processes that design around our patents, or become hostile to us or the patents or patent applications on which they are named as inventors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we have engaged in scientific collaborations in the past and will continue to do so in the future and our collaborators may develop adjacent or competing products that are outside the scope of our patents;
- we may not develop additional proprietary technologies that are patentable;
- any therapeutic candidates we develop may be covered by third parties' patents or other exclusive rights;
- the patents of others may harm our business; or
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Risks Related to Our Business Operations and Compliance with Government Regulations

Our operations and financial results could be adversely impacted by the COVID-19 pandemic in the United Kingdom, United States and the rest of the world.

Beginning in late 2019, an outbreak of a novel strain of coronavirus, COVID-19, began to spread globally. In March 2020, the World Health Organization characterized COVID-19 as a pandemic. The COVID-19 pandemic and the related adverse public health developments, including orders to shelter-in-place, travel restrictions, and the imposition of additional requirements on businesses, have adversely affected workforces, organizations, healthcare communities, economies, and financial markets globally, leading to an economic downturn and increased market volatility. Many governments also imposed restrictions on travel. These factors have also disrupted the normal operations of businesses across industries, including ours, and caused significant disruption in the operations of third party manufacturers and contract research organizations, or CROs, upon whom we rely.

In response to the spread of COVID-19 as well as public health directives and orders, we implemented a number of measures to ensure employee safety and business continuity, including limiting access to our laboratory and manufacturing facilities to only those individuals required to execute their job responsibilities and restricted the number of staff working concurrently in any given laboratory, as well as work-from-home policies. Such measures are no longer in effect.

As a result of the COVID-19 pandemic or any other disruption, we may experience disruptions that could 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;
- 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 clinical trials;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others;
- limitations in resources that would otherwise be focused on the conduct of our business or our clinical trials, including because of sickness or the desire to avoid contact with large groups of people or as a result of government-imposed “shelter in place” or similar working restrictions;
- delays in receiving approval from local regulatory authorities to initiate our planned clinical trials;
- delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials;
- interruption in global shipping that may affect the transport of clinical trial materials, such as investigational drug product used in our clinical trials;
- changes in regulations as part of a response to the COVID-19 pandemic which may require us to change the ways in which our clinical trials are conducted, or to discontinue the clinical trials altogether, or which may result in unexpected costs; and
- delays in necessary interactions with regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government or contractor personnel.

Additionally, certain third parties with whom we engage, including our collaborators, contract organizations, third party manufacturers, suppliers, clinical trial sites, regulators and other third parties with whom we conduct business are similarly adjusting their operations and assessing their capacity in light of the COVID-19 pandemic. If these third parties experience shutdowns or continued business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively impacted. For example, as a result of the COVID-19 pandemic, there could be delays in the manufacturing supply chain for our clinical trials, which could delay or otherwise impact our ongoing clinical programs in oncology and respiratory disease. We may also experience delays in procurement of materials for certain aspects of our studies due to the pandemic, which could impact our ability to conduct prespecified analysis.

Additionally, certain preclinical studies for our discovery research programs are conducted by CROs, which could be discontinued or delayed as a result of the pandemic. It is also likely that the disproportionate impact of COVID-19 on hospitals and clinical sites will have an impact on recruitment and retention for our clinical trials.

In addition, certain of our clinical trial sites have experienced, and others may experience in the future, delays in collecting, receiving and analyzing data from patients enrolled in our clinical trials. For example, we experienced delays to our study of MRx-4DP0004 in patients with partly controlled asthma due to limited staff at sites, limitation or suspension of on-site visits by patients, or patients' reluctance to visit the clinical trial sites during the pandemic. We and our CROs have also made certain adjustments to the operation of such trials in an effort to ensure the monitoring and safety of patients and to minimize risks to trial integrity during the pandemic in accordance with the guidance issued by the FDA on March 18, 2020, which the FDA subsequently updated, and generally. We may need to make further adjustments in the future, including those based on additional and future regulatory requirements promulgated by the FDA and other regulatory authorities as a result of the COVID-19 pandemic. Many of these adjustments are new and untested, may not be effective, and may have unforeseen effects on the enrolment, progress and completion of these trials and the findings from these trials. While we are currently continuing our clinical trials and considering adding new clinical trial sites to accelerate patient recruitment, we may not be successful in adding trial sites, may experience delays in patient enrolment or in the progression of our clinical trials, may need to suspend our clinical trials, and may encounter other negative impacts to our trials, due to the effects of the COVID-19 pandemic.

The ultimate impact of the COVID-19 pandemic on our business operations is highly uncertain and subject to change and will depend on future developments which are difficult to predict, including the duration of the COVID-19 pandemic, the ultimate geographic spread of the disease, additional or modified government actions, new information that will emerge concerning the severity and impact of COVID-19 and other actions taken to contain or address its impact in the short and long term, among others. We do not yet know the full extent of potential delays or impacts on our business, our clinical studies, our research programs, healthcare systems or the global economy, and if the ultimate impact of the COVID-19 pandemic and the resulting uncertain economic and healthcare environment is more severe than we anticipated, we may not be able to execute on our current operating plan or on our strategy.

The global outbreak of COVID-19 continues to rapidly evolve. While the extent of the impact of the current COVID-19 pandemic on our business and financial results is uncertain, a continued and prolonged public health crisis such as the COVID-19 pandemic could have a material negative impact on our business, financial condition and operating results.

Our success is highly dependent on our ability to attract and retain highly skilled executive officers and employees.

To succeed, we must recruit, retain, manage and motivate qualified clinical, scientific, technical and management personnel, and we face significant competition for experienced personnel. We are highly dependent on the principal members of our management and scientific and medical staff. If we do not succeed in attracting and retaining qualified personnel, particularly at the management level, it could adversely affect our ability to execute our business plan and harm our operating results. In particular, the loss of one or more of our executive officers could be detrimental to us if we cannot recruit suitable replacements in a timely manner. We could in the future have difficulty attracting and retaining experienced personnel and may be required to expend significant financial resources in our employee recruitment and retention efforts.

Many of the other biotechnology companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide higher compensation, more diverse opportunities and better prospects for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are unable to continue to attract and retain high-quality personnel, the rate and success at which we can discover, develop and commercialize our therapeutic candidates will be limited and the potential for successfully growing our business will be harmed.

Additionally, we rely on our scientific founders and other scientific and clinical advisors and consultants to assist us in formulating our research, development and clinical strategies. These advisors and consultants are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. In addition, these advisors and consultants typically will not enter into non-compete agreements with us. If a conflict of interest arises between their work for us and their work for another entity, we may lose their services. Furthermore, our advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours. In particular, if we are unable to maintain consulting relationships with our scientific founders or if they provide services to our competitors, our development and commercialization efforts will be impaired and our business will be significantly harmed.

In order to successfully implement our plans and strategies, we will need to grow the size of our organization, and we may experience difficulties in managing this growth.

As of December 31, 2021, we had 106 employees, including 45 employees in the United Kingdom and four employees in the United States. Of these employees, 90 were engaged in research and development activities and 16 were engaged in administrative activities. In order to successfully implement our development and commercialization plans and strategies, and we expect to need additional managerial, operational, sales, marketing, financial and other personnel. Future growth would impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining and motivating additional employees;
- managing our internal development efforts effectively, including the commercial, clinical and regulatory development of MRx0518, MRx-4DP0004, MRx0005, MRx0029, Blautix and Thetanix and any other therapeutic candidates, while complying with any contractual obligations to contractors and other third parties we may have; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to successfully develop and commercialize MRx0518, MRx-4DP0004, MRx0005 MRx0029, Blautix and Thetanix and other therapeutic candidates will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services, including key aspects of clinical development and manufacturing. We cannot assure you that the services of independent organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by third party service providers is compromised for any reason, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain marketing approval of MRx0518 and MRx-4DP0004 and any other therapeutic candidates or otherwise advance our business. We cannot assure you that we will be able to manage our existing third-party service providers or find other competent outside contractors and consultants on economically reasonable terms, or at all.

If we are not able to effectively expand our organization by hiring new employees and/or engaging additional third-party service providers, we may not be able to successfully implement the tasks necessary to further develop and commercialize MRx0518, MRx-4DP0004, MRx0005, MRx0029, Blautix and Thetanix and other therapeutic candidates and, accordingly, may not achieve our research, development and commercialization goals.

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or our guidance.

Our quarterly and annual operating results may fluctuate significantly in the future, which makes it difficult for us to predict our future operating results. From time to time, we may enter into license or collaboration agreements or strategic partnerships with other companies that include development funding and significant upfront and milestone payments and/or royalties, which may become an important source of our revenue. These upfront and milestone payments may vary significantly from period to period and any such variance could cause a significant fluctuation in our operating results from one period to the next.

In addition, we measure compensation cost for stock-based awards made to employees at the grant date of the award, based on the fair value of the award as determined by our board of directors, and recognize the cost as an expense over the employee's requisite service period. As the variables that we use as a basis for valuing these awards change over time, including, after the closing of this offering, our underlying share price and stock price volatility, the magnitude of the expense that we must recognize may vary significantly.

Furthermore, our operating results may fluctuate due to a variety of other factors, many of which are outside of our control and may be difficult to predict, including the following:

- the timing and cost of, and level of investment in, research and development activities relating to our current therapeutic candidates and any future therapeutic candidates and research-stage programs, which will change from time to time;
- our ability to enroll patients in clinical trials and the timing of enrolment;
- the cost of manufacturing our current therapeutic candidates and any future therapeutic candidates, which may vary depending on FDA, EMA or other comparable foreign regulatory authority guidelines and requirements, the quantity of production and the terms of our agreements with manufacturers;
- expenditures that we will or may incur to acquire or develop additional therapeutic candidates and technologies or other assets;
- the timing and outcomes of clinical trials for MRx0518, MRx-4DP0004, MRx0005, MRx0029, Blautix and Thetanix, and any of our other therapeutic candidates, or competing therapeutic candidates;
- the need to conduct unanticipated clinical trials or trials that are larger or more complex than anticipated;
- competition from existing and potential future products that compete with MRx0518, MRx-4DP0004, MRx0005, MRx0029, Blautix and Thetanix and any of our other therapeutic candidates, and changes in the competitive landscape of our industry, including consolidation among our competitors or partners;
- any delays in regulatory review or approval of MRx0518, MRx-4DP0004, MRx0005, MRx0029, Blautix and Thetanix or any of our other therapeutic candidates;
- the level of demand for MRx0518, MRx-4DP0004, MRx0005, MRx0029, Blautix and Thetanix and any of our other therapeutic candidates, if approved, which may fluctuate significantly and be difficult to predict;
- the risk/benefit profile, cost and reimbursement policies with respect to our therapeutic candidates, if approved, and existing and potential future products that compete with MRx0518, MRx-4DP0004, MRx0005, MRx0029, Blautix and Thetanix and any of our other therapeutic candidates;
- our ability to commercialize MRx0518, MRx-4DP0004, MRx0005, MRx0029, Blautix and Thetanix and any of our other therapeutic candidates, if approved, inside and outside of the United States, either independently or working with third parties;
- our ability to establish and maintain collaborations, licensing or other arrangements;
- our ability to adequately support future growth;
- potential unforeseen business disruptions that increase our costs or expenses;
- future accounting pronouncements or changes in our accounting policies; and
- the changing and volatile global economic and political environment, including the economic impact of inflation, the COVID-19 pandemic and other geopolitical uncertainty and instability, such as the ongoing geopolitical tensions related to Russia's actions in Ukraine, resulting sanctions imposed by the U.S. and other countries, and retaliatory actions taken by Russia in response to such sanctions.

The cumulative effect of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our ordinary shares or ADSs could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated guidance we may provide.

Actual or anticipated changes to our estimates regarding future expenses, revenues and needs for additional financing, including values on financial instruments, such as warrants, share options and units may create unforeseen fluctuations in profits and tax liability and materially impact our financial results

Actual or anticipated changes to our estimates regarding future expenses, revenues and needs for additional financing, whether immediate or foreseeable, could result in our having to recognize additional liabilities on our balance sheet, or in further write-downs or impairments to our assets and could also have a material adverse effect on our business, results of operations and outlook. For example, we adjusted our unaudited interim condensed consolidated financial statements for the six months period ending June 30, 2021 when we determined that the warrants and units we assumed in connection with the Merger with Longevity should not be recorded as equity instruments and should be recorded as liabilities.

Changes to estimates or accounting treatments may result in differences to our reported results and to the taxable treatment of certain items resulting in variations in our liabilities, income and cash.

Our internal computer systems, or those of any of our CROs, manufacturers, other contractors or consultants or potential future collaborators, may fail or suffer security or data privacy breaches or other unauthorized or improper access to, use of, or destruction of our proprietary or confidential data, employee data, or personal data, which could result in additional costs, loss of revenue, significant liabilities, harm to our brand and material disruption of our operations.

Despite the implementation of security measures in an effort to protect systems that store our information, given their size and complexity and the increasing amounts of information maintained on our internal information technology systems, and those of our third-party CROs, other contractors (including sites performing our clinical trials) and consultants, these systems are potentially vulnerable to breakdown or other damage or interruption from service interruptions, system malfunction, natural disasters, terrorism, war and telecommunication and electrical failures, as well as security breaches from inadvertent or intentional actions by our employees, contractors, consultants, business partners, and/or other third parties, or from cyber-attacks by malicious third parties (including the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information), which may compromise our system infrastructure or lead to the loss, destruction, alteration or dissemination of, or damage to, our data. For example, companies have experienced an increase in frequency and sophistication of phishing and social engineering attacks from third parties in connection with the COVID-19 pandemic, and cybersecurity researchers anticipate an increase in cyberattack activity in connection with Russia's activities in Ukraine.

To the extent that any disruption or security breach were to result in a loss, destruction, unavailability, alteration or dissemination of, or damage to, our data or applications, or for it to be believed or reported that any of these occurred, we could incur liability and reputational damage and the development and commercialization of our therapeutic candidates could be delayed. We cannot assure you that our data protection efforts and our investment in information technology, or the efforts or investments of CROs, consultants or other third parties, will prevent significant breakdowns or breaches in systems or other cyber incidents that cause loss, destruction, unavailability, alteration or dissemination of, or damage to, our data that could have a material adverse effect upon our reputation, business, operations or financial condition. For example, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs and the development of our therapeutic candidates could be delayed. In addition, the loss of clinical trial data for our therapeutic candidates could result in delays in our marketing approval efforts and significantly increase our costs to recover or reproduce the data.

Furthermore, significant disruptions of our internal information technology systems or security breaches could result in the loss, misappropriation, and/or unauthorized access, use, or disclosure of, or the prevention of access to, data (including trade secrets or other confidential information, intellectual property, proprietary business information, and personal information), which could result in financial, legal, business, and reputational harm to us. For example, any such event that leads to unauthorized access, use, or disclosure of personal information, including personal information regarding our clinical trial subjects or employees, could harm our reputation directly, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information, which could result in significant legal and financial exposure and reputational damages that could potentially have an adverse effect on our business.

Notifications and follow-up actions related to a security incident could impact our reputation and cause us to incur significant costs, including legal expenses and remediation costs. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the lost data. We expect to incur significant costs in an effort to detect and prevent security incidents, and we may face increased costs and requirements to expend substantial resources in the event of an actual or perceived security breach. We also rely on third parties to manufacture our therapeutic candidates, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security incident were to result in a loss, destruction or alteration of, or damage to, our data, or inappropriate disclosure of confidential or proprietary information, we could be exposed to litigation and governmental investigations, the further development and commercialization of our therapeutic candidates could be delayed, and we could be subject to significant fines or penalties for any noncompliance with certain state, federal and/or international privacy and security laws.

Our insurance policies may not be adequate to compensate us for the potential losses arising from any such disruption in or, failure or security breach of our systems or third-party systems where information important to our business operations or commercial development is stored. In addition, such insurance may not be available to us in the future on economically reasonable terms, or at all. Further, our insurance may not cover all claims made against us and could have high deductibles in any event, and defending a suit, regardless of its merit, could be costly and divert management attention.

The collection, processing and cross-border transfer of personal information is subject to restrictive laws and regulations.

We are subject to privacy and data protection laws and regulations that apply to the collection, transmission, storage and use of personally identifiable information. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on compliance in this area, with the potential to affect our business.

In the EU, the collection and use of personal data (including health data) is governed by the provisions of the General Data Protection Regulation 2016/679 (the "**EU GDPR**") which became effective and enforceable across all then-current member states of the EU on May 25, 2018. In the United Kingdom, following the end of the transition period for the United Kingdom's withdrawal from the EU on December 31, 2021, the GDPR has been retained as part of domestic law by virtue of the European Union (Withdrawal) Act 2018. The retained law (the "**UK GDPR**") continues to apply alongside the Data Protection Act 2018 (the "**UK Data Protection Laws**"). The UK GDPR has been modified to reflect the fact that the United Kingdom is no longer a member of the EU. The EU GDPR and the UK GDPR are together referred to as the "**GDPR**."

The GDPR enhances data protection obligations for both processors and controllers of personal data, including by materially expanding the definition of what is expressly noted to constitute personal data, requiring additional disclosures about how personal data is to be used, creating mandatory personal data breach notification requirements in certain circumstances, and establishing onerous new obligations on services providers who process personal data solely on behalf of others, as well as obligations regarding the security and confidentiality of the personal data. The EU GDPR also imposes strict rules on the transfer of personal data out of the European Economic Area to third countries, including the United States. The UK GDPR contains equivalent rules on the transfer of personal data out of the United Kingdom. The GDPR has expanded its reach to include any business, regardless of its location, that processes personal data in relation to the offering of goods or services to individuals in the EU and/or the monitoring of their behavior. The UK GDPR has equivalent extra territorial application in relation to the offering of goods or services to individuals in the United Kingdom and/or the monitoring of their behavior. This expansion would incorporate any clinical trial activities in the United Kingdom or EU member states (as applicable). The GDPR prohibits controllers from processing "special categories of personal data" which includes health and genetic information of data subjects, unless a specific derogation applies (such as the data subject has given his explicit consent to the processing of such data). The GDPR also provides data subjects with a swathe of rights, including the right to object to the processing of their personal data, allows them to access their personal data, request deletion of personal data in certain circumstances, and provides an express right to seek legal remedies in the event the individual believes his or her rights have been violated. Failure to comply with the requirements of the GDPR may result in fines of up to 4% of an undertaking's total global annual turnover for the preceding financial year, or €20 million, whichever is greater. In addition to administrative fines, a wide variety of other potential enforcement powers are available to competent authorities in respect of potential and suspected violations of the GDPR, including extensive audit and inspection rights, and powers to order temporary or permanent bans on all or some processing of personal data carried out by noncompliant actors. While we have taken steps to comply with the GDPR, and implementing legislation in the United Kingdom and applicable member states, including by seeking to establish appropriate lawful bases for the various processing activities we carry out as a controller, reviewing our security procedures, and entering into data processing agreements with relevant customers and business partners, we cannot guarantee that our efforts to achieve and remain in compliance have been, and/or will continue to be, fully successful.

Businesses based in the United Kingdom who offer goods or services to individuals in the EU and/or monitor their behavior (and vice versa) are now subject to both the EU GDPR and the UK GDPR. This may result in some duplication of liabilities, expenses, costs, and other operational losses in connection with measures taken to comply with the two separate laws. In particular, there are now two parallel enforcement regimes, each with the power to impose fines up to the greater of either 4% of total global annual turnover, or €20 million (under the EU GDPR) or £17.5 million (under the UK GDPR).

In addition, the United Kingdom is now considered a "third country" under the EU GDPR and EU countries are considered "third countries" under the UK GDPR, which may have an impact on transfers of personal data between the United Kingdom and EU countries.

In respect of personal data transfers from the EU to the United Kingdom, on June 28, 2021, the European Commission adopted two adequacy decisions for the United Kingdom— one under the EU GDPR and the other for the Law Enforcement Directive 2016/680. This means that personal data can now flow freely from the EU to the United Kingdom where it benefits from an essentially equivalent level of protection to that guaranteed under EU law. The adequacy decisions also facilitate the correct implementation of the EU-UK Trade and Cooperation Agreement, which foresees the exchange of personal data, for example for cooperation on judicial matters. Both adequacy decisions include strong safeguards in case of future divergence such as a 'sunset clause', which limits the duration of adequacy to four years.

In respect of personal data transfers from the United Kingdom to the EU, transfers of personal data are expressly permitted under the UK Data Protection Laws.

The so-called "Schrems II" judgement, which was delivered by the Courts of Justice of the European Union in July 2020 poses a further risk which needs to be noted. The judgement applies both in the EU and the United Kingdom since it was delivered before the end of the transition period. The Schrems II judgement effectively renders unlawful transfers of personal data to entities in the US which are caught by section 702 of the Foreign Intelligence Surveillance Act, unless additional safeguards are put in place and it raises concerns that transfers to other countries may similarly be deemed unlawful depending on the applicable domestic legal framework. Before engaging in international personal data transfers, United Kingdom and EU entities are now required to assess the local laws which will apply to the data after it is transferred in the context of the personal data transfer, namely taking account of the nature of the data, volume, duration and frequency of the transfers, and likelihood of a request by a public authority.

Similarly, failure to comply with federal and state laws in the United States regarding privacy and security of personal information could further expose us to penalties under privacy and data protection laws. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our business.

Our employees, consultants and contractors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements or insider trading violations, which could significantly harm our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees, consultants or contractors could include intentional failures to comply with governmental regulations, comply with healthcare fraud and abuse and anti-kickback laws and regulations in the United States, the United Kingdom and other jurisdictions, or failure to report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of, including improper trading based upon information obtained in the course of clinical studies, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a robust compliance program, but it is not always possible to identify and deter employee misconduct, 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 comply with these laws or 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 and results of operations, including the imposition of significant fines or other sanctions.

Inadequate funding for the FDA, the SEC and other government agencies could hinder or otherwise prevent those agencies from performing normal business 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 products can be affected by a variety of factors, including government budget and funding levels and the ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the Securities and Exchange Commission (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. Disruptions at the FDA and other agencies, such as due to COVID-19 related factors, furloughs or government shutdowns, may also increase the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business.

Separately, in response to the COVID-19 pandemic, since March 2020 when foreign and domestic inspections of facilities were largely placed on hold, the FDA has been working to resume routine surveillance, bioresearch monitoring and pre-approval inspections on a prioritized basis. In 2020 and 2021, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. As of May 2021, the FDA noted it was continuing to ensure timely reviews of applications for medical products during the ongoing COVID-19 pandemic in line with its user fee performance goals and conducting mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. However, the FDA review timelines could be extended due to various factors, including where a pre-approval inspection or an inspection of clinical sites is required and due to the ongoing COVID-19 pandemic and other factors that disrupt normal operations, the FDA is unable to complete such required inspections during the review period. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic 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.

Healthcare legislative reform measures may have a negative impact on our business and results of operations.

In the United States, there have been, and continue to be, legislative and regulatory developments regarding the healthcare system that could prevent or delay marketing approval of our therapeutic candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell any therapeutic candidates for which we obtain marketing approval. Additionally, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state 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 products. While any proposed measures will require authorization through additional legislation to become effective, Congress and the current administration have each indicated that they will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological 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. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or successfully commercialize our drugs.

The withdrawal of the United Kingdom from the EU, commonly referred to as "Brexit," may adversely impact our ability to obtain regulatory approvals of our therapeutic candidates in the EU, result in restrictions, delays or increased costs for importing our therapeutic candidates into the EU, and may require us to incur additional expenses in order to develop, manufacture and commercialize our therapeutic candidates in the EU.

Following the result of a referendum in 2016, the United Kingdom left the EU on January 31, 2020, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the EU, the United Kingdom was subject to a transition period (the "**Transition Period**") during which EU rules continued to apply, which ended on December 31, 2020. Following negotiations, the two sides agreed on a Trade and Cooperation Agreement ("**TCA**"), which became effective on January 1, 2021

The TCA provides for a no tariff, no quota on goods trade deal. However, there will now be a need for border controls and checks in importing and exporting goods into the EU, potentially leading to delays and additional costs.

Currently, a significant proportion of the regulatory framework in the United Kingdom applicable to our business and our therapeutic candidates is derived from EU directives and regulations. In the immediate post-Brexit period, a lot of EU legislation has been retained as domestic legislation by virtue of the EU (Withdrawal) Act 2018 (as amended). However, the UK may choose to amend retained legislation over time. This could materially impact the existing regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our therapeutic candidates in the United Kingdom or the EU.

Following the Transition Period, the United Kingdom is no longer covered by the centralized procedures for obtaining EU-wide marketing authorization from the European Medicines Agency and a separate process for authorization of drug products, including our therapeutic candidates, will be required in the United Kingdom, the new processes being outlined by the Medicines and Healthcare Products Regulatory Agency (with existing applications via the centralized procedure being addressed by transitional arrangements). Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of the new or transitional processes or otherwise, could make it more difficult for us to commercialize our therapeutic candidates in the EU or in the United Kingdom and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom or the EU for our therapeutic candidates, or incur significant additional expenses to operate our business, which could significantly and materially harm or delay our ability to generate revenues or achieve profitability of our business.

Although the TCA means that we should not be required to pay new tariffs in connection with the importation of our therapeutic candidates from the UK into the EU and vice versa, this will depend upon whether the products satisfy complex rules of origin. If goods being imported into the EU from the UK are not treated under these rules as originating in the UK, EU tariffs may be payable. In the near term there is also a risk of disrupted import and export processes due to a lack of administrative processing capacity by the respective UK and EU customs agencies that may delay time-sensitive shipments and may negatively impact our product supply chain.

In addition, in order to benefit from no tariffs, a product must meet complex rules which certify its origins as being from the UK or the EU (or at least, being substantively processed in one or the other). Any further changes in international trade, tariff and import/export regulations as a result of Brexit or otherwise may impose unexpected duty costs or other non-tariff barriers on us. These developments, or the perception that any of them could occur, may significantly reduce global trade and, in particular, trade between the impacted nations and the United Kingdom.

It is also possible that Brexit may negatively affect our ability to attract and retain employees, particularly those from the EU, since free movement of workers between the UK and EU will now require visas and other permits in a number of circumstances, and hence make travel by our employees between our UK, Irish and Spanish facilities more difficult, time-consuming and expensive than previously was the case.

Our business may incur VAT in EU states where it is not established and does not make supplies. VAT incurred by the UK companies in the group will not have access to the EU's electronic system for claiming refunds. Although refunds should still be obtainable, claims will have to be made direct to the relevant tax authorities, which means reclaims could be significantly more complex and slower to process. Such differences have the potential to materially affect cash requirements and costs to the business.

Legal, political and economic uncertainty surrounding Brexit may be a source of instability in international markets, create significant currency fluctuations, adversely affect our operations in the United Kingdom and pose additional risks to our business, revenue, financial condition, and results of operations.

While our headquarters are in the United Kingdom, we have subsidiaries elsewhere in the EU, currently in Ireland and Spain, and rely on suppliers elsewhere in the EU. On the one hand, this is helpful to us since having an "establishment" in the EU is now required for compliance with a number of relevant regulatory matters, for example a clinical trials sponsor must either be established in the EU or, if not, appoint a legal representative in an EU27 country. However, since future UK laws and regulations, including financial laws and regulations, tax and free trade agreements, intellectual property rights, data protection laws, supply chain logistics, environmental, health and safety laws and regulations, immigration laws and employment laws, may diverge from EU law and regulation in the future, this may negatively impact foreign direct investment in the United Kingdom, increase costs, depress economic activity and restrict access to capital.

Although the TCA is agreed between the principals, there is still material clarification required on the detail of how higher-level principles will be reflected into day-to-day processes and operations. Hence there is still likely to be a degree of uncertainty concerning the United Kingdom's ongoing legal, political and economic relationship with the EU, which may be a source of instability in the international markets, create significant currency fluctuations, and/or otherwise adversely affect trading agreements or similar cross-border cooperation arrangements (whether economic, tax, fiscal, legal, regulatory or otherwise).

These developments, or the perception that any of them could occur, 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 limit 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 well as on the regulatory process in Europe. Asset valuations, currency exchange rates and credit ratings may also be subject to increased market volatility. The TCA is subject to regular (every five years) review provisions. In addition, each party has the right to take certain trade defense measures unilaterally (which could include the imposition of tariffs or quotas or suspension of certain aspects of the TCA) subject to binding arbitration procedures. Ultimately, either party has the right to require the "rebalancing" of rights and obligations under the TCA in circumstances where there has been a significant and persistent divergence in subsidy-control or environmental and labor regulation. Irrespective of the need to "rebalance" the TCA, each party also has the right to terminate it, by giving 12 months' notice. Accordingly, the nature of the TCA is such that it creates a lot of uncertainty for businesses.

The detail of how the United Kingdom's access to the European single market for goods, capital, services and labor within the EU, or single market, and the wider commercial, legal and regulatory environment, will impact our UK operations and customers remains to be fully understood. There may continue to be economic uncertainty surrounding the consequences of Brexit, which could adversely impact customer confidence resulting in customers reducing their spending budgets on our products, which could adversely affect our business, revenue, financial condition, results of operations and could adversely affect the market price of our shares and ADSs.

We are currently operating in a period of economic uncertainty and capital markets disruption, which has been significantly impacted by geopolitical instability due to the ongoing military conflict between Russia and Ukraine.

U.S. and global markets are experiencing volatility and disruption following the escalation of geopolitical tensions and the start of the military conflict between Russia and Ukraine. In February 2022, Russia launched a full-scale military invasion of Ukraine. Although the length and impact of the ongoing military conflict is highly unpredictable, the conflict in Ukraine could lead to market disruptions, including significant volatility in commodity prices, credit and capital markets. Additionally, Russia's prior annexation of Crimea, recent recognition of two separatist republics in the Donetsk and Luhansk regions of Ukraine and subsequent military interventions in Ukraine have led to sanctions and other penalties being levied by the United States, European Union and other countries against Russia, Belarus, the Crimea Region of Ukraine, the so-called Donetsk People's Republic, and the so-called Luhansk People's Republic, including agreement to remove certain Russian financial institutions from the Society for Worldwide Interbank Financial Telecommunication (SWIFT) payment system. Additional potential sanctions and penalties have also been proposed and/or threatened. Russian military actions and the resulting sanctions could adversely affect the global economy and financial markets and lead to instability and lack of liquidity in capital markets, potentially making it more difficult for us to obtain additional funds. Any of the abovementioned factors could affect our business, prospects, financial condition, and operating results. The extent and duration of the military action, sanctions and resulting market disruptions are impossible to predict, but could be substantial. Any such disruptions may also magnify the impact of other risks described in this Annual Report on Form 20-F.

Exchange rate fluctuations may adversely affect our results of operations and cash flows.

Our functional currency is pounds sterling, and our transactions are commonly denominated in that currency. However, we receive payments under our collaboration agreements in U.S. dollars and we incur a portion of our expenses in other currencies, primarily Euros. As a result, fluctuations in exchange rates, particularly between the pound sterling on the one hand and the U.S. dollar and Euro on the other hand, may adversely affect our reported results of operations and cash flows. Since the Brexit referendum in 2016, there has been a significant increase in the volatility of these exchange rates and an overall weakening of the pound sterling. Our business and the price of our shares and ADSs may be affected by fluctuations in foreign exchange rates between the pound sterling and these and other currencies, any of which may have a significant impact on our results of operations and cash flows from period to period.

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 have a material adverse effect on the success of 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 products. 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.

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 or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. 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 production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to Our ADSs and Ordinary Shares

The price of our ordinary shares or ADSs may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our ordinary shares or ADSs, and we could be subject to securities class action litigation as a result.

Our stock price is likely to be volatile. A public market has only been established for our ADSs since March 22, 2021, and such a market may not be sustained. The stock market in general, and the market for smaller biopharmaceutical companies in particular, have 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 price at which you purchase the shares. The lack of an active market may also reduce the fair market value of the ADSs and could also affect the market price for our ordinary shares on AIM. The price at which ADSs trade on Nasdaq may or may not be correlated with the price at which our ordinary shares trade on AIM.

The market price for our ordinary shares or ADSs may be influenced by many factors, including:

- the success of competitive products or technologies;
- actual or anticipated changes in our growth rate relative to our competitors;
- results of clinical trials of our therapeutic candidates or those of our competitors;
- developments related to any future collaborations;
- regulatory or legal developments in the United States and other countries;
- adverse actions taken by regulatory agencies with respect to our preclinical studies or clinical trials, manufacturing or sales and marketing activities;
- any adverse changes to our relationship with third party contractors or manufacturers;
- development of new therapeutic candidates that may address our markets and may make our existing therapeutic candidates less attractive;
- changes in physician, hospital or healthcare provider practices that may make our therapeutic candidates less useful;
- announcements by us, our collaborators or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;

- the level of expenses related to any of our therapeutic candidates or product development programs;
- failure to meet or exceed financial estimates and projections of the investment community or that we provide to the public;
- press reports or other negative publicity, whether or not true, about our business;
- the results of our efforts to discover, develop, acquire or in-license additional therapeutic candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- the trading volume of our ADSs on Nasdaq or ordinary shares on AIM;
- sales of our ADSs or ordinary shares by us, members of our senior management and directors or our shareholders;
- general economic, political, and market conditions and overall fluctuations in the financial markets in the United States, the United Kingdom, the EU, and other countries, including the global and regional impacts of the COVID-19 pandemic and the ongoing geopolitical tensions related to Russia's actions in Ukraine, resulting sanctions imposed by the U.S. and other countries, and retaliatory actions taken by Russia in response to such sanctions; and
- the other factors described in this "Risk Factors" section.

These and other market and industry factors may cause the market price and demand for our ordinary shares and ADSs to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from selling their ordinary shares or ADSs at or above the price paid for the ordinary shares or ADSs and may otherwise negatively affect the liquidity of our ordinary shares or ADSs.

Some companies that have experienced volatility in the trading price of their shares have been the subject of securities class action litigation. Any lawsuit to which we are a party, with or without merit, may result in an unfavorable judgment. We also may decide to settle lawsuits on unfavorable terms.

Any such negative outcome could result in payments of substantial damages or fines, damage to our reputation or adverse changes to our business practices. Defending against litigation is costly and time-consuming and could divert our management's and key employees' attention and our resources. Furthermore, during the course of litigation, there could be negative public announcements of the results of hearings, motions or other interim proceedings or developments, which could have a negative effect on the market price of our ordinary shares or ADSs.

Future sales, or the possibility of future sales, of a substantial number of ADSs representing our shares or our shares could adversely affect the price of such securities.

Future sales of a substantial number of ADSs or shares, or the perception that such sales will occur, could cause a decline in the market price of our shares or ADSs. If holders sell substantial amounts of ADSs on Nasdaq or ordinary shares on AIM, or if the market perceives that such sales may occur, the market price of the ADSs and the ordinary shares may fall and our ability to raise capital through an issue of equity securities in the future could be adversely affected.

The dual-listing of ordinary shares and ADSs is costly to maintain and may adversely affect the liquidity and value of our ordinary shares and ADSs.

Our ordinary shares trade on AIM and our ADSs trade on Nasdaq. For now, we plan to maintain a dual listing, which will generate additional costs, including increased legal, accounting, investor relations and other expenses that we did not incur prior to the listing of our ADSs on Nasdaq, in addition to the costs associated with the additional reporting requirements. We cannot predict the effect of this dual listing on the value of our ADSs and ordinary shares. However, the dual listing of ADSs and ordinary shares may dilute the liquidity of these securities in one or both markets and may adversely affect the development of an active trading market for our ADSs. The price of our ADSs could also be adversely affected by trading in our ordinary shares on AIM.

We are an "emerging growth company" and the reduced disclosure requirements applicable to emerging growth companies may make our ADSs less attractive to investors.

We are an emerging growth company as that term is used in the JOBS Act and may remain an emerging growth company until the earlier of (i) the last day of the fiscal year (A) following the fifth anniversary of the completion of the Merger, (B) in which we have total annual gross revenue of at least $1.07 billion, or (C) in which we are deemed to be a large accelerated filer, which means the market value of our outstanding ordinary shares that are held by non-affiliates exceeds $700 million as of the prior June 30, and (ii) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three year period. For so long as we remain an emerging growth company, we are permitted to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies and we intend to rely on certain of these exemptions. These exemptions include:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. We have elected to take advantage of this extended transition period.

We have elected to take advantage of certain of the reduced reporting obligations. In particular, we have not included all of the executive compensation information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our ADSs less attractive if we rely on certain or all of these exemptions. If some investors find our ADSs less attractive as a result, there may be a less active trading market for our ADSs and our ADS price may be more volatile.

We qualify as a foreign private issuer and, as a result, we will not be subject to U.S. proxy rules and will be subject to Exchange Act reporting obligations that, to some extent, are more lenient and less frequent than those of a U.S. domestic public company. This may limit the information available to holders of our ADSs.

We are a foreign private issuer, as such term is defined in Rule 405 under the Securities Act, and 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 a foreign private issuer, 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 are applicable to U.S. domestic public companies, including (i) the sections of the Exchange Act regulating the solicitation of proxies, consents or authorizations in respect of a security registered under the Exchange Act; (ii) the 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 (including the requirement applicable to emerging growth companies to disclose the compensation of our Chief Executive Officer and the other two most highly compensated executive officers on an individual, rather than an aggregate, basis); and (iii) 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. In addition, foreign private issuers are not required to file their annual report on Form 20-F until 120 days after the end of each fiscal year, while U.S. domestic issuers that are accelerated filers are required to file their annual report on Form 10-K within 75 days after the end of each fiscal year. Foreign private issuers also are exempt from Regulation Fair Disclosure, aimed at preventing issuers from making selective disclosures of material information. Accordingly, there may be less publicly available information concerning our business than there would be if we were a U.S. public company and you may not have the same protections afforded to shareholders of US-listed companies that are not foreign private issuers.

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 Nasdaq corporate governance listing standards.

As a foreign private issuer listed on Nasdaq, we will be subject to corporate governance listing standards. However, Nasdaq rules permit a foreign private issuer like us to follow the corporate governance practices of its home country in lieu of certain Nasdaq corporate governance listing standards. Certain corporate governance practices in England, which is our home country, may differ significantly from Nasdaq corporate governance listing standards. For example, neither the corporate laws of England nor our articles of association require a majority of our directors to be independent; we may include non-independent directors as members of our nominations and remuneration committees; and our independent directors would not necessarily hold regularly scheduled meetings at which only independent directors are present. We are required to follow the AIM Rules for Companies published by London Stock Exchange plc, and have adopted the Corporate Governance Code published by the Quoted Companies Alliance. Therefore, our shareholders may be afforded less protection than they otherwise would have under Nasdaq corporate governance listing standards applicable to U.S. domestic issuers. See "Item 16.G—Corporate Governance— Foreign Private Issuer Exemption" for the exemptions to the Nasdaq corporate governance rules applicable to foreign private issuers.

We may lose our foreign private issuer status in the future, which could result in significant additional cost and expense.

We are a foreign private issuer, as such term is defined in Rule 405 under the Securities Act, however, under Rule 405, 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 a majority of our shareholders, directors or management are U.S. citizens or residents and we fail to meet additional requirements necessary to avoid loss of foreign private issuer status. Although we may elect to comply with certain U.S. regulatory provisions, our loss of foreign private issuer status would make such provisions mandatory. The regulatory and compliance costs to us under U.S. securities laws as a U.S. domestic issuer may be significantly higher. 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 than the forms available to a foreign private issuer. For example, the annual report on Form 10-K requires domestic issuers to disclose executive compensation information on an individual basis with specific disclosure regarding the domestic compensation philosophy, objectives, annual total compensation (base salary, bonus, and equity compensation) and potential payments in connection with change in control, retirement, death or disability, while the annual report on Form 20-F permits foreign private issuers to disclose compensation information on an aggregate basis.

We would also have to mandatorily comply with U.S. federal proxy requirements, and our officers, directors, and principal shareholders will become subject to the short-swing profit disclosure and recovery provisions of Section 16 of the Exchange Act. We may also be required to modify certain of our policies to comply with good governance practices associated with U.S. domestic issuers. Such conversion and modifications will involve additional costs. 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.

We will incur increased costs as a result of simultaneously having our ADSs listed in the United States and our ordinary shares admitted to trading on AIM in the United Kingdom, and our senior management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a company whose securities are publicly listed in the United States, we incur significant legal, accounting and other expenses, even though our ordinary shares are admitted to trading on AIM, and these expenses may increase after we are no longer an EGC. We will be subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Protection Act, as well as rules adopted, and to be adopted, by the SEC and Nasdaq. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, we expect these rules and regulations to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly, which will increase our operating expenses. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain sufficient coverage, particularly in light of recent cost increases related to coverage. We cannot accurately predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

In addition, as a public company we will be required to incur additional costs and obligations in order to comply with SEC rules that implement Section 404 of the Sarbanes-Oxley Act. Under these rules, beginning with our second annual report on Form 20-F after we become a company whose securities are publicly listed in the United States, we will be required to make a formal assessment of the effectiveness of our internal control over financial reporting, and once we cease to be an emerging growth company, we will be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaging 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 our internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are designed and operating effectively, and implement a continuous reporting and improvement process for internal control over financial reporting.

The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation to meet the detailed standards under the rules. During the course of its testing, our management may identify material weaknesses or deficiencies which may not be remedied in time to meet the deadline imposed by the Sarbanes-Oxley Act. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the market price of our stock could decline and we could be subject to sanctions or investigations by the stock exchange on which our ordinary shares are listed, the SEC or other regulatory authorities.

Further, being a U.S. listed company and an English public company with ordinary shares admitted to trading on AIM impacts the disclosure of information and requires compliance with two sets of applicable rules. From time to time, this may result in uncertainty regarding compliance matters and result in higher costs necessitated by legal analysis of dual legal regimes, ongoing revisions to disclosure and adherence to heightened governance practices. As a result of the enhanced disclosure requirements of the U.S. securities laws, business and financial information that we report is broadly disseminated and highly visible to investors, which we believe may increase the likelihood of threatened or actual litigation, including by competitors and other third parties, which could, even if unsuccessful, divert financial resources and the attention of our management and key employees from our operations.

If we do not develop and implement all required accounting practices and policies, including proper and effective internal control over financial reporting, we may be unable to provide the financial information required of a U.S. publicly traded company in a timely and reliable manner 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 shares and ADSs.

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be re-evaluated frequently. Our 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 in accordance with generally accepted accounting principles. We continue to improve the process of documenting, reviewing and improving our internal controls and procedures for compliance with Section 404, which requires annual management assessment of the effectiveness of our internal control over financial reporting. Having already added to our accounting and finance personnel in the year we continue our recruitment of personnel with certain skill sets that are needed as an English public company listed in the U.S.

Implementing any appropriate changes to our internal controls may distract our officers and employees from day-to-day business operations, entail substantial costs to modify our existing processes, and take significant time to complete. These changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements on a timely basis, could increase our operating costs and harm our business.

Any delays or deficiencies in our internal controls could penalize us, including by limiting our ability to obtain financing, either in the public capital markets or from private sources and hurt our reputation and could thereby impede our ability to implement our growth strategy. In addition, any such delays or deficiencies could result in our failure to meet the requirements to maintain our ADSs listed on a national securities exchange.

Our Articles of Association and the Deposit Agreement for our ADSs provide that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act and that certain claims may only be instituted in the courts of England and Wales, which could limit our securityholders' ability to choose the judicial forum for disputes with us or our directors, shareholders, officers, or others.

Section 22 of the Securities Act creates concurrent jurisdiction for U.S. federal and state courts over all causes of action arising under the Securities Act. Accordingly, both U.S. state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, we have amended our Articles of Association to provide that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act. The Deposit Agreement similarly provides for such an exclusive forum for such causes of action. This exclusive forum provision will not apply to suits brought to enforce any liability or duty created by the Exchange Act. Any person or entity purchasing or otherwise acquiring any interest in any of our securities shall be deemed to have notice of and consented to the foregoing provisions.

We have amended our Articles of Association to provide that any action asserting a claim that is governed by the internal affairs doctrine, such as, for example, an action asserting a claim of breach of fiduciary duty owed by any of our directors, officers, or other employees, including the ability to bring such a claim, shall be governed by and construed in accordance with the laws of England and Wales, and that any such claims may only be instituted in the courts of England and Wales.

Although we believe these exclusive forum provisions benefit us by providing increased consistency in the application of U.S. federal securities laws and the laws of England and Wales in the types of lawsuits to which they apply, these provisions may limit a shareholder's ability to bring a claim in a judicial forum of its choosing for disputes with us or any of our directors, shareholders, officers, or others, or may increase the cost of doing so, both of which may discourage lawsuits with respect to such claims. Our shareholders will not be deemed to have waived our compliance with the U.S. federal securities laws and the rules and regulations thereunder as a result of our exclusive forum provision. Further, in the event a court finds the exclusive forum provisions contained in our Articles of Association or the Deposit Agreement to be unenforceable or inapplicable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could harm our results of operations.

If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, the price and trading volume of our shares and ADSs could decline.

The trading market for our shares and ADSs is influenced by the research and reports that equity research analysts publish about us and our business. As a company admitted to trading on AIM, our equity securities are currently subject to coverage by a number of analysts. Equity research analysts may elect not to provide research coverage of our ADSs, and such lack of research coverage may adversely affect the market price of our ADSs. We will not have any control over the analysts or the content and opinions included in their reports. If any of the equity research analysts who cover us downgrade our shares or ADSs or issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our target preclinical studies or clinical studies and/or operating results fail to meet the expectations of analysts, the price of our shares or ADSs could decline. If one or more equity research analysts ceases coverage of us or fails to publish reports on us regularly, demand for our shares or ADSs could decrease, which in turn could cause the trading price or trading volume of our shares or ADSs to decline.

Concentration of ownership of our ordinary shares (including ordinary shares represented by ADSs) among our existing senior management, directors and principal shareholders may prevent new investors from influencing significant corporate decisions and matters submitted to shareholders for approval.

Members of our senior management, directors and current beneficial owners of 5% or more of our ordinary shares and their respective affiliates will, in the aggregate, beneficially own approximately 15.6% of our issued and outstanding ordinary shares, based on the number of ordinary shares issued and outstanding as of March 25, 2022. As a result, depending on the level of attendance at general meetings of our shareholders, these persons, acting together, would be able to significantly influence all matters requiring shareholder approval, including the election, re-election and removal of directors, any merger, scheme of arrangement, or sale of all or substantially all of our assets, or other significant corporate transactions, and amendments to our articles of association. In addition, these persons, acting together, may have the ability to control the management and affairs of our company. Accordingly, this concentration of ownership may harm the market price of our ADSs by:

- delaying, deferring, or preventing a change in control;
- entrenching our management and/or the board of directors;
- impeding a merger, scheme of arrangement, takeover, or other business combination involving us; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

In addition, some of these persons or entities may have interests different than yours. For example, because many of these shareholders purchased their shares at prices substantially below the current market price for an ordinary share on AIM and have held their shares for a longer period, they may be more interested in selling our company to an acquirer than other investors, or they may want us to pursue strategies that deviate from the interests of other shareholders.

Because we do not anticipate paying any cash dividends on our ordinary shares (including ordinary shares represented by ADSs) in the foreseeable future, capital appreciation, if any, will be your sole source of gains and you may never receive a return on your investment.

You should not rely on an investment in our ADSs to provide dividend income. 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 paid. Therefore, we must have distributable profits before issuing a dividend. We have never declared or paid a dividend on our ordinary shares in the past, and we currently intend to retain our future earnings, if any, to fund the development of our technologies and therapeutic candidates and the growth of our business. As a result, capital appreciation, if any, on our ADSs will be your sole source of gains for the foreseeable future. Investors seeking cash dividends should not purchase our ADSs.

Securities traded on AIM may carry a higher risk than securities traded on other exchanges, which may impact the value of your investment.

Our ordinary shares are currently traded on AIM. Investment in equities traded on AIM is sometimes perceived to carry a higher risk than an investment in equities quoted on exchanges with more stringent listing requirements, such as the Main Market of the London Stock Exchange, New York Stock Exchange or Nasdaq. This is because AIM imposes less stringent corporate governance and ongoing reporting requirements than those other exchanges. In addition, AIM requires only half-yearly, rather than quarterly, financial reporting. The value of our ordinary shares may be influenced by many factors, some of which may be specific to us and some of which may affect AIM companies generally, including the depth and liquidity of the market, our performance, a large or small volume of trading in our ordinary shares, legislative changes and general economic, political or regulatory conditions, and that the prices may be volatile and subject to extensive fluctuations. Therefore, the market price of our ordinary shares, the ADSs, or the ordinary shares underlying the ADSs, may not reflect the underlying value of our company.

Fluctuations in the exchange rate between the U.S. dollar and the British pound sterling may increase the risk of holding ADSs and ordinary shares.

The share price of our ordinary shares is quoted on AIM in British pounds sterling, while our ADSs trade on Nasdaq in U.S. dollars. Fluctuations in the exchange rate between the U.S. dollar and the British pound sterling may result in differences between the value of our ADSs and the value of our ordinary shares, which may result in heavy trading by investors seeking to exploit such exchange rate differences. In addition, as a result of fluctuations in the exchange rate between the U.S. dollar and the British pound sterling, the U.S. dollar equivalent of the proceeds that a holder of the ADSs would receive upon the sale in the United Kingdom of any ordinary shares withdrawn from the depositary, and the U.S. dollar equivalent of any cash dividends paid in British pounds sterling on ordinary shares represented by the ADSs, could also decline.

Holders of our ADSs have fewer rights than our shareholders and must act through the depositary to exercise their rights.

Holders of our ADSs do not have the same rights as our shareholders who hold our ordinary shares directly and may only exercise their voting rights with respect to the underlying ordinary shares in accordance with the provisions of the deposit agreement. Holders of the ADSs will appoint the depositary or its nominee as their representative to exercise the voting rights attaching to the ordinary shares represented by the ADSs. When a general meeting is convened, if you hold ADSs, you may not receive sufficient notice of a shareholders' meeting to permit you to withdraw the ordinary shares underlying your ADSs to allow you to vote with respect to any specific matter. We will use commercially reasonable efforts to cause the depositary to extend voting rights to you in a timely manner, but we cannot assure you that you will receive voting materials in time to instruct the depositary to vote, and it is possible that you, or persons who hold their ADSs through brokers, dealers or other third parties, will not have the opportunity to exercise a right to vote. Furthermore, the depositary will not be liable for any failure to carry out any instructions to vote, for the manner in which any vote is cast or for the effect of any such vote. As a result, you may not be able to exercise your right to vote and you may lack recourse if your ADSs are not voted as you request. In addition, in your capacity as an ADS holder, you will not be able to call a shareholders' meeting.

You may be subject to limitations on transfers of your ADSs.

Your ADSs are transferable on the books of the depositary. However, the depositary may close its transfer books at any time or from time to time when deemed necessary or advisable by it in good faith in connection with the performance of its duties or at our reasonable written request, subject in all cases to compliance with applicable U.S. securities laws. In addition, 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 deems it advisable to do so because of any requirement of law or of any government or governmental body, or under any provision of the deposit agreement, or for any other reason, subject to certain rights to cancel ADSs and withdraw the underlying ordinary shares. Temporary delays in the cancellation of 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 because we are paying a dividend on our ordinary shares or similar corporate actions.

The depositary for our ADSs is entitled to charge holders fees for various services, including annual service fees.

The depositary for our ADSs is entitled to charge holders fees for various services, including for the issuance of ADSs upon deposit of ordinary shares (other than in the case of ADSs issued pursuant to the merger), cancellation of ADSs, distributions of cash dividends or other cash distributions, distributions of ADSs pursuant to share dividends or other free share distributions, distributions of securities other than ADSs and annual service fees. In the case of ADSs issued by the depositary into The Depository Trust Company, or DTC, the fees will be charged by the DTC participant to the account of the applicable beneficial owner in accordance with the procedures and practices of the DTC participant as in effect at the time. The depositary for our ADSs will not generally be responsible for any United Kingdom stamp duty or stamp duty reserve tax arising upon the issuance or transfer of ADSs.

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.

Although we do not have any present plans to declare or pay any dividends, in the event we declare and pay any dividend, the depositary for the ADSs has agreed to pay to you the 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 register under U.S. securities laws any offering of ADSs, ordinary shares or other securities received through such distributions. We also 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.

Your right to participate in any future rights offerings may be limited, which may cause dilution to your holdings.

Under English law, shareholders usually have preemptive rights to subscribe on a pro rata basis in the issuance of new shares for cash. The exercise of preemptive rights by certain shareholders not resident in the United Kingdom may be restricted by applicable law or practice in the United Kingdom and overseas jurisdictions. We may from time to time distribute rights to our shareholders, including rights to acquire our securities. However, we cannot make rights available to you in the United States unless we register the rights and the securities to which the rights relate under the Securities Act or an exemption from the registration requirements is available. Also, under the deposit agreement, the depositary bank will not make rights available to you unless either both the rights and any related securities are registered under the Securities Act, or the distribution of them to ADS holders is exempted from registration under the Securities Act. We are under no obligation to file a registration statement with respect to any such rights or securities or to endeavor to cause such a registration statement to be declared effective. Moreover, we may not be able to establish an exemption from registration under the Securities Act. If the depositary does not distribute the rights, it may, under the deposit agreement, either sell them, if possible, or allow them to lapse. Accordingly, you may be unable to participate in our rights offerings and may experience dilution in your holdings. We are also permitted under English law to disapply preemptive rights (subject to the approval of our shareholders by special resolution or the inclusion in our articles of association of a power to disapply such rights) and thereby exclude certain shareholders, such as overseas shareholders, from participating in a rights offering (usually to avoid a breach of local securities laws).

We may be a passive foreign investment company, which could result in adverse U.S. federal income tax consequences to U.S. investors owning the ADSs or our ordinary shares.

A non-U.S. corporation, such as our company, will be considered a PFIC for any taxable year if either (i) at least 75% of its gross income is passive income or (ii) at least 50% of the value of its assets (based on an average of the quarterly values of the assets during a taxable year) is attributable to assets that produce or are held for the production of passive income.

Based upon our current and projected income and assets, and projections as to the value of our assets, we do not anticipate that we will be a PFIC for the 2022 taxable year or the foreseeable future. However, no assurance can be given in this regard because the determination of whether we will be or become a PFIC is a factual determination made annually that will depend, in part, upon the composition of our income and assets, and we have not and will not obtain an opinion of counsel regarding our classification as a PFIC. Fluctuations in the market price of the ADSs may cause us to be classified as a PFIC in any taxable year because the value of our assets for purposes of the asset test, including the value of our goodwill and unbooked intangibles, may be determined by reference to the market price of the ADSs from time to time (which may be volatile). If our market capitalization subsequently declines, we may be or become classified as a PFIC for the 2022 taxable year or future taxable years. Furthermore, the composition of our income and assets may also be affected by how, and how quickly, we use our liquid assets and any future fundraising activity. Under circumstances where our revenues from activities that produce passive income significantly increases relative to our revenues from activities that produce non-passive income, or where we determine not to deploy significant amounts of cash for active purposes, our risk of becoming classified as a PFIC may substantially increase. It is also possible that the IRS may challenge the classification or valuation of 4D Pharma's assets, including its goodwill and other unbooked intangibles, or the classification of certain amounts received by 4D Pharma, including from JPMorgan, as depositary, which may result in 4D Pharma being, or becoming classified as, a PFIC for the 2022 taxable year or future taxable years.

If we were treated as a PFIC for any taxable year during which a U.S. investor held an ADS or an ordinary share, certain adverse U.S. federal income tax consequences could apply to the U.S. Holder. See "Item 10. Additional Information—E. Taxation—U.S Federal Income Tax Consequences—Passive foreign investment company rules."

We may be unable to use U.K., Irish and Spanish carryforward tax losses to reduce future tax payments or benefit from favorable U.K. tax legislation.

As a U.K. resident trading entity with Irish, Spanish, U.S, and British Virgin Island ("**BVI**") subsidiaries, we are subject to U.K. corporate taxation with Corporation tax in the other jurisdictions also applicable. Due to the nature of our business, we have generated losses since inception. As of December 31, 2021, we had gross cumulative carryforward tax losses of $109 million, $5.7 million and $0.6 million respectively in the UK, Ireland and Spain. There were no taxable losses carried forwards in the BVI, nor were there any in the US as we recognized tax on profits. Subject to any relevant 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 available to carry forward and offset against future operating profits.

As a company that carries out extensive research and development activities, we benefit from the U.K. research and development tax credit regime under the scheme for small and medium-sized enterprises, ("**SMEs**"), or in some instances we access the Research and Development Expenditure Credit ("**RDEC**") scheme in place of this. Under the SME scheme, we are able to surrender to the UK tax authorities some of our trading losses that arise from our qualifying research and development activities for a cash payment using an enhanced effective rate of up to 33.35% of such qualifying research and development expenditures (again subject to certain restrictions but including enhanced deductions), while the RDEC scheme offers up to 13% (10.53% after tax) against profits. We may not be able to continue to claim payable research and development tax credits under the SME Scheme in the future if we cease to qualify as an SME, based on size criteria concerning employee headcount, turnover and gross assets. Qualifying expenditures largely are comprised of employment costs for research staff, research materials, outsourced CRO costs and R&D consulting costs incurred as part of research projects. Under the SME scheme specified subcontracted qualifying research expenditures are eligible for a cash rebate of up to 21.67% and may be ineligible to qualify for the more stringent rules of the RDEC scheme.

Recent proposed changes to the SME scheme, which becomes effective for the Company periods commencing in January 2022, will cap the available claim under the schemes to a multiple of payroll taxes and restrict expenditure on research and development used in the calculation to UK based costs. This cap is likely to significantly limit the value we can claim.

In the event we generate revenues in the future, we may benefit from the U.K. "patent box" regime that allows profits attributable to revenues from patents or patented products with a UK nexus to be taxed at an effective rate of 10%. We are the owners of several patents which cover our product candidates, and accordingly, future upfront fees, milestone fees, product revenues and royalties could be taxed at this tax rate. When taken in combination with the enhanced relief available on our research and development expenditures, we expect a long-term lower effective rate of corporation tax to apply to us. If, however, there are unexpected adverse changes to the U.K. research and development tax credit regime or the "patent box" regime, or for any reason we are unable to qualify for such advantageous tax legislation, or we are unable to use net operating loss and tax credit carryforwards and certain built-in losses to reduce future tax payments, our business, results of operations, and financial condition may be adversely affected. This may impact our ongoing requirement for investment and the timeframes within which additional investment is required.

We may be subject to securities litigation, which is expensive and could divert management attention.

The market price of our ADSs may be volatile and, in the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

Changes and uncertainties in the tax system in the countries in which we have operations, could cause us to experience fluctuations in our tax obligations and effective tax rate materially adversely affecting our financial condition and results of operations, and reducing net returns to our shareholders.

We are subject to a variety of taxes and tax collection obligations in the United Kingdom and in other jurisdictions where we record tax expense, including indirect taxes, based on current tax payments and our estimates of future tax payments. We may recognize additional tax expense and be subject to additional tax liabilities, including tax collection obligations, due to changes in tax law such as legislation, including regulations, administrative practices, outcomes of court cases, and changes to the global tax framework. Further, our effective tax rate and cash taxes paid in a given financial statement period may be adversely impacted by results of our business operations including changes in the mix of costs and revenue among different jurisdictions, acquisitions, investments, entry into new geographies, the relative amount of foreign earnings, changes in foreign currency exchanges rates, changes in our stock price, intercompany transactions, changes to accounting rules, expectation of future profits, changes to trading rules post Brexit, changes in our deferred tax assets and liabilities and our assessment of their realizability, and changes to our ownership or capital structure. Fluctuations in our tax obligations and effective tax rate could adversely affect our business.

In the ordinary course of our business, there are numerous transactions and calculations for which the ultimate tax determination is uncertain. Although we believe that our tax positions and related provisions reflected in the financial statements are fully supportable, we recognize that these tax positions and related provisions may be challenged in the future by various tax authorities. These tax positions and related provisions are reviewed on an ongoing basis and are adjusted as additional facts and information become available, including changes in interpretation of tax laws, developments in case law, and closing of statute of limitations. To the extent that the ultimate results differ from our original or adjusted estimates, our effective tax rate can be adversely affected.

The provision for income taxes involves a significant amount of management judgment regarding interpretation of relevant facts and laws in the jurisdictions in which we operate. Future changes in applicable laws, projected levels of taxable income and tax planning could change the effective tax rate and tax balances recorded by us. In addition, should tax authorities review our income tax returns filed by us then they may raise issues regarding our filing positions, timing and amount of income and deductions, and the allocation of income among the jurisdictions in which we operate. A significant period of time may elapse between the filing of an income tax return and the ultimate resolution of an issue raised by a tax authority with respect to that return. Any adjustments as a result of any examination may result in additional taxes or penalties being assessed on or imposed against us. If the ultimate result of any audit differs from original or adjusted estimates, it could have a material impact our effective tax rate and tax liabilities.

While we have transfer pricing policies in place for trade with subsidiaries in multiple countries the tax authorities could come to a different determination on the values and amounts of such transfers. Such a determination could lead to additional tax liabilities and may also incur fines and penalties which may have a material impact on our brought forwards losses and our tax liability.

At any one time, multiple tax years could be subject to audit by various taxing jurisdictions. As a result, we could be subject to higher than anticipated tax liabilities as well as ongoing variability in our disclosed tax rates as audits close and exposures are re-evaluated.

We continue to analyze our exposure for taxes and related liabilities and have estimated our outstanding tax liability in our US entity at $17 thousand at December 31, 2021. We do have provisions for deferred tax liabilities relating to the increases in value arising on recognition of the fair value of acquired over the amounts paid and we had deferred tax provisions of $14 thousand at December 31, 2021 after offsetting deferred tax liabilities against losses which are available for offset.

If a U.S. person is treated as owning at least 10% of our ordinary shares (including ordinary shares represented by ADSs), such holder may be subject to adverse U.S. federal income tax consequences.

If a U.S. person is treated as owning (directly, indirectly or constructively) at least 10% of the value or voting power of our ordinary shares, such person may be treated as a "United States shareholder" with respect to us or to any of our subsidiaries, if we or any of our subsidiaries constitute a "controlled foreign corporation" (in each case, as such terms are defined under the U.S. Internal Revenue Code of 1986, as amended (the "**Code**")). Certain United States shareholders of a controlled foreign corporation may be required to annually report and include in its U.S. taxable income, as ordinary income, its pro rata share of "Subpart F income," "global intangible low-taxed income" and certain investments in U.S. property by controlled foreign corporations, whether or not we make any distributions to such United States shareholder. A failure by a United States shareholder to comply with its reporting obligations may subject the United States shareholder to significant monetary penalties and other adverse tax consequences, and may extend the statute of limitations with respect to the United States shareholder's U.S. federal income tax return for the year for which such reporting was due. We cannot provide any assurances that we will assist investors in determining whether we or any of our non-U.S. subsidiaries are controlled foreign corporations or whether any investor is a United States shareholder with respect to any such controlled foreign corporations. We also cannot guarantee that we will furnish to United States shareholders information that may be necessary for them to comply with the aforementioned obligations. United States investors should consult their own advisors regarding the potential application of these rules to their investments in us. The risk of being subject to increased taxation may deter our current shareholders from increasing their investment in us and others from investing in us, which could impact the demand for, and value of, our ADSs.

The rights of our shareholders may differ from the rights typically offered to shareholders of a U.S. corporation. Particularly, protections found in provisions under the U.K. Takeover Code may delay or discourage a takeover attempt, including attempts that may be beneficial to holders of our ADSs.

We are incorporated under English law. The rights of holders of ordinary shares and, therefore, certain of the rights of holders of our ADSs, are governed by English law, including the provisions the U.K. Companies Act and by our articles of association.

The U.K. Takeover Code applies, amongst other things, to an offer for a public company whose registered office is in the United Kingdom and whose securities are admitted to trading on a multilateral trading facility in the United Kingdom, which includes AIM. We are therefore subject to the U.K. Takeover Code.

The U.K. Takeover Code provides a framework within which takeovers of certain companies organized in the United Kingdom are regulated and conducted. The following is a brief summary of some of the most important rules of the U.K. Takeover Code:

In connection with a potential offer, if, following an approach by or on behalf of a potential bidder, the company is "the subject of rumor or speculation" or there is an "untoward movement" in the company's share price, there is a requirement for the potential bidder to make a public announcement about a potential offer for the company, or for the company to make a public announcement about its review of a potential offer.

When a person or group of persons acting in concert (i) acquires, whether by a series of transactions over a period of time or not, interests in shares carrying 30% or more of the voting rights of a company (which percentage is treated by the Takeover Code as the level at which effective control is obtained) or (ii) increases the aggregate percentage interest they have when they are already interested in not less than 30% and not more than 50%, they must make a cash offer to all other shareholders at the highest price paid by them or any person acting in concert with them in the 12 months before the offer was announced.

When interests in shares carrying 10% or more of the voting rights of a class have been acquired for cash by an offeror (i.e. a bidder) or any person acting in concert with them in the offer period (i.e. before the shares subject to the offer have been acquired) or within the previous 12 months, the offer must be in cash or be accompanied by a cash alternative for all shareholders of that class at the highest price paid by the offeror or any person acting in concert with them in that period. Further, if an offeror or any person acting in concert with them acquires for cash any interest in shares during the offer period, the offer must be in cash or accompanied by a cash alternative at a price at least equal to the price paid for such shares during the offer period.

If after an announcement is made, the offeror or any person acting in concert with them 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 accordingly.

The board of directors of the offeree company must appoint a competent independent adviser whose advice on the financial terms of the offer must be made known to all the shareholders, together with the opinion of the board of directors of the offeree company.

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 company.

All shareholders must be given the same information.

Those issuing documents in connection with a takeover must include statements taking responsibility for the contents thereof.

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 requirements are laid down for the disclosure of dealings in relevant securities during an offer, including the prompt disclosure of positions and dealings in relevant securities by the parties to an offer and any person who is interested (directly or indirectly) in 1% or more of any class of relevant securities.

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.

As an English public company, certain capital structure decisions will require shareholder approval, which may limit our flexibility to manage our capital structure.

English law provides that a board of directors may only allot shares (or grant rights to subscribe for, or to convert any security into, shares) with the prior authorization of shareholders by ordinary resolution, being a resolution passed by a simple majority of votes cast at a general meeting in person or by proxy, such authorization stating the aggregate nominal amount of shares that it covers and being valid for a maximum period of five years, each as specified in the articles of association or relevant shareholder resolution. In either case, this authorization would need to be renewed by our shareholders upon expiration (i.e., at least every five years). Typically, English public companies renew the authorization of their directors to allot shares on an annual basis at their annual general meeting.

English law also generally provides shareholders with preemptive rights when new shares are issued for cash. However, it is possible for the articles of association, or for shareholders to pass a special resolution at a general meeting, being a resolution passed by at least 75% of the votes cast, in person or by proxy, to disapply preemptive rights. Such a disapplication of preemptive rights may be for a maximum period of up to five years from the date of adoption of the articles of association, if the disapplication is contained in the articles of association, or from the date of the shareholder special resolution, if the disapplication is by shareholder special resolution, but not longer than the duration of the authority to allot shares to which the disapplication relates. In either case, this disapplication would need to be renewed by our shareholders upon its expiration (i.e., at least every five years). Typically, English public companies renew the disapplication of preemptive rights on an annual basis at their annual general meeting.

English law also generally prohibits a public company from repurchasing its own shares without the prior approval of shareholders by ordinary resolution, being a resolution passed by a simple majority of votes cast, at a general meeting in person or by proxy, and other formalities. Such approval may be for a maximum period of up to five years. See "Description of 4D Pharma Securities and Articles of Association."

Claims of U.S. civil liabilities may not be enforceable against us.

We are incorporated under English law. All of our assets are located outside the United States. The majority of our senior management and board of directors reside outside the United States. As a result, it may not be possible for investors to effect service of process within the United States upon such persons or to enforce judgments obtained in U.S. courts against them or us, including judgments predicated upon the civil liability provisions of the U.S. federal securities laws.

The United States and the United Kingdom do not currently have a treaty providing for the reciprocal recognition and enforcement of judgments (other than arbitration awards) in civil and commercial matters. Consequently, a final judgment for payment given by a court in the United States, whether or not predicated solely upon U.S. securities laws, would not automatically be recognized or enforceable in England and Wales. In addition, uncertainty exists as to whether the English and Welsh courts would entertain original actions brought in England and Wales against us or our directors or senior management predicated upon the securities laws of the United States or any state in the United States. Any final and conclusive monetary judgment for a definite sum obtained against us in U.S. courts would be treated by the courts of England and Wales as a cause of action in itself and sued upon as a debt so that no retrial of the issues would be necessary, provided that certain requirements are met consistent with English law and public policy. Whether these requirements are met in respect of a judgment based upon the civil liability provisions of the U.S. securities laws is an issue for the English court making such decision. If an English court gives judgment for the sum payable under a U.S. judgment, the English judgment will be enforceable by methods generally available for this purpose.

As a result, U.S. investors may not be able to enforce against us or our senior management, board of directors or certain experts named herein who are residents of the United Kingdom or countries other than the United States any judgments obtained in U.S. courts in civil and commercial matters, including judgments under the U.S. federal securities laws.

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 results to the plaintiff(s) in any such action.

The deposit agreement governing our ADSs provides that owners and holders of ADSs irrevocably waive the right to a trial by jury in any legal proceeding arising out of or relating to the deposit agreement or the ADSs, including claims under U.S. federal securities laws, against us or the depositary to the fullest extent permitted by applicable law. If this jury trial waiver provision is prohibited by applicable law, an action could nevertheless proceed under the terms of the deposit agreement with a jury trial. Although we are not aware of a specific federal decision that addresses the enforceability of a jury trial waiver in the context of U.S. federal securities laws, it is our understanding that jury trial waivers are generally enforceable. Moreover, insofar as the deposit agreement is governed by the laws of the State of New York, New York laws similarly recognize the validity of jury trial waivers in appropriate circumstances. In determining whether to enforce a jury trial waiver provision, New York courts and federal courts will consider whether the visibility of the jury trial waiver provision within the agreement is sufficiently prominent such that a party has knowingly waived any right to trial by jury. We believe that this is the case with respect to the deposit agreement and the ADSs.

In addition, New York courts will not enforce a jury trial waiver provision in order to bar a viable setoff or counterclaim of fraud or one which is based upon a creditor's negligence in failing to liquidate collateral upon a guarantor's demand, or in the case of an intentional tort claim (as opposed to a contract dispute). 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 any provision of U.S. federal securities laws and the rules and regulations promulgated thereunder.

If any owner or holder of our ADSs brings a claim against us or the depositary in connection with matters arising under the deposit agreement or the ADSs, including claims under U.S. federal securities laws, such owner or holder 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 or the depositary. If a lawsuit is brought against us 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 results 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.

ITEM 4. INFORMATION ON THE COMPANY

A. History and Development of the Company

We were founded in 2014 under the legal name 4D pharma plc and registered as a private limited company under the laws of England and Wales with the company number 08840579. Our headquarters and principal executive offices are located at 5th Floor, 9 Bond Court, Leeds, LS1 2JZ, United Kingdom, telephone: +44 (0) 113 895 0130. Our website address is: www.4dpharmaplc.com. Information on our website is not incorporated by reference into or otherwise part of this annual report. We have included our website address in this annual report solely for informational purposes. The SEC also maintains a website that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC. The address of this website is http://www.sec.gov.

We are a pharmaceutical company developing Live Biotherapeutic Products, a novel class of drug derived from the human microbiome. Our differentiated approach focuses on understanding mechanism of action and the interactions of our LBPs with host biology. Our pipeline of therapeutic candidates includes single strain LBPs targeting major diseases in multiple therapeutic areas with the potential to address significant unmet patient needs.

On March 22, 2021, we consummated a merger (the "**Merger**") with Longevity Acquisition Corporation ("**Longevity**"), a publicly-traded special purpose acquisition company, pursuant to which we issued Nasdaq-listed ADSs to the shareholders of Longevity and assumed warrants previously issued by Longevity, and Longevity became our wholly-owned subsidiary.

At closing, Longevity merged with and into Dolphin Merger Sub Limited ("**Merger Sub**"), our wholly owned subsidiary, with Merger Sub continuing as the surviving company. Each of Longevity's common shares issued and outstanding prior to the effective time of the merger (excluding shares held by the Company and Longevity and dissenting shares, if any) was automatically converted into the right to receive certain per share merger consideration (as defined below), and each warrant to purchase Longevity's ordinary shares and right to receive Longevity's ordinary shares that were outstanding immediately prior to the effective time of the merger was assumed by us and automatically converted into a warrant to purchase our ordinary shares and a right to receive our ordinary shares, payable in our ADSs, respectively. The per share merger consideration consisted of 7.5315 ordinary shares, payable in ADSs (each ADS representing 8 ordinary shares), for each issued and outstanding ordinary share of Longevity. Longevity had $11.6 million at the time of the merger after paying all of its debtors.

Concurrently with the completion of the merger, on March 22, 2021, we raised £18.0 million ($25.0 million) through the issuance of 16,367,332 ordinary shares at a share price of £1.10 ($1.53) per share. On April 16, 2021, a further £1.4 million ($2.0 million) was raised through the issuance of 1,317,680 ordinary shares at a share price of £1.10 ($1.52) per share to Duncan Peyton and Alexander Stevenson, the Company's CEO and CSO, respectively.

Our ordinary shares are listed on the London Stock Exchange's AIM market under the symbol "DDDD," our American Depositary Shares are listed on the Nasdaq Global Market under the symbol "LBPS" and our warrants trade on the Nasdaq Global Market under the symbol "LBPSW."

We are an Emerging Growth Company. As such, for a period of up to five years we are eligible, and intend to, take advantage, of certain exemptions from various reporting requirements applicable to other public companies that are not Emerging Growth Companies, such as not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002.

We will remain an Emerging Growth Company until the earliest of: (i) the last day of our fiscal year during which we have total annual gross revenues of at least $1.07 billion; (ii) the last day of our fiscal year following the fifth anniversary of the closing of our merger with Longevity; (iii) the date on which we have, during the previous three-year period, issued more than $1.0 billion in non-convertible debt; and (iv) the date on which we are deemed to be a Large Accelerated Filer under the Exchange Act, with at least $700 million of equity securities held by non-affiliates.

For information regarding our capital expenditures, see "Item 5. Operating and Financial Review and Prospects—B. Liquidity and Capital Resources."

B. Business Overview

We are a pharmaceutical company developing LBPs, a novel class of drug derived from the human microbiome. Our differentiated approach, as described above, has generated a pipeline of single strain LBPs targeting oncological, respiratory, immune-inflammatory, CNS and gastrointestinal diseases. In recent years, we believe this approach has been validated by clinical results in our programs in immune-oncology, gastrointestinal and respiratory disease.

Our LBPs are a novel class of drugs based on live organisms, namely single strains of naturally-occurring bacteria. These bacteria are not genetically modified and are originally isolated from healthy human donors. Our therapeutic candidates are therefore 'live' drugs that can provide therapeutic benefit via their interaction with host biology, whether by their structural components such as peptides, primary or secondary metabolites or other means. In contrast, biologics, such as antibodies, are not 'live' compounds and, generally speaking, are not naturally occurring molecules. As naturally occurring, non-engineered, commensal bacteria originally isolated from healthy human donors, our LBPs are expected, and to date have been found, to be well tolerated compared to other drug modalities such as small molecules or biologics, given that they are single strains of naturally-evolved human commensal microbes that act on the gut-body network without significant risk of systemic exposure. To date, this has meant that we can accelerate our therapeutic candidates from discovery and pre-clinical testing into clinical trials faster than traditional therapeutic modalities such as small molecules or biologics. For all of our clinical-stage LBP candidates to date, regulators including the FDA have allowed us to conduct first-in-human clinical trials in our target patient population without requiring us to first conduct traditional Phase I safety studies in healthy volunteers or long-term animal toxicology testing. These factors may reduce the cost and time to generate meaningful in-patient clinical data for our therapeutic candidates compared to small molecules or biologics targeting the same diseases.

To further advance our product pipeline, we have developed MicroRx, our LBP discovery platform. MicroRx interrogates our proprietary library of bacterial isolates for therapeutic functionality and comprehensively characterizes the bacterial isolates using a range of complementary tools and technologies. By developing a thorough understanding of the mechanism of action of our therapeutic candidates and their interaction with host biology, we can develop LBPs that target disease pathology rationally and effectively and further expand our robust sector-leading patent portfolio with additional patents relating to LBP functionality.

The functionality of bacteria and their impact on human biology is diverse, and has allowed us to develop a broad pipeline of therapeutic candidates across multiple therapeutic areas. We initially focused on the gastrointestinal disease space in IBD and IBS, a logical starting point for developing a modality based around organisms found in the human gut. However, as our research expertise and the MicroRx discovery platform have advanced, we were able to leverage our knowledge of the human microbiome and its diverse interactions with various host systems to realize the potential of LBPs to treat diseases manifest in organs and tissues distal to the gut. Our observation that candidates in our proprietary library were having systemic, not just gut-localized, effects led us to explore new applications and disease areas.

To this end, our key clinical focus areas now include immuno-oncology and respiratory disease, with preclinical candidates MRx0029 and MRx0005 targeting CNS. We have completed three clinical trials and currently have four more ongoing. Our clinical and preclinical Live Biotherapeutic development programs are illustrated below.

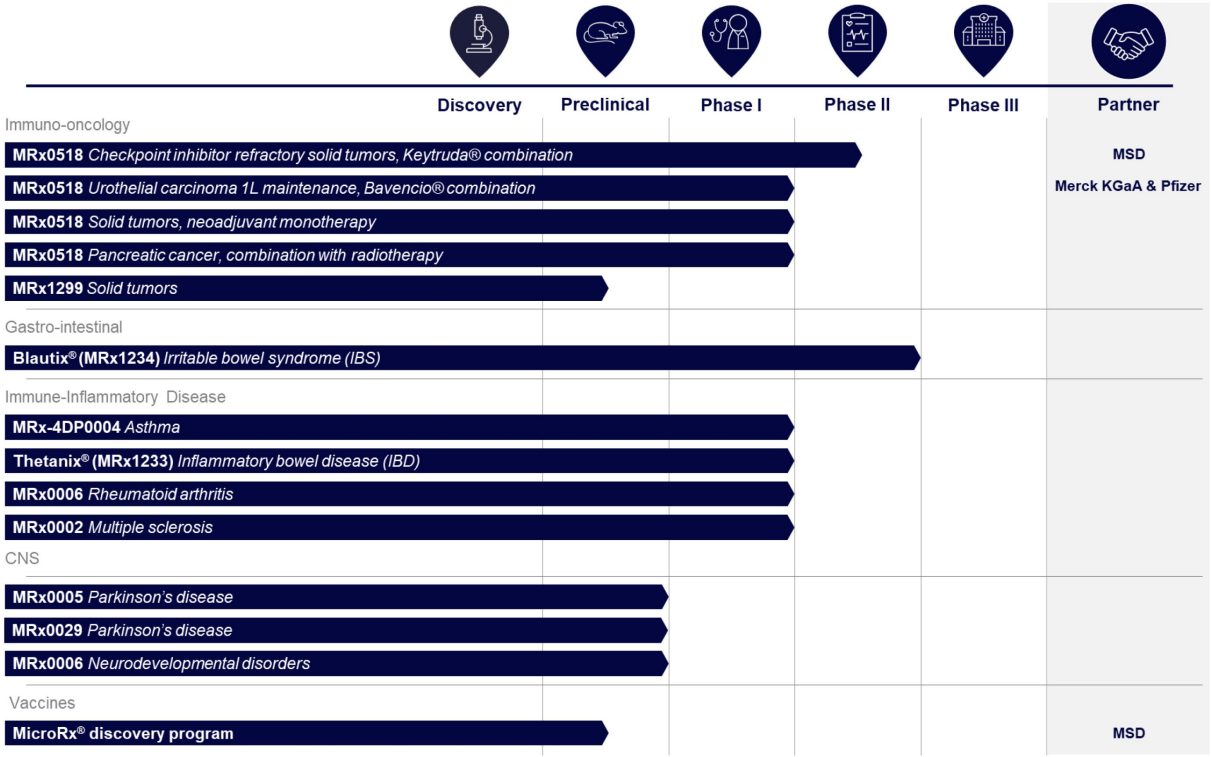


Figure 1 - 4D Pharma's pipeline of LBP therapeutic candidates.

One of our key focus areas is immuno-oncology, and with our lead therapeutic candidate, MRx0518, to our knowledge, we delivered the first positive proof-of-concept data with a Live Biotherapeutic in the treatment of cancer. MRx0518 is a strain of *Enterococcus gallinarum* that was discovered with MicroRx and exhibits an immunostimulatory host-response profile that indicated strong potential as an immuno-oncology candidate. The anti-tumor activity of its immuno-stimulatory profile was demonstrated in multiple preclinical tumor models. MRx0518 is currently being evaluated in cancer patients in three ongoing clinical trials, including a Phase I/II trial in solid tumor in combination with the ICI Keytruda (pembrolizumab) in patients with metastatic NSCLC, RCC, UC, TNBC HNSCC and MSI-H that are refractory to prior anti-PD-1/PD-L1 therapy. Results from the completed part A of this clinical trial demonstrated a DCR of 42% in 12 patients with mRCC and mNSCLC, which was considered a meaningful clinical benefit significantly above the 10% DCR threshold predefined with our collaborator, MSD, to warrant further investigation of the combination in Part B. During Part A of this clinical trial, MRx0518 was well tolerated and had no treatment-related serious adverse events or drug discontinuations and, importantly, no increase of immune-related adverse events commonly associated with ICI therapy.

Part B of the study is currently enrolling, and will assess clinical benefit in addition to safety, up to an additional 30 patients per tumor type with metastatic NSCLC, RCC and UC that are refractory to prior anti-PD-1/PD-L1 therapy. Additionally, new cohorts of 10 patients with new tumor types are being enrolled in the study, including patients with TNBC, HNSCC and MSI-H tumors that are also refractory to prior anti-PD-1/PD-L1 therapy. On March 23, 2022, we announced that in Part B of this study, the RCC group has met its primary efficacy endpoint ahead of enrollment completion. The primary efficacy endpoint for Part B of the study is more than three out of 30 patients per tumor group achieving clinical benefit, defined as complete response, partial response, or stable disease for at least six months. Four out of the first 16 evaluable RCC patients enrolled in Part B achieved clinical benefit, each having achieved at least 6 months of stable disease. MRx0518 continues to be safe and well tolerated.

We have two other ongoing studies of MRx0518 in oncology. We commenced a Phase I trial of MRx0518 as a neoadjuvant monotherapy in patients undergoing surgical resection of solid tumors, which is being conducted at Imperial College London. At the Society for Immunotherapy of Cancer's 35th Annual Meeting ("**SITC 2020**"), we announced initial results from Part A of this trial in 17 patients, demonstrating MRx0518 monotherapy immunomodulatory activity. Additional data subsequently presented at the European Society for Medical Oncology (ESMO) Congress 2021 ("**ESMO 2021**") showed that treatment with MRx0518 was associated gene expression and metagene signature changes associated with anti-tumor immune activity. We are currently designing Part B of this Phase I clinical trial.

We also initiated a Phase I clinical trial of MRx0518 in potentially resectable pancreatic cancer in combination with hypofractionated radiotherapy, which is part of our strategic collaboration with MD Anderson. Study treatment has been well tolerated to date and this study continues to enroll.

In February 2021, we announced a clinical trial collaboration and supply agreement with Merck KGaA, Darmstadt, Germany and Pfizer Inc. for Bavencio (avelumab), under which 4D Pharma is conducting a Phase II clinical trial to evaluate Bavencio (to be supplied under a free of charge supply agreement) in combination with MRx0518 as a first-line maintenance therapy for patients with locally advanced or metastatic urothelial carcinoma that has not progressed with first-line platinum-containing chemotherapy. This study is expected to commence is 2022. Meanwhile, we are engaged in business development activities with the goal of expanding the development of MRx0518 into new settings and are actively exploring additional collaboration opportunities.

In addition to progressing lead oncology LBP MRx0518, we continue to use the MicroRx platform to discover and develop additional LBP candidates with potential applications in cancer treatment through novel mechanisms of action. In July 2021 we published pre-clinical research relating to a second-generation oncology LBP MRx1299 improving the activity of CAR-T. The research, conducted in collaboration with the Philipps-University Marburg, Germany, and Universitätsklinikum Würzburg, Germany, and published in Nature Communications, demonstrated the ability of the bacterium Megasphaera massiliensis or its short chain fatty acid ("**SCFA**") metabolite pentanoate to enhance the anti-tumor activity of cytotoxic T lymphocytes ("**CTL**") and CAR-T therapies in animal models of cancer, resulting in better tumor clearance.

We continue to utilize the MicroRx platform to discover promising new LBP candidates for major diseases with significant unmet need. As part of our CNS portfolio, we have identified novel LBP candidates that act upon multiple aspects of the pathology of neurodegenerative diseases in preclinical models, including gut-barrier function, neuroinflammation and protection of neurons critical to healthy CNS function. A first-in-human clinical study for our lead CNS therapeutic candidates, MRx0005 and MRx0029, in Parkinson's disease patients is expected to commence in 2022, having received FDA IND clearances in February 2022. As part of our commitment to CNS research and drug development, in December 2020, we became an industry partner of the Parkinson's Progression Markers Initiative, a longitudinal study sponsored by The Michael J. Fox Foundation for Parkinson's Research to better understand Parkinson's disease and accelerate the development of new treatments. Our involvement in this project was extended by a further 12 months in December 2021. In addition, in April 2021 we entered into a collaboration with Parkinson's UK, a non-profit organization focused on advancing the understanding of Parkinson's disease and improving treatments, to establish a Patient Advisory Board (PAB) comprised of people living with Parkinson's. Supported by Parkinson's UK, the PAB provides valuable patient-centric perspective to 4D Pharma as we continue to advance novel Live Biotherapeutics into the clinic to treat neurodegenerative conditions such as Parkinson's. The PAB will also focus on raising awareness of the issues people with Parkinson's face with current treatment options.

We are also developing therapeutic candidates for our respiratory disease portfolio. MicroRx enabled the discovery of MRx-4DP0004, an immunomodulatory single strain Live Biotherapeutic candidate that demonstrated marked effects in preclinical trials of respiratory inflammation, particularly in the lungs. MRx-4DP0004 significantly reduced both neutrophilic and eosinophilic airway infiltration concurrently in a preclinical disease model of severe steroid-resistant asthma. Our Phase I/II clinical trial of MRx-4DP0004 in partly controlled asthma is, to our knowledge, the world's first clinical trial of a Live Biotherapeutic in the indication. In December 2021, we announced that Part A of this trial achieved the primary endpoint of safety and tolerability, and that multiple secondary endpoints showed positive trends in improving asthma control. Part B is expected to enroll up to 90 patients and will assess clinical efficacy in addition to exploratory immune and microbiome biomarkers and safety.

In our gastro-intestinal disease portfolio, we currently have two LBP candidates in clinical development, Blautix and Thetanix. Blautix is being developed as the first therapeutic to potentially treat all patients with IBS, regardless of clinical subtype. Our Phase II study of Blautix in patients with IBS-C (constipation predominant) and IBS-D (diarrhea-predominant) showed that Blautix achieved a statistically significant overall response rate compared to placebo in the combined IBS-C/D analysis group, and demonstrated positive trends in overall response rate for both IBS-C and IBS-D subgroups independently, with an effect size versus placebo comparable to that of other approved IBS therapeutics. Blautix was well tolerated, with a safety profile comparable to placebo, an advantage compared to many currently approved IBS therapeutics which are associated with side effects linked to their mechanism of action. The Phase II trial results provide a strong foundation for the continued development of Blautix as the first therapeutic with the potential to treat both major subtypes of IBS, and this data will inform regulatory engagement around the design of a potential Phase III pivotal program.

Thetanix is a single-strain human, gut commensal bacteria that has an anti-inflammatory mechanism and is currently under investigation for the treatment of IBD. Thetanix received an Orphan Drug Designation for pediatric Crohn's disease from the FDA. We have successfully completed a Phase Ib clinical trial of Thetanix in pediatric Crohn's disease patients. The Phase Ib clinical trial demonstrated that Thetanix was well tolerated, with no treatment-related serious adverse events or drug discontinuations and indicated preliminary signals of clinical activity. We are exploring strategic options for Thetanix, including parallel development in pediatric and adult populations in both Crohn's disease and ulcerative colitis, as well as potential partnerships.

In addition to our internal development programs, we are seeking to realize the value and potential of the MicroRx platform through collaborations in new areas. In 2019, we entered into a research collaboration and option to license agreement with MSD to discover and develop LBPs for vaccines. We received a non-refundable, upfront payment of $2.5 million and an equity investment by MSD of $5 million upon initiation of this agreement. This collaboration pairs our proprietary MicroRx platform with MSD's expertise in the development and commercialization of novel vaccines, to discover and develop LBPs as vaccines in up to three undisclosed indications. If MSD successfully develops vaccines under this agreement, we will be eligible to receive milestone payments of up to approximately $1 billion as well as high single-digit royalties on sales. To date, we have screened and characterized hundreds of LBPs with immuno-modulatory potential and selected from this group lead LBPs with desirable immuno-modulatory properties for further evaluation and development. See "Item 4. Information on the Company—B. Business Overview—Collaborations—Research Collaboration and Option to License Agreement with Merck."

Our Strategy

Our goal is to pioneer a novel class of safe and effective therapeutic derived from the gut microbiome that have the potential to transform the way many diseases are treated.

Key elements of our strategy include:

- **Continuing to be a leading innovator in the microbiome field, with a rigorous approach that focuses highly on the functionality of our LBPs.** We have invested highly in our research, manufacturing and clinical capabilities to put ourselves at the front of the pack in the microbiome space. This expertise has generated what we believe is a comprehensive, sector-leading intellectual property portfolio in the microbiome space.
- **Delivering what we believe are differentiated LBPs in multiple indications.** We intend to deliver what we believe are differentiated therapeutics that leverage the inherent advantages of LBPs in multiple indications. We seek to continue to deliver positive clinical data, particularly in our immuno-oncology program, with a goal to develop the first LBP approved for the treatment of cancer. We continue to work to push LBPs into new therapeutic areas, such as our preclinical LBP therapeutic candidates MRx0005 and MRx0029 that leverages the gut-brain axis and is currently being assessed in Parkinson's disease.
- **Working with partners to realize the full potential of our sector-leading capabilities.** MicroRx is a unique LBP discovery and development platform and, alongside building our internal pipeline of LBP candidates, the platform also enables us to build valuable partnerships and collaborations. We believe the collaboration with MSD to discover and develop LBPs for vaccines, in addition to the proof-of-concept data generated to date across multiple programs, has validated the MicroRx platform and 4D Pharma's approach to LBP development. We will seek to engage additional new partners that wish to explore the potential of LBPs in disease areas of interest through collaborations.

Background on LBPs

Microbiome

Throughout the history of medicine, pharmaceuticals have been originally derived from complex mixtures, whether that be plant extracts, serum therapies, blood transfusions or fecal material transplant. Over time, researchers were able to accurately identify and characterize the specific components of the complex mixtures that were exerting the desired therapeutic effects. These components could then be isolated and developed as single entities, allowing the optimization of blunt unrefined natural mixtures with high levels of functional redundancy, into potent and precise therapeutics which are the small molecules, antibodies, therapeutic proteins and vaccines used to treat or prevent disease today.

Another complex mixture is the gut microbiome, the trillions of bacteria, and their gene products, that colonize the human gastro-intestinal tract. The gut microbiome contains more cells than there are in the entire human host and carries around 500 times more genetic information than the human genome. These bacteria and all of their genetic information has function, whether that be metabolic function, interaction with the host, or their interaction with other organisms in the microbiome. Consequently, the gut microbiome plays a significant role in human health and disease.

The gut microbiome is commonly understood to influence gastrointestinal diseases such as IBD and IBS. However, gut bacteria also impact the host through systemic modulation of the human immune system, metabolism and even neurological function, and are increasingly understood to play a key role in the cause, progression and treatment of diseases outside the gut, from cancer to immune-mediated diseases and CNS conditions. Understanding and leveraging this precise functionality offers a new approach to the treatment of a broad range of diseases, from cancer to asthma and conditions of the CNS.

Live Biotherapeutic Products

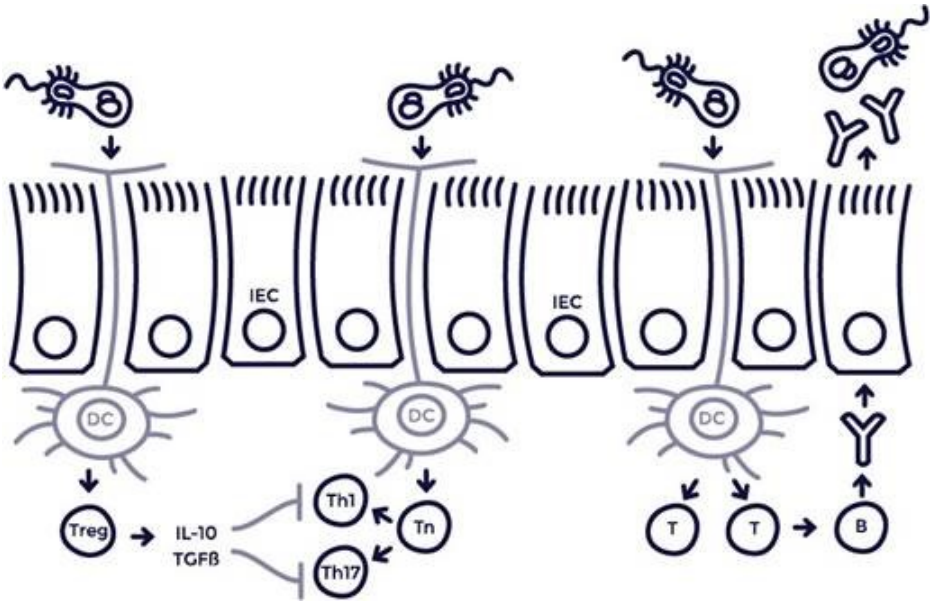


Figure 2. LBPs interact with the host by a variety of mechanisms. Although typically initiated in the gut, the resulting changes in downstream pathways are diverse and can produce effects in distal areas of the body. IEC = intestinal epithelial cell; DC = dendritic cell; Treg = T regulatory cell; IL-10 = interleukin-10; TGF-β = Transforming growth factor beta; Th1 = T-helper 1 cell; Th17 = T-helper 17 cell; Tn = naïve T cell; T = T-cell; B = B-cell.

We are developing LBPs, a novel class of medicines that contain live organisms, which have the potential to prevent, treat, or cure disease. In 2012, the FDA set the first guidelines for this new modality, which have set the administration, regulatory and manufacturing standards by which such products must be developed; these were updated in 2016. While several different types of LBPs are currently being developed, including fecal microbiota transplants, bacterial consortia and genetically engineered modified organisms, we are developing single strain LBPs utilizing non-engineered commensal bacteria found in the human gut microbiome.

Driven by our unique LBP discovery engine MicroRx, we have built an end-to-end drug development company with capabilities across the development process, from discovery and preclinical development, through manufacturing and scale-up, to execution of clinical trials. Advances in technology and our consequent understanding of the microbiome have enabled us to develop the MicroRx platform for the efficient discovery of single strain LBPs. This process enables us to take our library of single strains of gut commensal bacteria originally isolated from the complex microbiomes of healthy human donors, and screen for strains that demonstrate functional profiles of interest with strong potential to treat disease. Once the single strains are identified, we can characterize the functionality of the bacteria, including gaining a deep understanding of mechanism of action, and progress them into further development as therapeutic candidates. Our in-depth characterization and understanding of our LBP candidates further strengthens the discovery capabilities of our platform.

Key aspects of our approach to drug development include the following:

- **A functional, not correlative approach**. Our approach focuses on understanding and exploiting function and characterizing the mechanisms by which our single strain LBP candidates interact with host biology. In this sense, our approach is analogous to the traditional development of small molecules and biologics, rational selection and development based on functionality and mechanism, rather than attempting to reverse engineer a 'healthy' microbiota profile and its correlation with a given disease.
- **Inherent advantages of LBPs**. The side effects associated with existing medicines are a concern for both patients and clinicians, and these can lead to sub-optimal treatment regimens or termination of development programs. Our LBPs are naturally occurring, non-engineered strains originally isolated from healthy human donors, and consequently, we have not observed any drug related serious adverse effects in any of our clinical studies conducted to date, which have included dosing in over 500 individuals with our LBPs. This significantly accelerates the development timeline from discovery to clinical proof-of-concept, enabling us to conduct first-in-human studies in patients, rather than traditional Phase I safety studies in healthy volunteers and without long-term animal toxicology studies, and thus generate clinically relevant data much earlier than with traditional drug types.
- **Orally-administered single strain LBPs.** Our therapeutic candidates are pharmaceutical formulations of single strains of bacteria originally isolated from healthy human donors, selected using our MicroRx platform based on a desired functional profile investigated and demonstrated using *in vitro* and *in vivo* models. Additionally, our candidates can exhibit polypharmacy, acting on multiple disease relevant pathways to exert their therapeutic effects. Our LBPs are not required to engraft or "colonize" the gut to achieve activity, in the same way that a small molecule drug does not need to stay in the body forever to exert a therapeutic effect. Consequently, the activity of our LBP candidates should not be dependent on the composition of the resident microbiome, and do not require preconditioning with antibiotics to create an ecological niche for engraftment.
- **Well-developed manufacturing capability**. We have invested heavily in our manufacturing capability and infrastructure since our inception, and now have significant expertise in the manufacturing of LBPs. Our therapeutic candidates are manufactured at our cGMP-certified facility, with nine candidates now taken through the development and scale-up process to clinical-scale, with production capacity up to small-to-mid-scale commercial supply. This level of capability gives us ultimate control over the supply of our therapeutic candidates for clinical development and developing and optimizing processes in-house has generated valuable know-how and intellectual property. We are also able to integrate manufacturing considerations into our candidate selection and early development, reducing later development risk and accelerating the progression of candidates into the clinic.
- **A comprehensive intellectual property estate in the microbiome space.** As of January 2022, our patent portfolio is comprehensive and includes patents and pending applications that cover our therapeutic candidates in the US and other countries internationally. Our LBPs in clinical development are protected by patent filings in major territories including the United States.

MicroRx

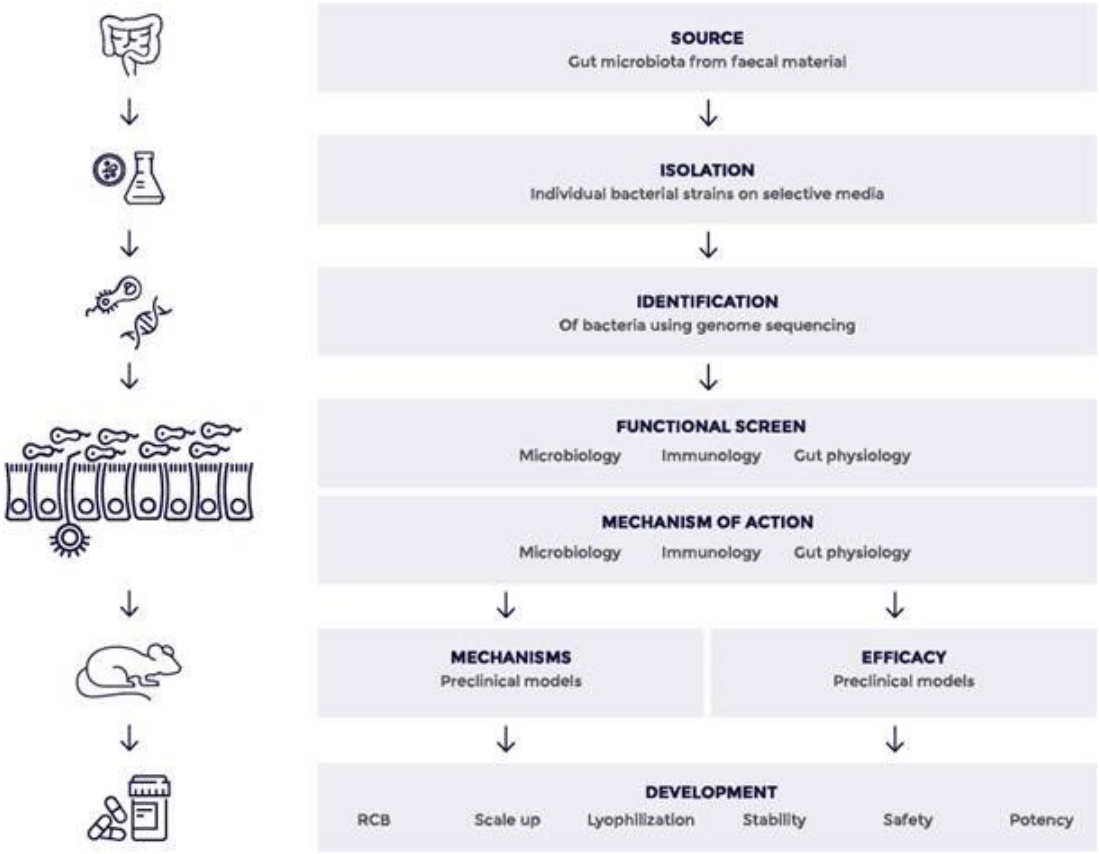


Figure 3. A high-level overview of the processes that underpin the MicroRx discovery platform

Our proprietary drug discovery platform, MicroRx, drives the development of our therapeutic candidates and is highly differentiated in the microbiome space, based on its level of productivity in populating our pipeline with novel LBP candidates in multiple therapeutic areas. We use MicroRx to interrogate our extensive proprietary library of bacterial isolates to identify Live Biotherapeutic candidates for a target disease, based on a deep understanding of functionality and mechanism, looking for specific functional signatures relevant to disease pathways.

We select our LBPs based on their preclinical activity and potential to be translated into commercially viable therapeutic candidates and elucidate their functionality and interactions with human biology. As bacteria of the human gut microbiome have co-evolved with their hosts over millions of years to allow co-existence of bacteria and the host, LBPs have inherent advantages for use in the human body as LBPs are derived from naturally occurring sources. Traditional pharmaceutical drug discovery involves multiple rounds of hit and lead optimization to identify a clinical candidate, a process which can take many years and is highly capital intensive. In addition, the side effects associated with existing medicines are a concern for both patients and clinicians, and these can lead to sub-optimal treatment regimens or termination of development programs and in some cases, an inability to commence treatment. Our LBPs are naturally occurring, non-engineered strains originally isolated from healthy human donors, and we have not observed any serious adverse effects in any of our clinical studies conducted to date. As we do not need to optimize our LBPs to be tolerated in the human body, we can enter clinical development in shorter timeframes than traditional modalities such as small molecules and biologics.

MicroRx is a multi-faceted and modular platform, and can easily integrate new technologies, tools, techniques and assays to refine the platform through an iterative process, constantly improving our ability to identify single strain LBPs with functional profiles that demonstrate high therapeutic potential in specific diseases. Moreover, the adaptable platform can be targeted to identify strains with specific characteristics, phenotypes or functions of interest to us or our partners with regard to a specific target disease.

MicroRx is comprised of the following key areas:

Library. We have built a large and diverse bacterial culture collection that captures the significant inter-individual variability of the human gut microbiome by sampling donors that encompass a wide range of diets, ages, ethnicities, geographies and lifestyles. This 'untargeted' strategy has built a library that includes novel organisms that had previously never been isolated, an aspect that has advantageously assisted with developing robust intellectual property that protects our therapeutic candidates. To support the expansion of our library we have developed culturomics techniques to capture lesser-known taxa.

Discovery. Strains from our growing proprietary library are first screened for their ability to activate specific host receptors or pathways using a battery of reporter cell lines of both human and animal origin. Multiple aspects of the host-microbe interaction are investigated using complex co-culture systems, spheroids and organoid-based assays to mimic the *in vivo* environment and improve clinical translatability. Cytokine and metabolite production, cell differentiation and gene expression patterns are all evaluated at this stage to identify and characterize the complex interaction between the specific strains and the host at the cellular and molecular level. Genome mining is also used to identify strains with particular genes, or types of genes, of interest, as well as to characterize candidate strains.

Preclinical. Bacteria with specific signatures and functional profiles of interest are assayed *in vivo* in industry-standard disease-relevant animal models, characterizing interaction with the host at both systemic and target tissue level by evaluating a broad panel of markers, including cytokines and chemokines, metabolites, gene expression patterns, tissue histology, and frequency and activation status of immune cell subsets. We often utilize multiple disease models to generate a robust and comprehensive understanding of a candidate's in vivo activity. For candidates where a strong efficacy profile in animal models is observed, we attempt to elucidate their mechanism of action and identify putative effector molecules by using a multi-omics approach that incorporates genome mining, metabolomics, proteomics and lipidomics to analyze different bacterial cellular fractions or compartments. Strain engineering approaches are used to confirm the activity of potential effector molecules.

Process Development and Manufacturing. Progressing promising candidates into further development that cannot be manufactured to scale is futile, and it is for this reason that we have a pilot-scale manufacturing facility that runs alongside our research facility to ensure that lead strains have the potential for 'manufacturability' on a commercial scale. Lead candidates that demonstrate 'manufacturability' are then be transferred from this pilot lab to our commercial-scale manufacturing facility to undergo process optimization to produce batches of clinic-ready drug product. As LBPs are a new drug modality, we saw fit to invest in manufacturing and developing expertise. This approach has provided significant competitive advantages, allowing us to maintain ultimate control over drug from discovery to entering the clinic, relying on no external forces in progressing our therapeutic candidates.

Product Development Strategy and Portfolio

We are advancing our LBPs in multiple diseases, with our key focus areas being immuno-oncology, immune-inflammatory disease, CNS conditions and gastro-intestinal diseases. Our approach to identifying LBPs has, in a relatively short period of time, allowed us to conduct clinical trials on four therapeutic candidates to date with single strain LBPs in multiple disease areas, and provide valuable data on safety, tolerability, pharmacodynamic responses, immune biomarkers and clinical outcomes. Additionally, we have an in-house team of bioinformaticians that provide microbiome and metabolomics analysis from results obtained in our ongoing clinical trials. These analyses will assist us in the further development of these assets, and others in new indications.

Beyond the assets generated thus far, we intend to continue to invest in the discovery of new therapeutic candidates and add new pipeline therapeutic candidates that leverage the broad functional potential of LBPs effectively to tackle disease areas of high unmet need. We believe our function-driven approach to LBP development will continue to be fruitful, adding to our number of clinical stage programs and further strengthening our intellectual property position.

We intend to enter into more partnerships and collaborations utilizing our technology and expertise, including licensing deals for existing development candidates, or research collaboration deals using MicroRx, akin to our collaboration with MSD to discover LBPs for vaccines. We intend to collaborate to develop LBPs for new indications and leverage the complementary abilities of 4D Pharma and our partners to accelerate the development of current and novel programs.

Immuno-oncology Portfolio

The immune system acts as a surveillance system made up of a plethora of cell types, that enable a coordinated response in the body to detect and control disease and infection. When this system malfunctions and does not respond appropriately, this can enable progression of a range of diseases, including cancer.

Treatment of many types of advanced and metastatic cancer have been revolutionized in the last decade by the emergence of cancer immunotherapy. Leading immunotherapies that target programmed cell death protein/ligand 1 (PD-1/PD-L1) immune checkpoint pathways are monoclonal antibody biologics that target extracellular proteins on cells that enable the tumors to dampen the body's immune response to cancer. ICIs, such as Keytruda, Opdivo and Bavencio leverage the power of the human immune system to attack cancer cells by 'taking the brakes off' the body's immune response to cancer and amplifying the immune system's attack on malignant cells by binding to PD-1 or PD-L1, and preventing the dampening effect on the immune response.

While existing immunotherapies have been a remarkable success and have fundamentally changed the way that patients with cancers such as NSCLC and RCC are treated, many patients will stop responding to checkpoint immunotherapy (secondary, or acquired resistance), or not respond at all (primary resistance). At present, there are no therapeutics approved specifically for patients that fail on a checkpoint immunotherapy, and this represents a large unmet need for patients and clinicians.

MRx0518 is our lead immuno-oncology candidate, and is being assessed in the following three clinical trials:

- in combination with Keytruda in patients with solid tumors that are resistant to prior ICIs;
- as a monotherapy treatment in the neoadjuvant setting in patients undergoing surgical resection of solid tumors; and
- in combination with hypofractionated radiotherapy in the neoadjuvant setting in patients with potentially resectable pancreatic cancer.

The Keytruda combination clinical trial and pancreatic cancer clinical trial are part of our strategic collaboration with MD Anderson to evaluate 4D Pharma's Live Biotherapeutic oncology pipeline across a range of cancer settings. The collaboration brings together MD Anderson's translational medicine and clinical research capabilities with our expertise in the discovery and development of LBPs. See the section "Item 4. Information on the Company—B. Business - Overview—Collaborations —Collaboration with University of Texas MD Anderson" for more information about our collaboration with MD Anderson.

In addition to lead oncology candidate MRx0518, we have second generation oncology candidates in preclinical development, such as MRx1299, which have differentiated mechanisms of action to MRx0518 that may be more suitable for the treatment of additional tumor types.

MRx0518

Our lead product candidate in our immuno-oncology program is MRx0518, a strain of *Enterococcus gallinarum* that was discovered with MicroRx. MRx0518 exhibits an immunostimulatory host-response profile that indicated strong potential as an immuno-oncology candidate in preclinical trials. Additionally, the functionality of MRx0518 is well-characterized, demonstrating the primary mechanism of action by which it exerts its anti-tumor activity, via flagellin mediated activation of toll-like receptor 5 (TLR5). MRx0518 is now being assessed in four separate clinical trials, and to our knowledge, has delivered the first proof-of-concept data of a Live Biotherapeutic in a cancer setting.

MRx0518 preclinical data

Our approach to drug development is exemplified by MRx0518. Unlike other microbiome drug discovery strategies that have looked for correlations between specific species of bacteria and response of patients to therapies such as checkpoint inhibitors that do not necessarily indicate causation, we exploited the power of our MicroRx platform to select for potent immunostimulatory activity exhibited by the candidate, agnostic of any prior knowledge of species.

In Vitro Assays

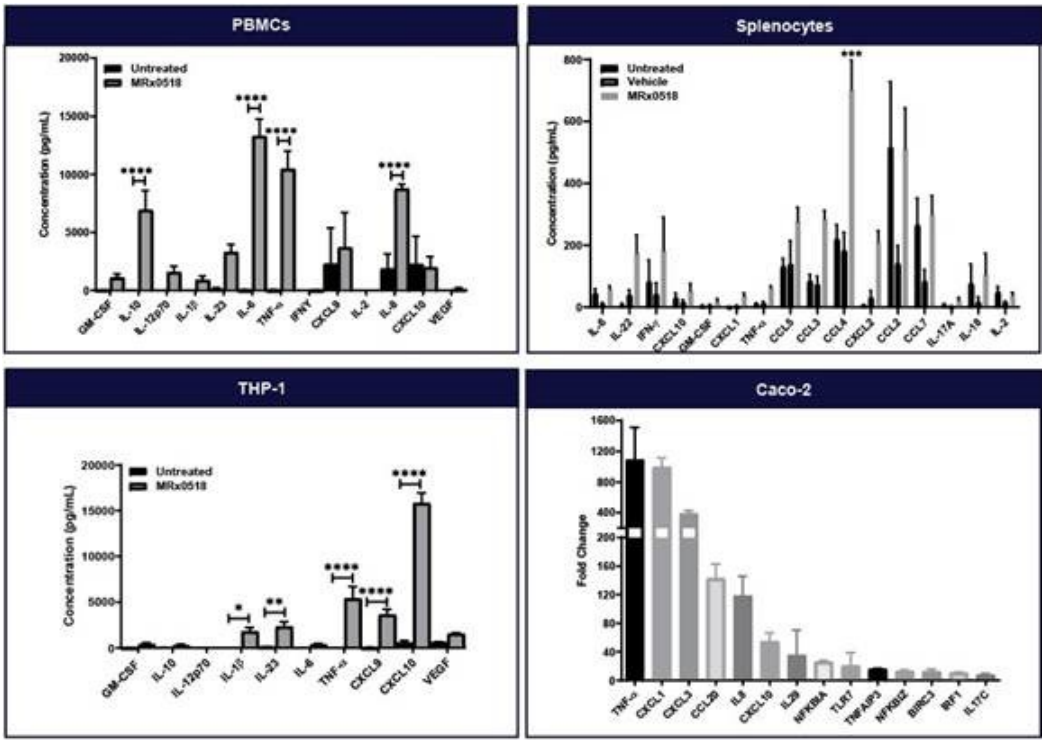


Figure 4. Results of *in vitro* assays, demonstrating the effects of MRx0518 on peripheral blood mononuclear cells (PBMCs), splenocytes, THP-1 cells (cell-line derived from an acute monocytic leukemia patient) and Caco-2 cells (cell-line derived from a patient with colon carcinoma). Significance relative to vehicle: * ($p < 0.05$), ** ($p < 0.01$), * ($p < 0.001$), **** ($p < 0.0001$).**

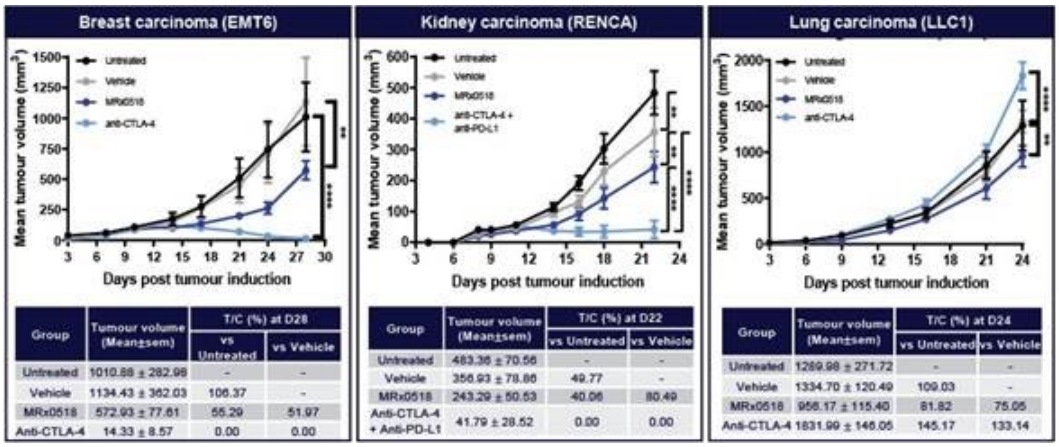
Screening of our proprietary library against a variety of *in vitro* assays enabled the discovery of MRx0518, a single strain of *Enterococcus gallinarum*. MRx0518 was able to induce a strong innate immune response in a range of *in vitro* assays (see Figure 4), in addition to a strong adaptive immune response, increasing ratios of CD4+ and CD8+ T-cells in PBMC co-culture assays, and reducing differentiation of T regulatory cells. The immuno-stimulatory phenotype observed *in vitro* was characterized by a distinct transcriptomic signature and induction of inflammatory mediators (IL-8, TNF-α, IL-1ß, IL-6, IL-23, CXCL9, CXCL10).

Statistical analysis for this study was performed using ANOVA followed by multiple comparisons tests, with *p < 0.05, **p < 0.01, ***p < 0.001 and ****p < 0.0001 between untreated and MRx0518 treated cells (see Figure 4). The level of statistical significance between treatments was expressed as a p-value between 0 and 1. The smaller the p-value, the stronger the evidence that the null hypothesis should be rejected. A p-value less than 0.05 (p < 0.05) is considered statistically significant, while it is considered highly significant as p < 0.001. It indicates strong evidence against the null hypothesis, as there is less than a 5% probability that the null is correct (and the results are random). Therefore, the null hypothesis is rejected, and the alternative hypothesis (there is an effect of treatment) is accepted.

A statistically significant outcome for primary efficacy endpoints is typically one of the requirements for FDA approval of a product. A statistically significant outcome indicates that the probability of the outcome occurring at random is less than the pre-established allowed error level, frequently set at 0.05 (or 1 in 20).

Preclinical Mouse Models

MRx0518 demonstrated an immunostimulatory signature, which translated into *in vivo* anti-tumor activity in syngeneic mouse tumor models of breast (EMT6), kidney (RENCA) and lung (LLC1) cancers when dosed as a monotherapy, reducing tumor size between 35% to 51% compared to controls (see **Figure 5**).



Group	Tumour volume (Mean±sem)	T/C (%) at D28	
		vs Untreated	vs Vehicle
Untreated	1010.88 ± 282.98	-	-
Vehicle	1134.43 ± 362.03	106.37	-
MRx0518	572.93 ± 77.61	56.29	51.97
Anti-CTLA-4	14.33 ± 8.57	0.00	0.00

Group	Tumour volume (Mean±sem)	T/C (%) at D22	
		vs Untreated	vs Vehicle
Untreated	483.36 ± 70.56	-	-
Vehicle	356.93 ± 78.86	49.77	-
MRx0518	243.29 ± 50.53	40.06	80.49
Anti-CTLA-4 + Anti-PD-L1	41.79 ± 28.52	0.00	0.00

Group	Tumour volume (Mean±sem)	T/C (%) at D24	
		vs Untreated	vs Vehicle
Untreated	1289.98 ± 271.72	-	-
Vehicle	1334.70 ± 120.49	109.03	-
MRx0518	956.17 ± 115.40	81.82	75.05
Anti-CTLA-4	1831.99 ± 146.05	145.17	133.14

Figure 5 - Results of preclinical trials of MRx0518 monotherapy in syngeneic mouse models of breast (EMT6), kidney (RENCA) and lung (LLC1) cancer. Significance relative to vehicle: ** (p < 0.01), ** (p < 0.0001).**

Effects of MRx0518 on the tumor and intestinal microenvironment *in vivo* was also assessed in preclinical mouse models. MRx0518 increased intra-tumoral populations of T cells, CD8+ T cell and NK cells (see **Figure 6**); in addition to genetic expression of chemokines, cytokines and TLRs within the tumor. Moreover, MRx0518 increased splenic Tγδ cell, NK cell, cDC1, plasma blasts and plasma cell populations.

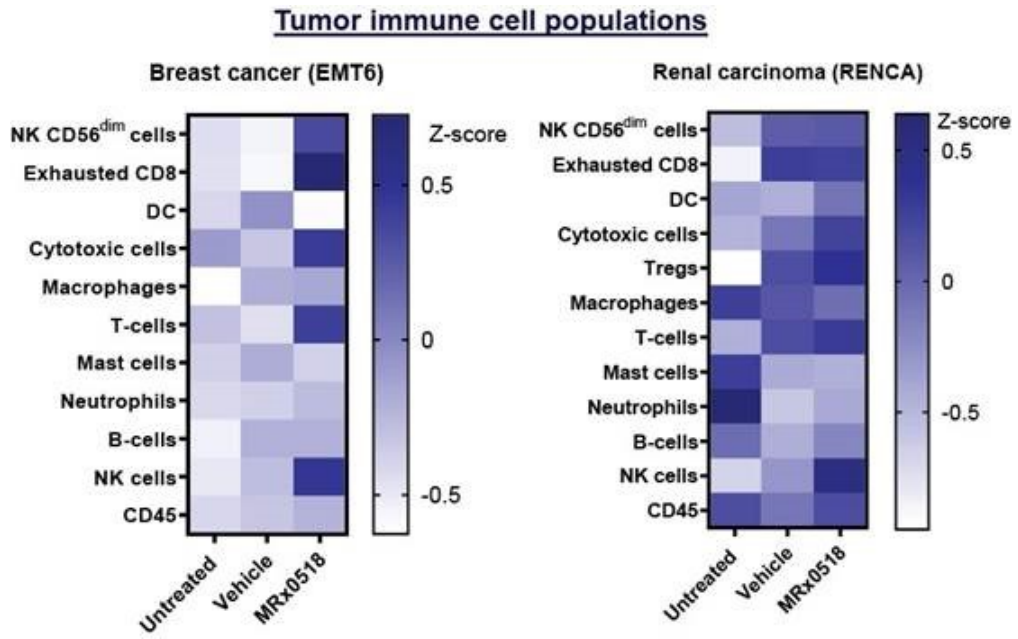


Figure 6 - Quantification of cell subsets utilizing tumor tissues and analysis via NanoString PanCancer IO360 Gene Expression Profile showed that MRx0518 administration in animal models led to increased intra-tumor populations of cytotoxic cells, T cells, CD8+ T cells and NK cells.

Significant work has also been carried out to elucidate the mechanism by which MRx0518 exerts its immunostimulatory effects (see **Figure 7**). While LBPs are poly-pharmaceutical and act on multiple biological pathways, in our preclinical trials we demonstrated that much of MRx0518's activity stems from its agonism of toll-like receptor 5 (TLR5), a component of the innate immune system, through its flagellin. In addition, our preclinical mouse model study showed that MRx0518 also activates nuclear factor kappa-light-chain-enhancer of activated B cells (NFκB). Furthermore, the flagellin of MRx0518 was shown to be more immunostimulatory than flagellin from other species, and a reference strain of *Enterococcus gallinarum*. These findings, in tandem with the other preclinical results showing MRx0518's specific effect on immune cell subsets and anti-tumor activity, were indicative of significant potential as an LBP immunotherapy.

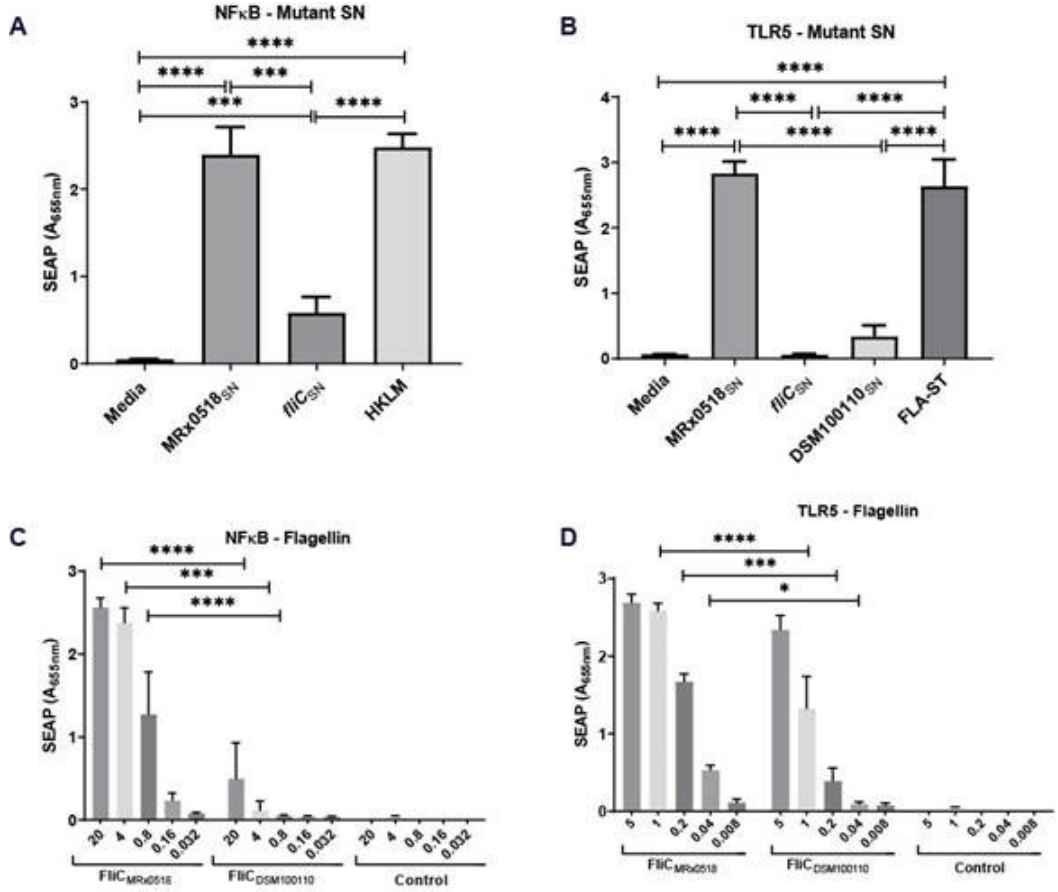


Figure 7. Activation of NF-κB and TLR5 pathway by *E. gallinarum* MRx0518 treatments. NF-κB (A) and TLR5 (B) activation after 22 h incubation with *E. gallinarum* MRx0518 (MRx0518LV), heat-killed MRx0518 (MRx0518HK) and culture supernatant (MRx0518SN) in HEK-Blue hTLR5 and THP1-Blue NF-kB reporter cell lines. A MOI of 10:1 was used with MRx0518LV and a 100:1 MOI equivalent was used with MRx0518HK and MRx0518SN. Heat-killed *Listeria monocytogenes* (HKLM) and *Salmonella* Typhimurium flagellin (FLA-ST) were used as positive controls for each cell line and YCFA was included as a negative control for MRx0518SN. NF-κB (C) and TLR5 (D) activation after 22 h incubation with *E. gallinarum* MRx0518 culture supernatant (MRx0518SN) and trypsin-treated supernatant (MRx0518Trypsin) (MOI 100:1 equivalent). YCFA = Yeast extract-Casein hydrolysate-fatty acid medium. Significance relative to vehicle: * (p < 0.05), ** (p < 0.01), * (p < 0.001), **** (p < 0.0001).**

Phase I/II clinical trial: MRx0518 in combination with Keytruda in solid tumors refractory to prior ICI

Our lead immuno-oncology product candidate, MRx0518, is being evaluated in an ongoing Phase I/II clinical trial in solid tumors in combination with ICI Keytruda in patients with metastatic NSCLC, RCC, UC, TNBC, HNSCC and MSI-H tumors that are refractory to prior anti-PD-1/PD-L1 therapy. This trial is a clinical collaboration with MSD, the maker of Keytruda. All patients enrolled in this clinical trial had previously responded to ICIs, and then developed resistance and progressive disease. The clinical trial evaluates whether the combination of MRx0518 and Keytruda can affect a response in patients that with resistance to ICIs, thus turning non-responders into responders.

The trial is formed of two parts. Part A was an initial safety phase in 12 patients with RCC or NSCLC, evaluating the safety and tolerability of the combination with MRx0518 and Keytruda over the dose limiting toxicity period of one three-week treatment cycle. Patients enrolled in Part A are eligible to remain on study treatment for up to two years to evaluate clinical benefit. Following successful completion of Part A and positive recommendation from the safety review committee, the Part B cohort expansion phase will enroll up to 30 patients per tumor type cohort with metastatic NSCLC, RCC and UC, and up to 10 patients in each cohort of TNBC, HNSCC and MSI-H tumors, to evaluate clinical benefit in addition to safety and tolerability.

Part A has been successfully completed and the safety review committee recommended proceeding to Part B of the study. Of the 12 patients enrolled into Part A of the trial, five patients (42%) demonstrated clinical benefit (defined as a complete response, partial response or stable disease for six months or longer) on treatment with MRx0518 and Keytruda (see **Figure 8**). These include three patients achieving partial responses with radiological scans giving evidence of target tumor shrinkage of greater than 30% from baseline. To the best of our knowledge, we, through this data, delivered the first ever proof-of-concept data in the treatment of cancer using LBPs. We and MSD, the study collaborators, pre-defined the clinical benefit threshold in this trial to support further investigation as 10%, which has been substantially exceeded in the Part A cohort.

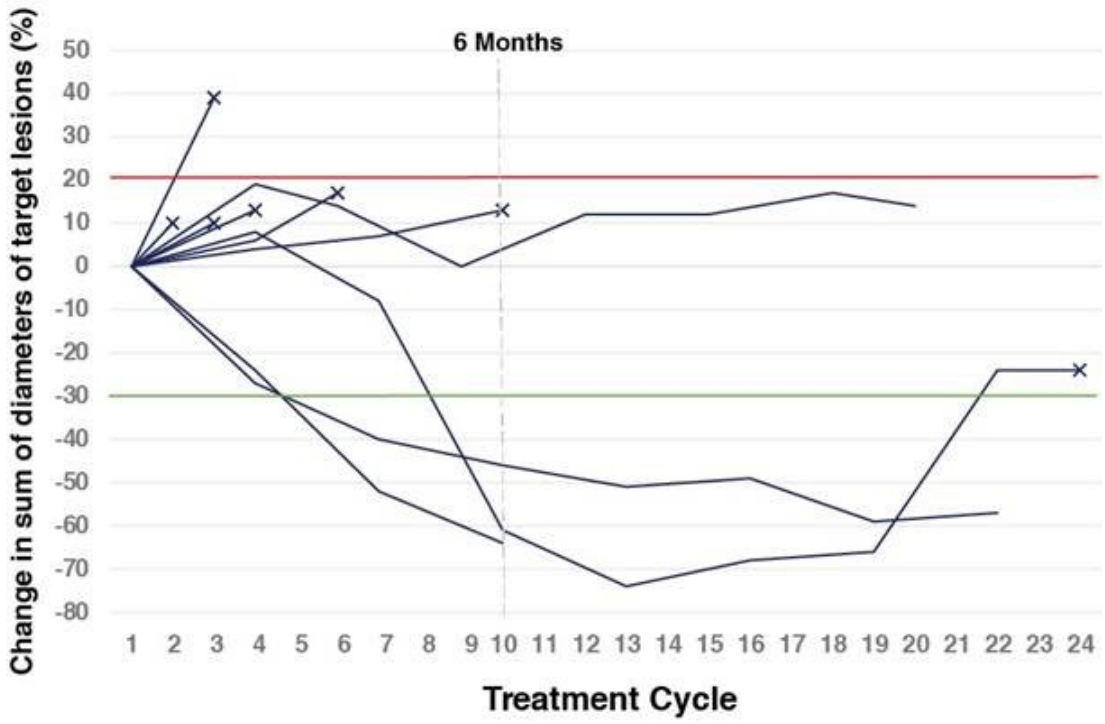


Figure 8. **Percentage change in sum of diameters of target tumors per RECIST v1.1 in patients enrolled in Part A of Phase I/II MRx0518 and Keytruda combination trial (NCT03637803), as of October 23, 2020. Radiological assessment was not possible for two patients who were withdrawn from the study due to progression-related adverse events. 'X' denotes when patients discontinued.**

During Part A of this clinical trial, MRx0518 showed no treatment-related serious adverse effects or drug discontinuations and, importantly, no increase of immune-related adverse events that are often associated with ICI therapy.

Of the 12 patients enrolled in Part A of the combination trial, seven patients were evaluated at the first scheduled restaging scan at nine weeks, and five were withdrawn prior to the first scheduled restaging scan due to clinical evidence of disease progression. Of these five patients, three had progression confirmed by radiological assessment. Radiological assessment was not possible for two patients who were withdrawn from the study as a result of progression-related adverse events. The early withdrawals ahead of the first scheduled restaging scan reflect the challenges of treating patients with advanced metastatic, progressive and refractory cancer, and the unmet needs of these patients.

It should be noted that the patient population in the study are highly refractory, having stopped responding to prior checkpoint immunotherapy, and all patients have received multiple lines of therapy and had progressive disease with no alternative treatment options known to provide benefit available. Additionally, one responder has NSCLC harboring an epidermal growth factor receptor (EGFR) mutation, who has had seven previous lines of therapy. NSCLC patients harboring EGFR mutations have been shown to be much less likely to show clinical benefit from PD-1/PD-L1 checkpoint inhibitors, indicating the potential for MRx0518 to induce response to checkpoint immunotherapy in refractory patients.

The Part B cohort expansion phase of the study is currently enrolling. Encouraged by the results of Part A of this clinical trial, we have opened additional trial sites to accelerate recruitment and delivery of more clinical data of the open-label study. These efforts will add up to an additional 30 patients per tumor type cohort of metastatic NSCLC, RCC and UC that are refractory to prior anti-PD-1/PD-L1 therapy. Additionally, new cohorts of 10 patients with new tumor types are being enrolled in the study, including patients with TNBC, HNSCC and MSI-H high tumors that are also refractory to prior anti-PD-1/PD-L1 therapy. On March 23, 2022, we announced that in Part B of this study, the RCC group has met its primary efficacy endpoint ahead of enrollment completion. The primary efficacy endpoint for Part B of the study is more than three out of 30 patients per tumor group achieving clinical benefit, defined as complete response, partial response, or stable disease for at least six months. Four out of the first 16 evaluable RCC patients enrolled in Part B achieved clinical benefit, each having achieved at least 6 months of stable disease. MRx0518 continues to be safe and well tolerated.

Phase I clinical trial: MRx0518 as a neoadjuvant monotherapy

We also have an ongoing Phase I clinical trial of MRx0518 as a neoadjuvant monotherapy in patients undergoing surgical resection of solid tumors, which is being conducted at Imperial College London. Patients enrolled are diagnosed with resectable tumors and a tumor sample was taken at baseline. MRx0518 was then dosed as a monotherapy for two to four weeks prior to resection, at which point another tumor sample was taken. Changes in systemic immune and intratumoral biomarkers were then analyzed to assess the effect of MRx0518 monotherapy on immune cell populations and gene expression over the dosing period..

Initial results from Part A of this trial were presented at SITC 2020 in November 2020 (see **Figure 9**). For the 17 patients enrolled in Part A of this clinical trial, following MRx0518 treatment, relative increases in cytotoxic cells, CD8+ T cells and other immune subsets associated with anti-tumor activity were observed in paired tumor samples. Upregulation of key immuno-stimulatory anti-tumor cytokines and chemokines, such as IL-12 and CXCL10, was also observed in post-treatment plasma samples. Gene expression analysis identified significant expression changes in 98 genes ($p<0.05$) in paired samples as a result of MRx0518 treatment, including upregulation of pathways associated with antigen presentation, costimulatory signaling, cytokine and chemokine signaling, known to promote anti-tumor immune activity. Crucially, the changes in intratumor immune subsets observed echoed findings in the preclinical setting with MRx0518.

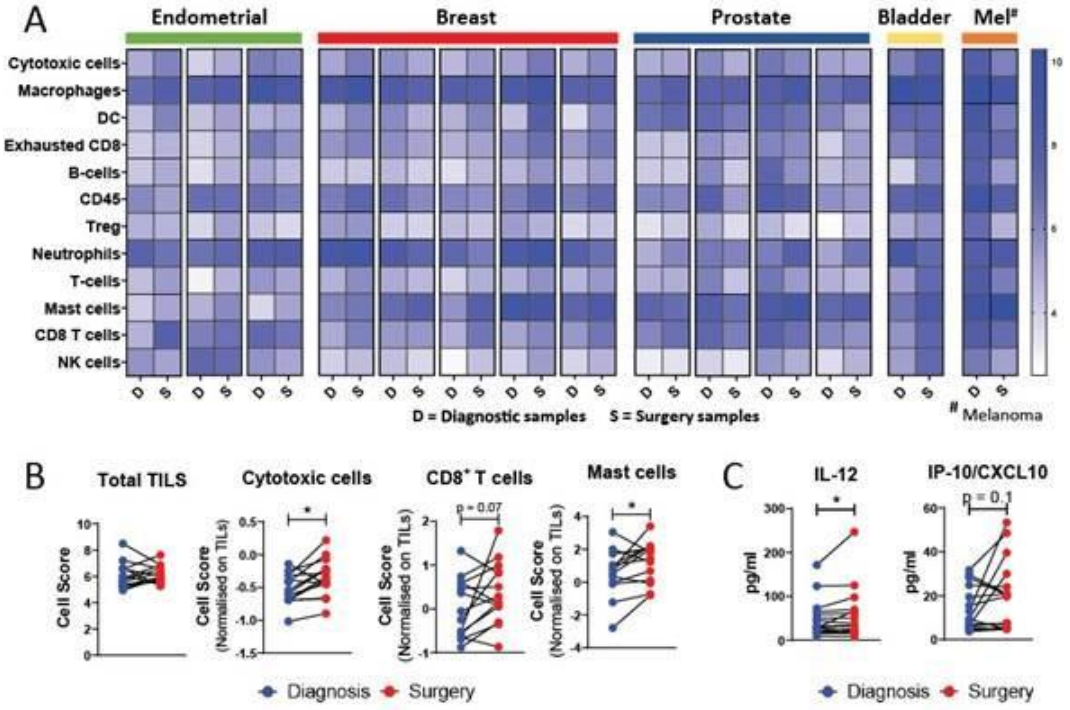


Figure 9. Relative frequency of immune cell subsets in diagnostic and surgery tumour samples were evaluated in the Phase I MRx0518 neoadjuvant monotherapy trial, evaluated using the NanoString IO360 platform and nSolver (A-B). Systemic cytokine concentrations were evaluated in plasma (Luminex) (C). P values calculated using paired t-test (* = p < 0.05).

Further analyses from this study were presented at ESMO 2021, showing that neoadjuvant MRx0518 treatment was associated with significant gene and metagene signature changes in solid tumors. Gene expression profiling of paired tumor samples pre- and post-MRx0518 monotherapy across multiple solid tumor types (N=15) showed that treatment with MRx0518 for two to four weeks was associated with anti-tumor immune activity including antigen presentation, innate immune processes, and interferon response. Analysis of paired tumor samples also identified significant increases in mast cells, Th1, CD8+ T cell, neutrophil, endothelial cell and inflammatory chemokine metagene signatures following MRx0518 monotherapy. Effects were particularly pronounced in the cohort of breast cancer patients (N=7), with significant increases observed in total and activated dendritic cells, CD8+ T cells and cytotoxic cells in the tumor micro-environment. Functional metagene analysis also identified positive changes in prognostic indicators and metagene signatures predictive of immunotherapy response in patients with breast cancer, including inflammatory chemokines, cytotoxicity, lymphoid scores, and the Tumor Inflammation Signature (TIS) - demonstrated to retrospectively predict clinical benefit of anti-PD-(L)1 ICI therapy efficacy in various cancer types. We are currently designing Part B of this Phase I clinical trial.

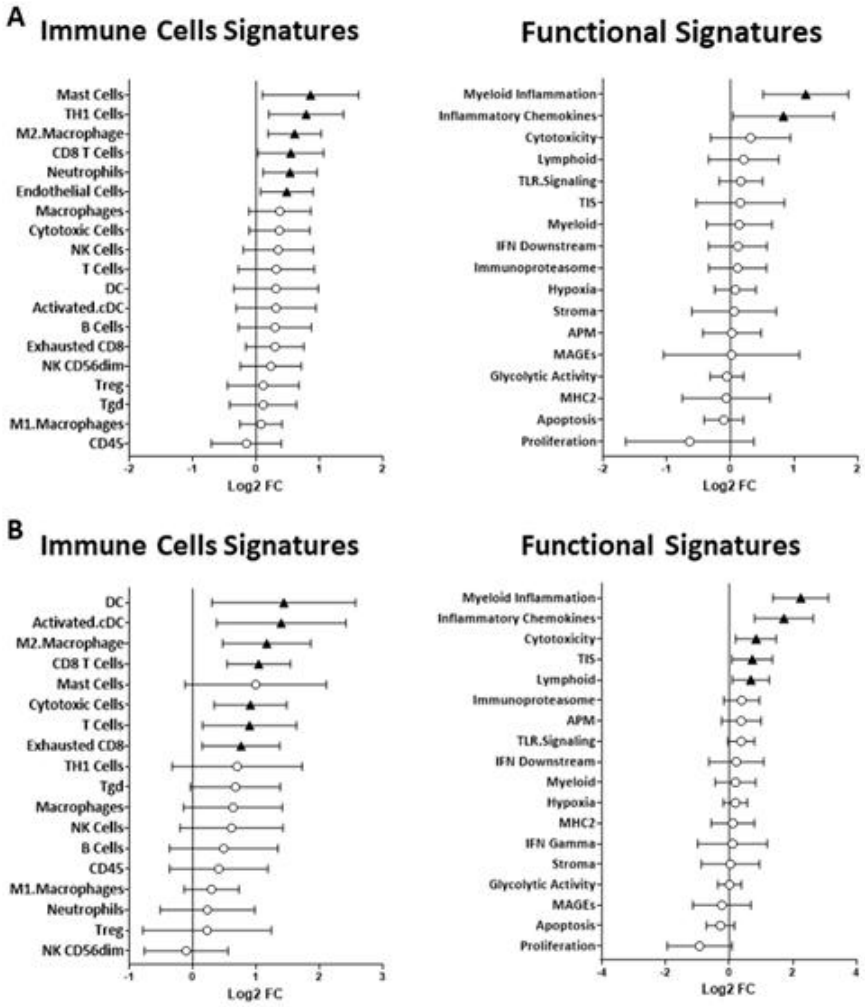


Figure 10. Changes in expression of metagene signatures in paired tumour samples before and after MRx0518 monotherapy for 2 to 4 weeks. Forest plots show the Log2 mean fold change, 95% confidence intervals, of immune cell type and functional score signatures in pre- vs post-treatment in all paired tumour samples (A) or breast cancer cohort paired tumors (B). Triangles (▲) indicate significant difference ($p<0.05$) as assessed by univariate analysis.

Phase I clinical trial: MRx0518 as a neoadjuvant monotherapy in combination with hypofractionated radiotherapy

A third clinical trial of MRx0518 is ongoing in potentially resectable pancreatic cancer, as part of our strategic collaboration with MD Anderson. Pancreatic Ductal Adenocarcinoma (PDAC) is the third leading cause of cancer death in the United States. Outcomes are poor, with five-year overall survival as low as 9%. Complete microscopic (R0) resection represents a requisite component of cure for PDAC, and as such, neoadjuvant therapies are increasingly important to optimize surgical outcomes and maximize long-term survival. Recent studies have shown that patients who received preoperative hypofractionated radiation had improved chances of R0 resection (63% versus 31%).

Our single center, open-label, Phase I clinical trial will treat 15 potentially resectable PDAC patients with a regimen for approximately six to nine weeks, before, during and after a course of hypofractionated radiation until the time of resection. The clinical trial will evaluate the safety of MRx0518 with radiation and whether MRx0518 can elicit an immunogenic profile that may be beneficial in decreasing systemic failure and improving local control. Efficacy outcomes will include incidence of major pathologic response, tumor infiltrating lymphocytes, overall survival, progression-free survival, local control, distant control and margin status. The study will evaluate immune infiltrates and stromal cells within and near the tumor as well as evaluating circulating immune cells, tumor cells and tumor DNA. We anticipate completing recruitment of this Phase I open-label study in 2022.

Phase II clinical trials: MRx0518 in combination with Bavencio as a first-line maintenance therapy for locally advanced or metastatic urothelial carcinoma

Highly encouraged by signals of clinical activity observed so far with MRx0518 combined with no observed treatment-related serious adverse effects or drug discontinuations, including in a particularly difficult-to-treat refractory patients, we are actively exploring additional drug combinations and settings in which to evaluate MRx0518. We are also active in seeking collaborations with industrial partners operating in the pharmaceutical industry to expand the MRx0518 clinical development program.

In February 2021, we entered into a collaboration agreement with Merck KGaA, Darmstadt, Germany ("**Merck KGaA**") and Pfizer, who co-developed and co-commercialized Bavencio (avelumab). This collaboration allows us to evaluate MRx0518 in an earlier treatment setting in patients with locally advanced or metastatic UC which has not progressed with first-line platinum-containing chemotherapy. Under the agreement, we will be the sponsor of the clinical trial. Merck KGaA and Pfizer are providing Bavencio without cost to us for the clinical trials. The study is expected to commence in 2022.

The parties granted each other licenses for rights to inventions and other intellectual property rights created in the design or performance of the study. The parties also granted each other licenses under patents which include or rely on data generated in the study to permit mutual freedom to operate. We have the first right to prosecute jointly owned patents. We retain the rights to all 4D Pharma owned inventions. The collaboration will continue until the completion of all of the obligations from all parties, but any party may terminate the agreement upon a party's material breach if not cured within 30 days of written notice or immediately if any regulatory authority takes any action or objects to the terminating party to supplying its compound for purposes of the study.

Second generation oncology candidates

Beyond our lead immuno-oncology candidate MRx0518, the MicroRx platform has continued to identify new LBP candidates exhibiting novel mechanisms of action with the potential to treat different types of cancers, such as MRx1299.

MRx1299 was selected using MicroRx and has an immunostimulatory host response profile. MRx1299 increased *in vitro* cytokine production by peripheral blood mononuclear cells (PBMCs) and splenocytes, and CD8+/Treg ratio in treated PBMCs, reduced clonogenic survival of various cancer cell lines; and reduced tumor growth by adoptive cell transfer in syngeneic cancer models *in vivo* (see **Figure 11**).

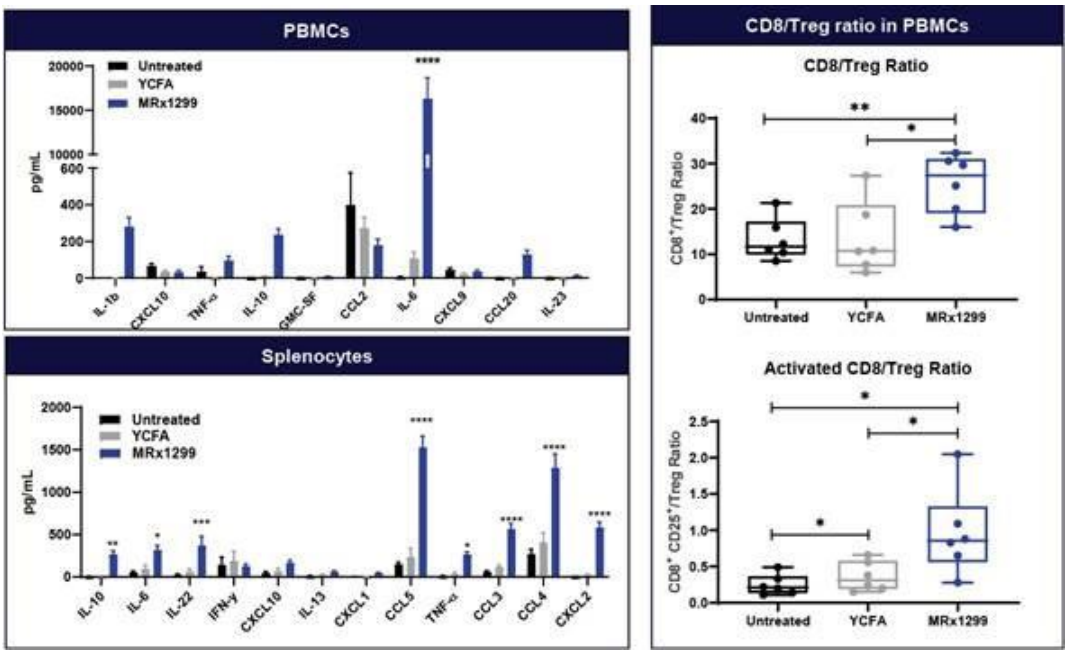


Figure 11. **MRx1299-induced immune activation was investigated in different cell types. MRx1299 induces a cytokine/chemokine signature in peripheral blood mononuclear cells (PBMCs) and splenocytes *in vitro* that includes IL-6, IL-22, IL-10, TNF-α, CXCL2, CXCL10, CCL3, CCL4 and CCL5, and increases the CD8+/Treg ratio in PBMCs *in vitro.* YCFA = Yeast extract-Casein hydrolysate-fatty acid medium. Significance relative to vehicle: * (p < 0.05), ** (p < 0.01), *** (p < 0.001), **** (p < 0.0001).**

The mechanism of action of MRx1299 is mediated in part by its metabolite profile - MRx1299 produces short chain fatty acids which act as potent histone deacetylase inhibitors. Treatment with MRx1299 increased acetylated H3 and H4 nuclear staining in melanoma and colorectal cancer cell lines, and acetylation corresponded to reduced clonogenic growth (see **Figure 12** and **Figure 13**). Pretreatment with MRx1299 enhanced the anti-tumor activity of adoptively transferred cytotoxic T lymphocytes in an animal model of melanoma, increasing tumor infiltration and production of effector cytokines.

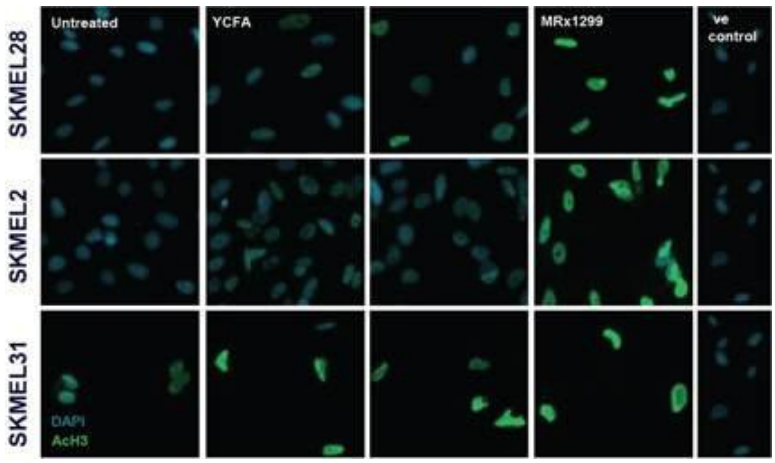


Figure 12. **MRx1299 increased acetylated H3 and H4 nuclear staining in melanoma cell lines. YCFA = Yeast extract-Casein hydrolysate-fatty acid medium.**

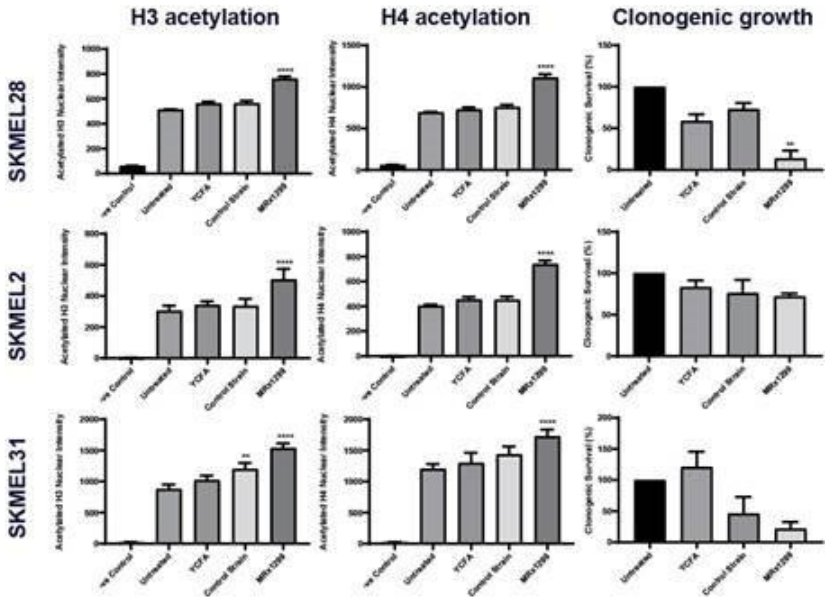


Figure 13. **MRx1299-induced histone acetylation correlated with reduced clonogenic growth in preclinical models of melanoma and colon carcinoma. YCFA = Yeast extract-Casein hydrolysate-fatty acid medium. Significance relative to vehicle: * ($p < 0.05$), ** ($p < 0.01$), *** ($p < 0.001$), **** ($p < 0.0001$).**

In July 2021 we published pre-clinical research relating to a second-generation oncology LBP MRx1299 improving the activity of CAR-T. The research, conducted in collaboration with the Philipps-University Marburg, Germany, and Universitätsklinikum Würzburg, Germany, and published in *Nature Communications*, demonstrated the ability of the bacterium *Megasphaera massiliensis* or its SCFA metabolite pentanoate to enhance the anti-tumor activity of CTL and CAR-T therapies in animal models of cancer, resulting in better tumor clearance.

Respiratory Disease Portfolio

Asthma

A significant number of patients with asthma are poorly controlled by current treatments, leading to exacerbations, hospitalization and mortality. Most biologic therapeutics approved for more severe patients only address the allergic or eosinophilic sub-types of asthma, meaning other patient sub-types remain under-served. These drugs must be administered via subcutaneous or intravenous delivery, and many come with warnings of serious side effects like anaphylaxis. There is significant need for a patient-friendly, oral, add-on therapy to reduce exacerbations, providing additional treatment options before patients are put on biologics, and which addresses under-served sub-groups.

MRx-4DP0004

MicroRx enabled the discovery of MRx-4DP0004, a Live Biotherapeutic candidate with unique effects on inflammation, particularly in the lungs. MRx-4DP0004 demonstrates an ability to address both neutrophilic and eosinophilic lung inflammation concurrently. The candidate is currently being evaluated in a Phase I/II study in patients with uncontrolled asthma.

Respiratory Preclinical Data

Studies in a murine model of severe neutrophilic asthma of MRx-4DP004 showed a statistically significant reduction of lung inflammation in mice. MRx-4DP0004 markedly reduced the magnitude of the neutrophilic immune response, with a reduction of eosinophils also observed (see **Figure 15**). This was associated with a statistically non-significant increase in regulatory T cells (Tregs) in the lung. MRx-4DP0004 was associated with reduced numbers of dendritic cells (DCs) meaning that Tregs cells could interact directly with DCs by downregulating their surface expression of CD80/CD86, reducing the antigen-presenting ability of DCs and blocking the generation of allergen-specific T cell responses.

MRx-4DP0004 also lowered inflammation in the lung, strongly reducing peribronchiolar and perivascular infiltrates, and lung IL-1α, IL-1β, CXCL2. Additionally, histopathological analysis of lungs of mice exposed to house dust mites (HDM) showed that MRx-4DP0004 treatment strongly reduced peribronchiolar and perivascular inflammatory cell infiltration, resulting in lung histological appearance similar to that of untreated animals (see **Figure 15**).

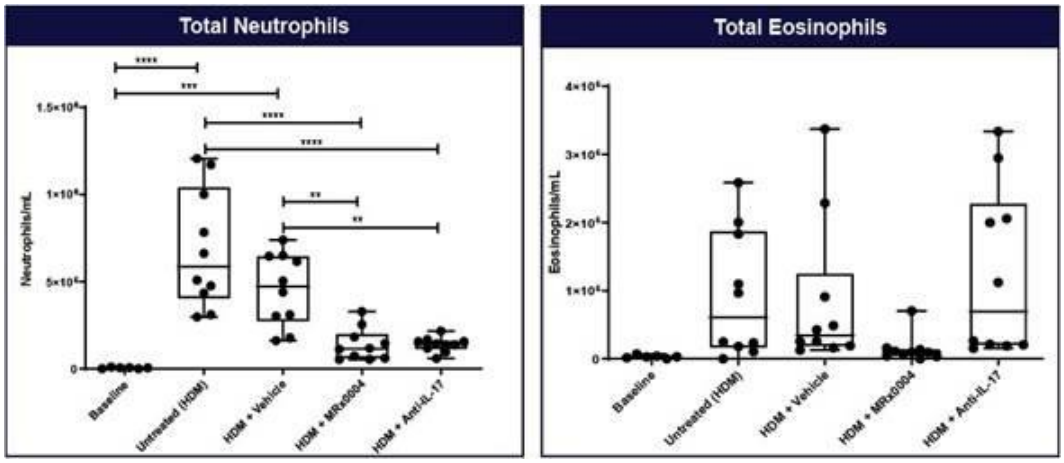


Figure 15. **Bronchoalveolar lavage fluid (BALF) cell counts of mice exposed to HDM, and treated therapeutically with MRx-4DP0004, anti-IL-17 or vehicle, with samples collected 24 h after final exposure. MRx-4DP0004 significantly reduced airway neutrophils, in addition to eosinophils. Significance relative to vehicle: Significance relative to vehicle: * (p < 0.05), ** (p < 0.01), *** (p < 0.001), **** (p < 0.0001).**

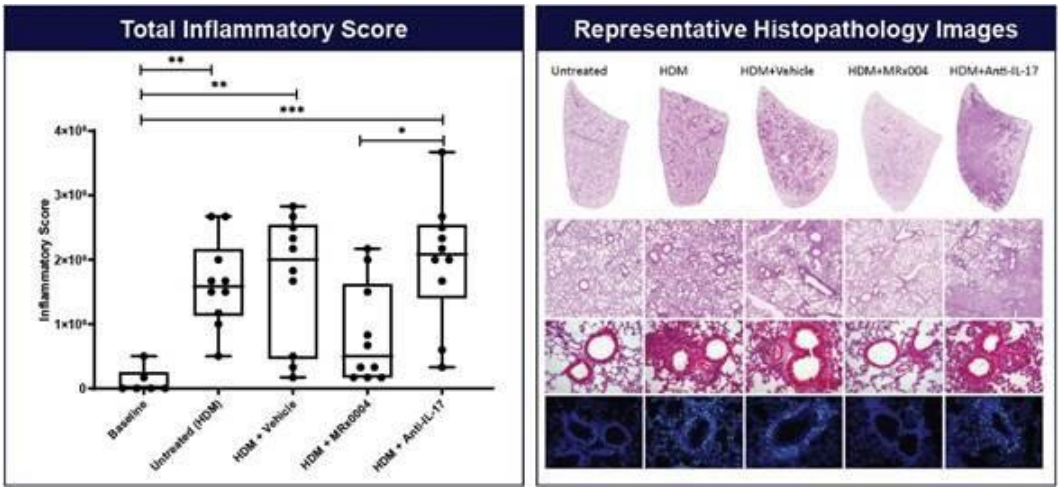


Figure 16. MRx-4DP0004 lowered inflammation in the lung, strongly reducing peribronchiolar and perivascular infiltrates, and lung IL-1α, IL-1β, CXCL2. In contrast, anti-IL-17 treated animals were comparable to vehicle-treated groups. Histopathological analysis of lungs of mice exposed to HDM, and treated with MRx-4DP0004, anti-IL-17 or vehicle, with samples collected 24 h after final exposure, showed that MRx-4DP0004 treatment strongly reduced peribronchiolar and perivascular inflammatory cell infiltration, resulting in lung histological appearance similar to that of untreated animals. HDM = house dust mite. Significance relative to vehicle: * (p < 0.05), ** (p < 0.01), * (p < 0.001).**

Phase I/II clinical trial in asthma

We are conducting a Phase I/II first-in-human, two-part clinical trial of MRx-4DP0004 in approximately 120 patients with partly controlled asthma. Patients on the study receive MRx-4DP0004 daily in addition to their long-term maintenance asthma medication of inhaled corticosteroid with or without long-acting beta agonist. The clinical trial assessed the safety and tolerability of MRx-4DP0004, in addition to clinical endpoints relating to asthma control, exacerbations, lung function and quality of life. A wide panel of host and microbiome biomarkers were also assessed that will contribute to mechanistic understanding of the candidate.

In December 2021 and January 2022, we announced that Part A of the trial in 34 patients achieved the primary endpoint of safety and tolerability and that multiple secondary endpoints showed positive trends in improving asthma control, supporting progression into Part B of the Phase I/II trial. At all timepoints throughout the treatment period, a significantly greater proportion of MRx-4DP0004 treated patients experienced reductions from baseline in Asthma Control Questionnaire (ACQ-6) score, as compared to placebo. At end of treatment, 83.3% of patients receiving MRx-4DP0004 experienced reductions in ACQ-6 score, compared to 56.3% in the placebo arm. Moreover, at end of treatment, 50.0% of patients receiving MRx-4DP0004 experienced reductions from baseline in ACQ-6 scores of 0.5 or more, compared to 37.5% in the placebo arm. In addition, at the end of treatment, 50.0% of patients receiving MRx-4DP0004 reduced their use of SABA, compared to 18.8% of patients receiving placebo. Overreliance on SABA rescue medication is associated with a greater risk of exacerbations, hospitalizations and mortality, and reduced SABA use is a key indicator of improved asthma control. 50.0% of patients receiving MRx-4DP0004 experienced a clinically meaningful increase in Asthma Quality of Life Questionnaire (AQLQ) scores of ≥0.5 at end of treatment, compared to 31.3% receiving placebo. MRx-4DP0004-treated patients' quality of life continued to improve over the treatment period. Mean measures of lung function including forced expiratory volume in the first second (FEV1, percentage of predicted), peak expiratory flow (PEF), and ratio of FEV1 to forced vital capacity (FEV1/FVC) for both MRx-4DP0004 and placebo treatment arms generally remained within normal ranges from baseline to end of treatment. One of 18 patients (5.6%) randomized to MRx-4DP0004 experienced an asthma exacerbation, compared to two of 16 patients (12.5%) randomized to placebo.

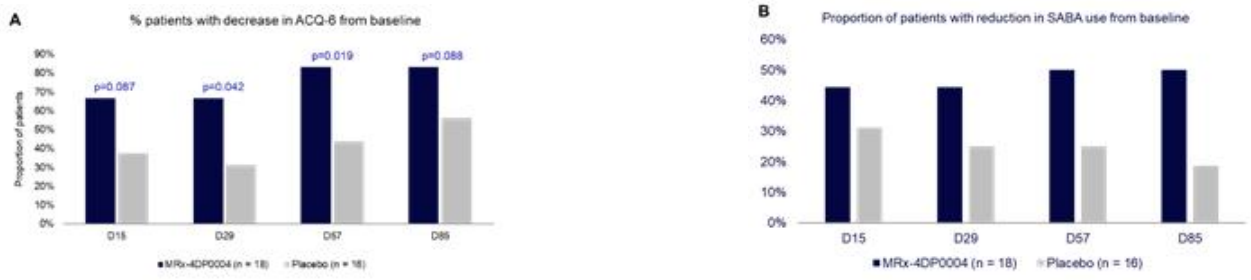


Figure 17. Phase I/II randomized placebo-controlled clinical trial of MRx-4DP0004 in patients with partly controlled asthma, Part A. Proportion of patients receiving MRx-4DP0004 or placebo achieving a decrease in Asthma Control Questionnaire (ACQ-6) score from baseline at different time points, p values calculated using one-sided Fisher's exact test, p<0.1 (A). Proportion of patients receiving MRx-4DP0004 or placebo who decreased their use of short acting beta agonist (SABA) rescue medication from baseline, total number of SABA puffs in 7 day period prior to visit.

To our knowledge, this is the world's first clinical trial of a single strain Live Biotherapeutic in this indication Part B is expected to enroll up to 90 patients and will assess clinical efficacy in addition to exploratory immune and microbiome biomarkers. The proportion of patients with reductions in ACQ-6 score at end of treatment will be the primary endpoint for Part B of the Phase I/II trial.

CNS Portfolio

Neurodegeneration is becoming a significant burden on the healthcare system. It has also proved elusive for the pharmaceutical industry to tackle this issue through traditional approaches. At 4D Pharma, we have most recently focused our MicroRx platform on the gut-brain axis. This work has identified two LBP candidates that demonstrate significant effects on many of the key aspects of Parkinson's disease pathology and represent potentially disease-modifying therapies, in addition to candidates that have effects on the behavior of animals in preclinical models that demonstrate potential in autism and psychiatric conditions.

Neurodegenerative disease

As the global population ages, age-related CNS conditions such as Alzheimer's disease, Parkinson's disease and other dementias will increase in prevalence. These conditions have long affected society, yet therapeutic options to treat these diseases remain limited, and no therapies exist that are known to slow, stop or reverse disease progression. Improving options for patients with neurodegenerative diseases therefore remains one of the biggest challenges in modern medicine.

Parkinson's disease ("**PD**") is one of the most common neurodegenerative diseases, affecting around 10 million people worldwide. The pathology of the disease involves deterioration of motor function due to loss of dopamine producing brain cells in the motor region of the brain, which has been linked to misfolded alpha-Synuclein proteins accumulating as Lewy bodies. The gut-brain axis has been implicated in the pathology of the disease, with patients experiencing gastrointestinal symptoms and gut microbiome symptoms long before the onset of motor symptoms.

Using MicroRx, a multi-targeted functional screening approach was employed that led to the selection of two strains of bacteria, MRx0005 and MRx0029. *In vitro*, the candidates decrease neuroinflammatory responses to stimuli including exogenous alpha-synuclein and protect against oxidative stress. MRx0029 also upregulated gene expression of proteins associated with gut barrier integrity such as Tight Junction Protein 1 and Occludin (see **Figure 18**).

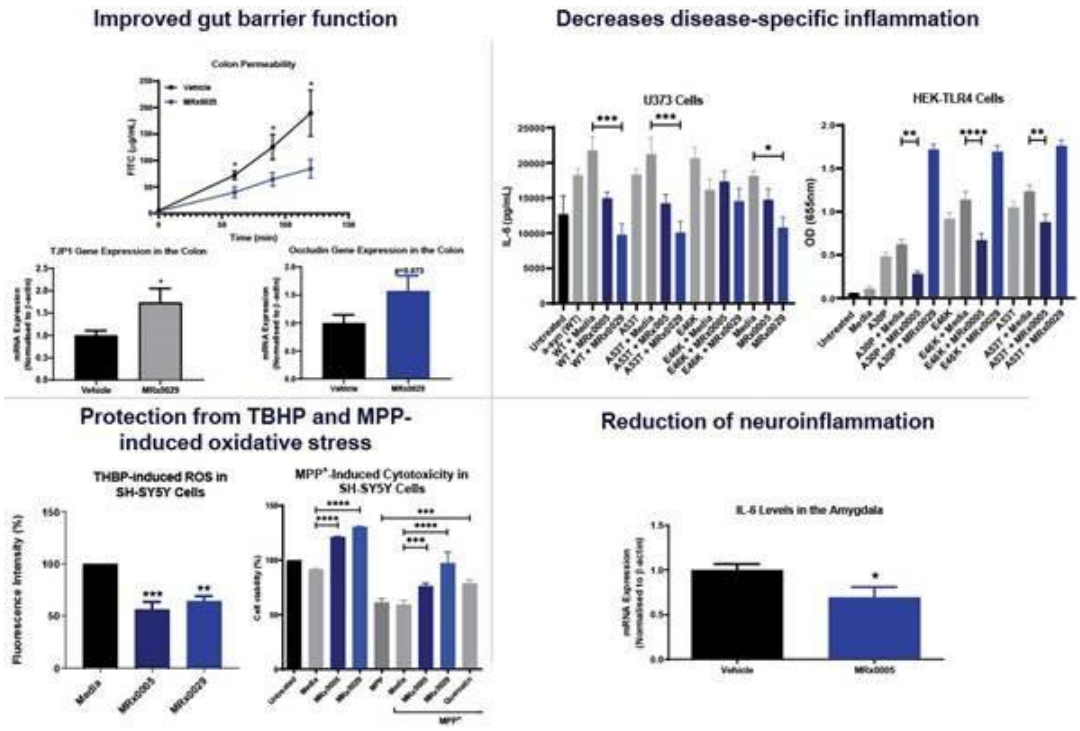


Figure 18. *In vitro*, MRx0029 was able to decrease gut permeability as measured by FITC/Ussing chambers, and increase gene expression of proteins associated with gut barrier functions such as Tight Junction Protein 1 and Occludin. The candidates also demonstrated neuroprotection from TBHP and MPP-induced oxidative stress in undifferentiated SH-SY5Y cells, and reduction in disease-specific neuroinflammation induced by both LPS and mutated alpha-Synuclein proteins. YCFA = Yeast extract, casitone and fatty acid medium; TBHP = ; MPP ; FITC = . Significance relative to vehicle: * (p < 0.05), ** (p < 0.01), * (p < 0.001).**

Notably, MRx0029 has shown promise as a potentially disease-modifying therapy, by indicating a potentially neuro-regenerative effect that could counteract the characteristic loss of dopaminergic neurons in PD (see **Figure 17**). MRx0029 induced neuronal differentiation in SH-SY5Y neuroblastoma cells towards a dopaminergic phenotype, via upregulation of microtubule-associated protein 2 ("**MAP2**") at the gene and cellular level, and upregulation of dopamine active transporter and LIM homeobox transcription factor 1-beta ("**LMX1B**") - markers of dopaminergic neurons.

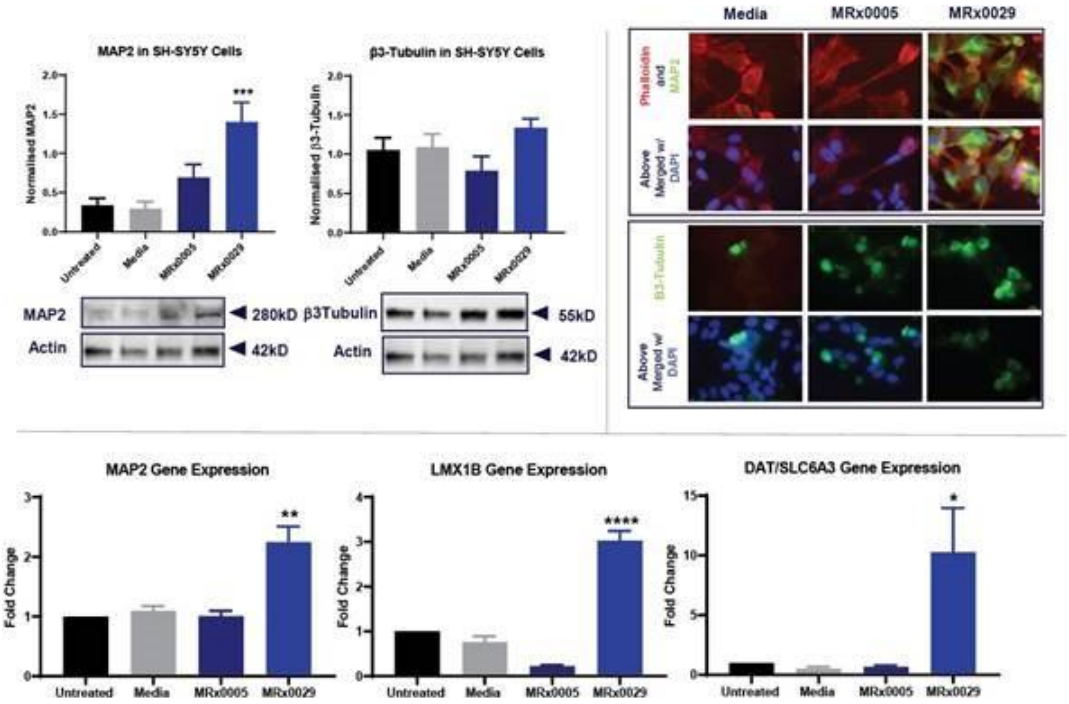


Figure 19. ***In vitro*** **treatment of neuroblastoma cells with MRx0029 demonstrated differentiation to a dopaminergic-like neuronal phenotype, and significantly upregulated expression of numerous markers of dopaminergic neurons, including MAP2, LMX1B and DAT. MPTP = 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine; TH = Tyrosine hydroxylase; 7-NI = 7-Nitroindazole; YCFA = Yeast extract, casitone and fatty acid medium; MAP2 = Microtubule-associated protein 2; LMX1B = LIM homeobox transcription factor 1-beta; DAT/SCL6A3 = dopamine active transporter. Significance relative to vehicle: * (p < 0.05), ** (p < 0.01), *** (p < 0.001), ## (no significant difference from vehicle + vehicle).**

In vivo in the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine ("**MPTP**") model of PD, MRx0029 reduced loss of tyrosine hydroxylase positive dopaminergic neurons, and MRx0005 was able to reduce deficits in dopamine and striatal 3,4-Dihydroxyphenylacetic acid ("**DOPAC**"), a metabolite of dopamine (see **Figure 20).**

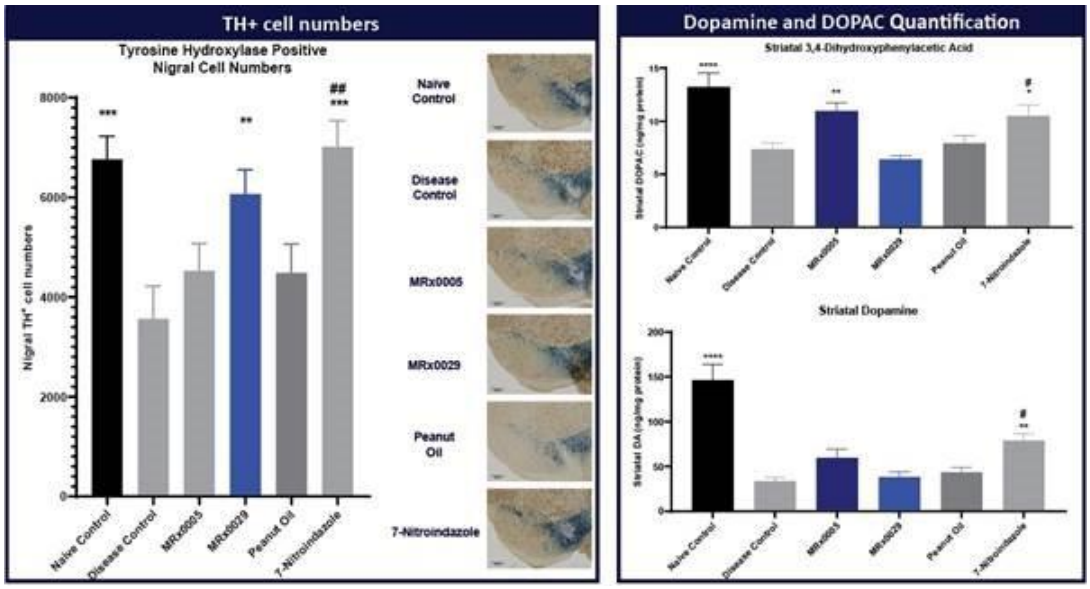


Figure 20. In the MPTP-induced animal model of PD, MRx0029 protected from the loss of TH+ neurons in MPTP-induced brain lesions, offering comparable neuroprotection to the 7-NI positive control. MRx0005 protected from loss of striatal dopamine and DOPAC in MPTP-treated mice, with a similar effect to the 7-NI positive control. MPTP = 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine; TH+ = tyrosine hydroxylase; 7-NI = 7-nitroindazole; DOPAC = 3,4-Dihydroxyphenylacetic acid. Significance relative to vehicle: * ($p < 0.05$), ** ($p < 0.01$), * ($p < 0.001$), ## (no significant difference from vehicle + vehicle).**

We have enlisted the help of key opinion leaders in PD clinical study design to assist in planning a first-in-human clinical trial in people with Parkinson's. In February 2022 we received FDA IND clearances for MRx0005 and MRx0029, and expect to commence the study in 2022.

Parkinson's Progression Markers Initiative

In December 2020, we became an industry partner of the Parkinson's Progression Markers Initiative ("**PPMI**"), a longitudinal study sponsored by The Michael J. Fox Foundation for Parkinson's Research to better understand Parkinson's disease and accelerate the development of new treatments. We will contribute to the efforts of the PPMI as members of the Partner Scientific Advisory Board closely involved in the design and execution of the study. In addition, we also joined a variety of PPMI Working Groups that provide a forum to discuss PPMI data and address Parkinson's clinical trial challenges with other PPMI industry and non-profit partners. In December 2021, our partnership with this initiative was extended by a further 12 months.

Autism spectrum disorder & psychiatric disease

Autism is a neurological development disorder that affects up to one in 54 children, with patients exhibiting a range of symptoms that include impaired social interactions, language and communication skills, patterns of thought and physical behaviors. While the cause of the condition is thought to involve a variety of genetic and environmental factors, the gut microbiome has been implicated due to comorbidity of gastrointestinal symptoms and an altered gut microbiome composition.

Our MicroRx platform has identified preclinical candidate MRx0006, a gut commensal strain of *Blautia stercoris*, that shows strong potential for the treatment of neurodevelopmental disorders.

In genetic BTBR and environmental maternal immune activation ("**MIA**") mouse models of autism, MRx0006 demonstrated statistically significant effects in a range of tests that assessed autism-like behaviors. The results in these models indicated reduced stereotyped behaviors, increased social interaction, reduced anhedonia, decreased depressive-like behavior, and decreased anxiety-like behaviors (see **Figure 21**).

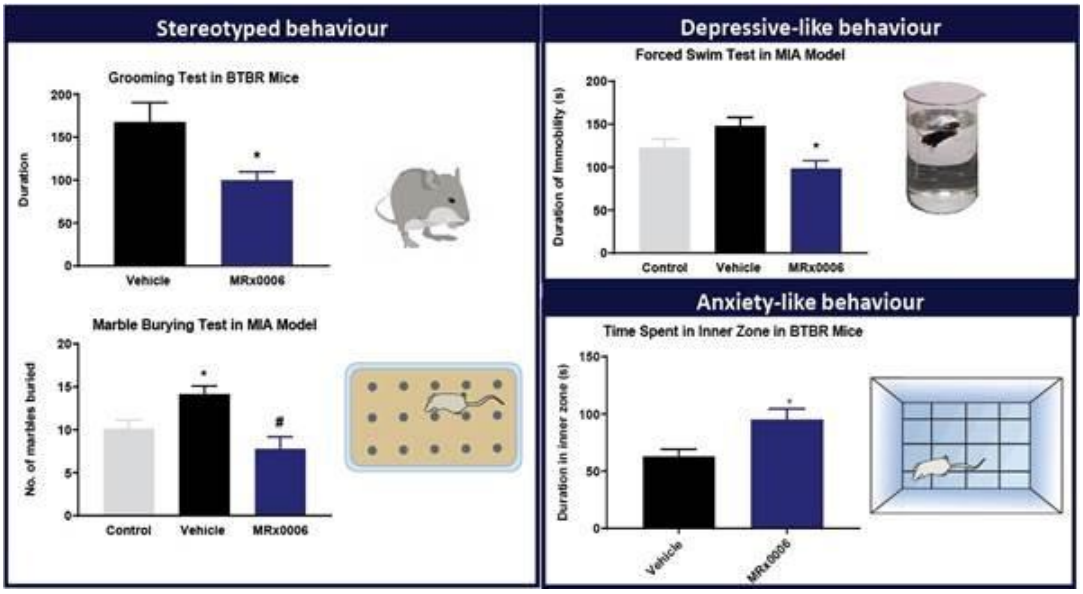


Figure 21. MRx0006 effect on social behaviors assessed in several models, including three-chamber test and urine sniffing test. BTBR = inbred BTBR T+tf/J mouse model of autism; MIA = maternal immune activation. Significance relative to vehicle: * ($p < 0.05$), ## (no significant difference from vehicle + vehicle).

Oxytocin and arginine vasopressin are neuropeptides synthesized in the hypothalamus and secreted from the posterior pituitary gland, that are implicated in social behaviors, in addition to feelings of trust, romance and aggression. MRx0006 demonstrated the ability to significantly increase expression of these neuropeptides, indicating potential to improve autistic-like behaviors (see **Figure 22**).

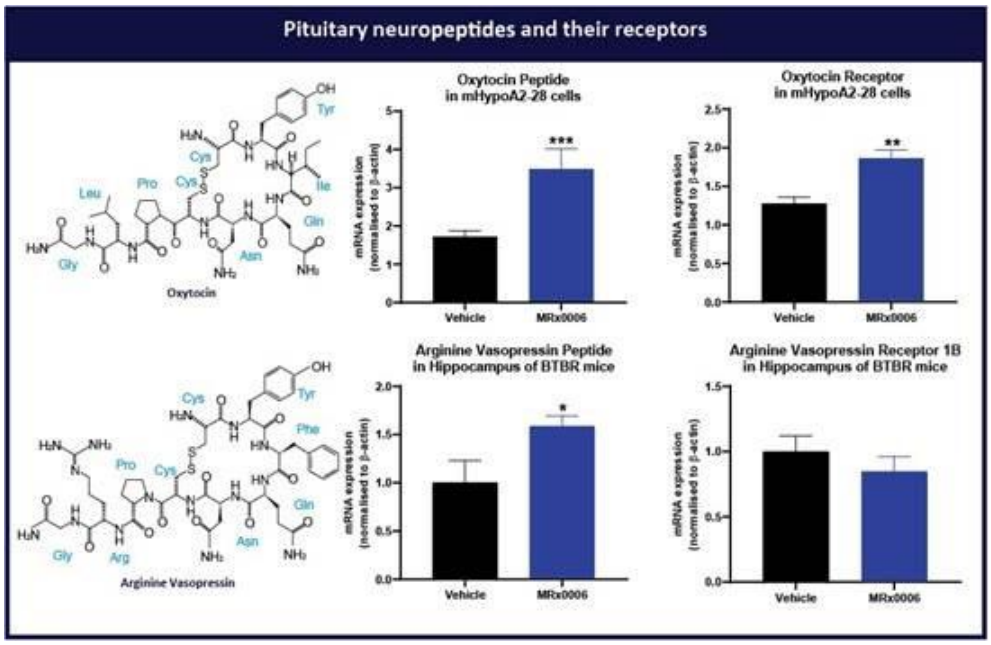


Figure 22. MRx0006 significantly increased oxytocin and oxytocin receptor mRNA expression in mHypoA2-28 cells. MRx0006 also significantly increased hippocampal arginine vasopressin mRNA expression in BTBR mice. Significance relative to vehicle: * (p < 0.05), ** (p < 0.01), * (p < 0.001).**

Immunology Portfolio

MicroRx has also produced candidates targeting immune-inflammatory diseases. These candidates are at the preclinical stage and have shown promising activity in disease relevant animal models. Manufacturing processes for both therapeutic candidates have been developed.

Multiple Sclerosis

Multiple sclerosis ("**MS**") encapsulates relapsing-remitting multiple sclerosis ("**RRMS**") and secondary progressive multiple sclerosis (**"SPMS"**), chronic demyelinating diseases of the CNS. RRMS is thought to affect nearly one million people in the United States, with around 85% of patients initially diagnosed with RRMS, which eventually progresses to SPMS over time.

MRx0002 is a strain in the *Bacteroides* genus and has demonstrated significant potential as an intervention for MS. MRx0002 was found to cause expansion of T regulatory cells and reduce dendritic cell subpopulations in splenocytes, modulate TLR2 and TLR4 signaling, strongly induce secretion of IL-10, inhibit NF-κB activation and improve gut barrier function *in vitro*.

Additionally, MRx0002 was able to completely prevent the onset of disease in an acute experimental autoimmune encephalomyelitis ("**EAE**") animal model of MS, and histological analysis in these models showed significantly reduced inflammation of the spinal cord. MRx0002 also showed a significant reduction in clinical scores compared to vehicle in a chronic EAE model (see **Figure 23**).

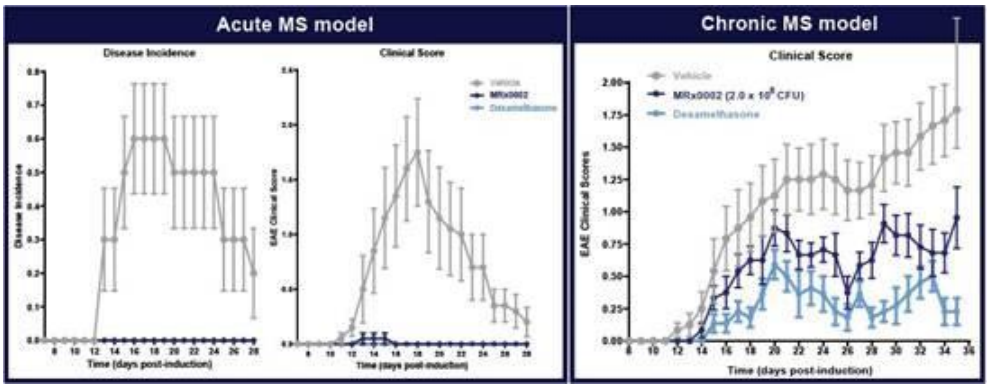


Figure 23. **In an acute experimental autoimmune encephalomyelitis (EAE) mouse model, MRx0002 completely prevented the onset of disease. In a chronic EAE model, MRx0002 also led to a significant reduction in clinical scores. PBS = Phosphate buffered saline; CFU = colony-forming unit.**

Rheumatoid Arthritis

Rheumatoid arthritis ("**RA**") is an autoimmune disease, characterized by chronic inflammation of the joints that erodes joints, bone and cartilage, eventually leading to progressive deformity. RA is estimated to affect around 1.5 million adults in the United States, with patients with chronic inflammation receiving injectable biologic therapies to manage their condition.

MRx0006 (*Blautia stercoris*) is a preclinical candidate that has shown significant potential in both *in vitro* and *in vivo* settings in treating RA. MRx0006 acts on the Th1/Th17 axis, and was able to decrease splenocyte proliferation response and secretion of inflammatory cytokines such as IL-10 and interferon gamma ("**IFNγ**") *in vitro*.

Moreover, MRx0006 was able to significantly improve clinical scores *in vivo* using a type II collagen ("**CII**")-induced arthritis model of RA (see **Figure 24**). MRx0006 also showed a distinct protection of joint architecture from inflammatory damage in histopathological assessment and scoring (see **Figure 25**).

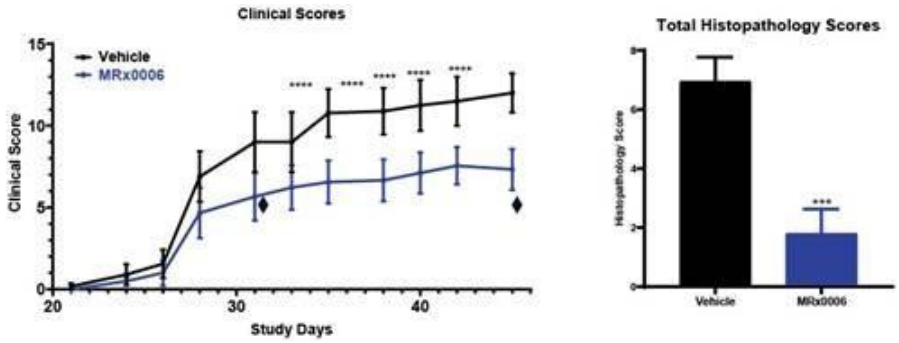


Figure 24. MRx0006 significantly reduced clinical scores (swelling of paws and joints), compared to vehicle following type II-collagen (CII) induction; and significantly reduced all hind limb histopathological scores, including joint inflammation, and cartilage and bone damage. Significance relative to vehicle: ♦ (p<0.05 compared to vehicle on given day), ** (p<0.0001 compared to Day 21 in vehicle); *** (p < 0.001).**

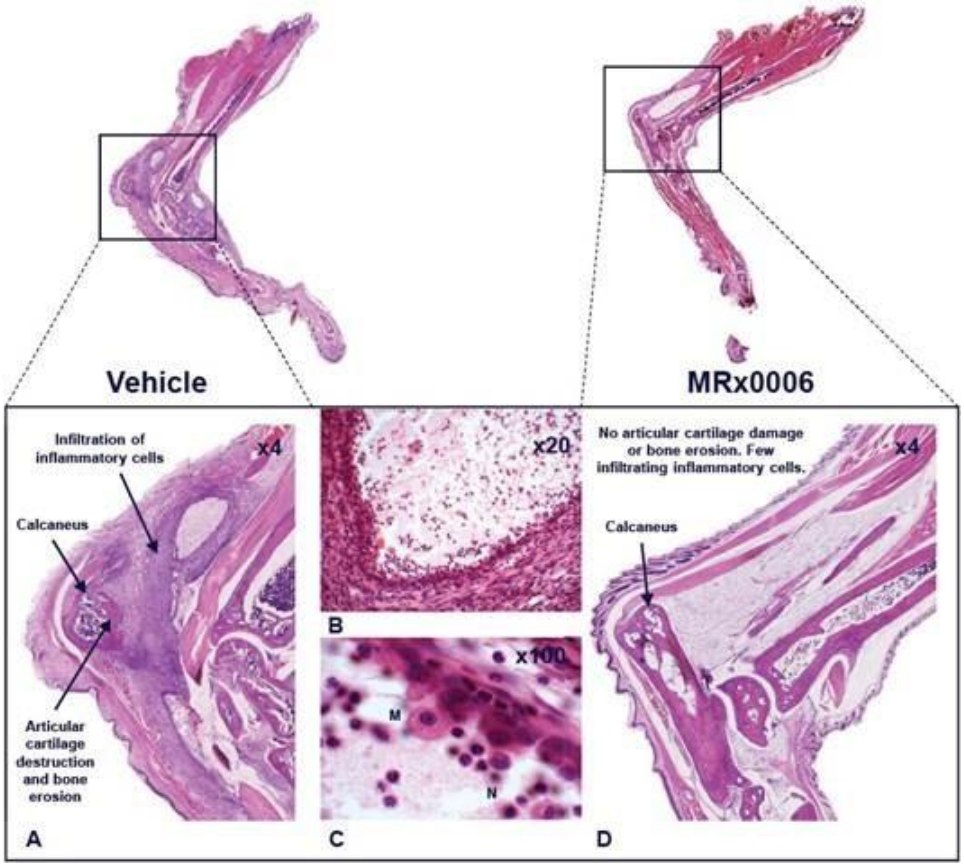


Figure 25. Representative H&E stained saggital sections of arthritic mouse hind limbs derived from subjects in the type II collagen (CII)-induced arthritis model of RA. Cartilage destruction, bone erosion and infiltration of inflammatory cells including macrophages (M) and neutrophils (N) were visible in vehicle-treated animals, whereas MRx0006 treated animals demonstrated few infiltrating inflammatory cells and minimal bone erosion.

Gastrointestinal Disease Portfolio

We have also investigated the efficacy of two therapeutic candidates in our gastrointestinal program in clinical trials, Blautix, a disease modifying therapeutic for IBS, and Thetanix, a single strain human gut commensal bacterium which has an anti-inflammatory mechanism and is under investigation for the treatment of IBD.

Blautix

IBS is a functional gastrointestinal condition affecting 10% to 15% of the U.S. and E.U. population, but with poorly understood etiology. The condition is currently defined symptomatically, patients are categorized as constipation predominant ("**IBS-C**"), diarrhea predominant ("**IBS-D**") or mixed ("**IBS-M**"). The occurrence of this mixed phenotype, and clinical observations that patients frequently switch between IBS-C and IBS-D, suggests a common underlying condition in which the microbiome may play a key role. However, current treatment options only address symptoms and do not address the underlying cause of the disease. Moreover, inherent in their mechanisms of action, available therapies cause severe and unpleasant side effects such as diarrhea.

Blautix is a single strain Live Biotherapeutic intended to address the underlying pathology of IBS and has the potential to become the first ever disease-modifying therapy suitable for all IBS patients regardless of clinical subtype. Blautix has a unique metabolism, consuming hydrogen and producing acetate, which promotes bacterial cross-feeding of the microbiota increasing diversity and stability, two attributes that have been demonstrated to be decreased in patients with IBS compared to healthy controls. Additionally, Blautix increases butyrate production and decreases hydrogen disulfide, leading to a reduction in the visceral hypersensitivity associated with IBS and improving gastrointestinal motility.

Blautix clinical data

Blautix completed a Phase Ib clinical trial in 24 patients with IBS and 24 healthy volunteers. The duration of the study was 14 days. The clinical trial demonstrated that Blautix was well tolerated, with no treatment-related serious adverse events or drug discontinuations, and increased microbiome diversity (Shannon diversity, p=0.04) and showed a trend to increased stability, which was associated with an improvement in symptoms in 82% of IBS subjects receiving Blautix compared to 50% of those who received placebo.

Following successful completion of the Phase Ib clinical trial, we commenced a Phase II multicenter randomized placebo-controlled clinical trial of Blautix in patients with IBS-C and IBS-D, BHT-II-002. The study enrolled a total of 158 patients with IBS-C and 195 patients with IBS-D. The study was designed with feedback from the FDA, using the FDA-recommended composite primary endpoint of overall response rate based on concurrent improvement in abdominal pain and bowel habit (stool frequency for IBS-C patients, or stool consistency for IBS-D patients) in the same week for at least four of the eight treatment weeks. The trial was intended as a signal finding Phase II study, to generate a signal of activity in both IBS-C and IBS-D and generate the clinical data to inform the design of a potential Phase III pivotal program towards registration.

In October 2020 we announced positive topline results from the Phase II clinical trial. Blautix demonstrated a statistically significant overall response rate compared to placebo in the combined IBS-C/D group Efficacy Evaluable Analysis Set ($p = 0.038$) and demonstrated positive, although not statistically significant, trends in improving overall response for both the IBS-C and IBS-D subgroups independently. Blautix was well tolerated, with a safety profile comparable to placebo with respect to adverse events and severe adverse events.

In May 2021, we presented additional positive analyses from the completed Phase II trial of our LBP Blautix in subjects with IBS-C or IBS-D at Digestive Disease Week. This further analysis of our data revealed strong and statistically significant activity on the key symptom of bowel habit, a potential approvable primary endpoint per regulatory guidelines. In the IBS-C group Efficacy Evaluable Analysis Set, Blautix demonstrated statistically significant ($p<0.1$) improvement in stool frequency ($p=0.054$), and the IBS-D group Efficacy Evaluable Analysis Set showed a statistically significant improvement in stool consistency ($p=0.042$). After eight weeks of treatment, evaluable IBS-C and IBS-D patients receiving Blautix reported a decrease from baseline in weekly average abdominal pain score. In addition, analysis of the data by geographical region shows that earlier topline results were impacted by an unusually high placebo response in patients in the UK and Ireland, and enhanced positive signals were seen in the larger US population.

Single strain LBP Blautix is the first therapeutic globally to have demonstrated efficacy in both IBS-C and IBS-D. The clinically meaningful overall response rates and improvements in bowel habit in both IBS-C and IBS-D in this signal finding Phase II trial, in spite of an unexpectedly high placebo response in certain patient groups, are highly encouraging for subsequent larger studies with increased statistical power. The Phase II clinical trial results provide a strong foundation for the continued development of Blautix as the first therapeutic with the potential to treat both major subtypes of IBS. The Phase II data will form the basis of regulatory engagement around the design of a potential Phase III pivotal trial.

Thetanix

Crohn’s disease is an IBD which can occur in any part of the gastro-intestinal tract, but primarily affects the small intestine. Approximately 15% to 25% of all Crohn’s disease patients present when they are younger than 18 years old and the manifestation of the disease in the pediatric population is clinically distinct. Patients suffer from diarrhea, rectal bleeding and abdominal pain, with many also experiencing weight loss, malnutrition and pubertal delay. Many of the standard therapies used in the adult population are problematic in children, including steroids and other systemic immunosuppressants long-term use of which can exacerbate growth retardation.

Thetanix is a single strain human gut commensal bacterium which has an anti-inflammatory mechanism and is under investigation for the treatment of IBD. Thetanix has FDA Orphan Drug Designation for pediatric Crohn's disease.

In multiple pre-clinical models of IBD , Thetanix demonstrated promising activity on the primary readouts in two different preclinical models with relevance to Crohn's disease, protecting against weight loss, preventing histopathological changes in the colon and attenuating expression of inflammatory mediators (see **Figure 26**). Using an *in vitro* co-culture assay, a pirin-like protein ("**PLP**") produced by Thetanix has been identified as a putative candidate effector molecule. Recombinant PLP was shown to be protective against colitis in a preclinical model and, like Thetanix, to act on NF-κB signaling *in vitro.*

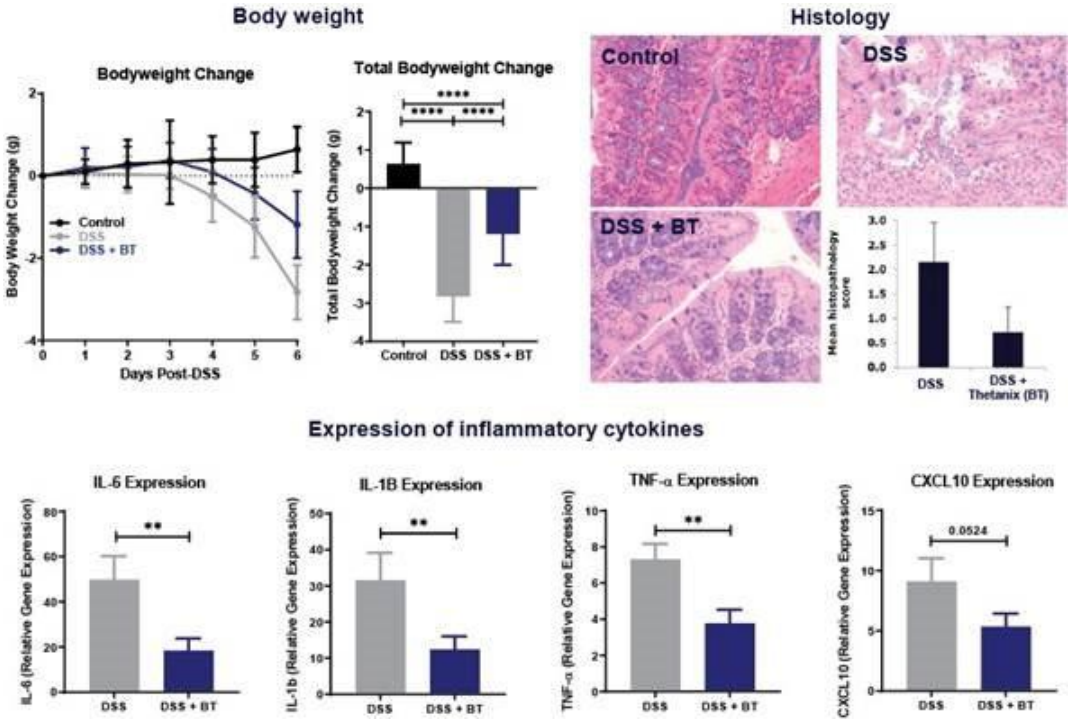


Figure 26. Thetanix protects against intestinal inflammation in dextran sodium sulfate (DSS) mouse models of colitis, reducing disease-associated bodyweight loss, downregulating inflammatory signals, and improving histopathology scores. BT = Thetanix. Significance relative to vehicle: ** ($p < 0.01$), ** ($p < 0.0001$).**

Thetanix Clinical Data

Thetanix has successfully completed a randomized, double-blind placebo-controlled Phase Ib clinical trial in pediatric patients with Crohn's disease. The study was conducted in two parts, a single-dose phase and a multiple-dose phase, and treated a total of 18 subjects aged 16 to 18 with Crohn's disease. In the single-dose phase, eight subjects were given a single dose of either Thetanix or placebo. In the multiple-dose phase, 10 subjects were given either Thetanix or placebo twice daily for seven days.

The Phase Ib study showed Thetanix was well tolerated, with no treatment-related serious adverse events or drug discontinuations, and reduced fecal calprotectin in a subset of patients, an established biomarker intestinal inflammation and indicative of clinical activity. Additionally, a significant difference in microbiome diversity (Shannon diversity, p=0.023) and evenness (microbiota evenness, p=0.03) was observed across the dosing period in Part B of the study. We are exploring strategic options for Thetanix, including the potential for parallel development in both pediatric and adult populations in both Crohn's disease and ulcerative colitis, as well as potential partnerships.

Manufacturing

As LBPs are a new drug modality, we saw fit to invest heavily in manufacturing and developing expertise in order to support rapid progression of our therapeutic candidates from discovery into and through the clinic. Our in-house facility in Leòn, Spain, can produce over 30 million capsules of cGMP drug product per year, with capacity to support all our ongoing trials and small-to-mid scale commercial supply.

To date we have taken nine strains through process development and scale-up to be able to manufacture clinic-ready product. Having in-house control of production has been a significant advantage in a field that has experienced significant hurdles relating to manufacturing. It also generates valuable know-how and intellectual property with returns across our pipeline and platform. We will continue to leverage the competitive advantage of our in-house production capabilities to support our expanding clinical development activities.

A number of raw materials are used to produce our product candidates. The bulk of the raw materials are items that are also used by other pharmaceutical producers, so are generally not difficult for us to obtain. We are dependent only on suppliers of raw materials solely for use in the preclinical and clinical development stages of our product candidates. The raw materials have relatively low-price volatility.

Sales and Marketing

As we are in the development stage of our therapeutic candidates, we are not yet a commercial organization. However, we do intend to commercialize our products, and to do so by assembling our own sales and marketing team, or utilizing the capabilities of select partners and collaborators.

Competition

The sector in which we operate is highly dynamic, with new breakthroughs made regularly that shift the paradigm of treatment of human disease. While we believe that our MicroRx platform and existing candidates enable us to make significant contributions within the biopharmaceutical sector, our competitors may develop or market therapies that are more effective, safer or less costly than any that we are commercializing, or may obtain regulatory or reimbursement approval for their therapies more rapidly than we may obtain approval for ours.

As we are developing medicines based on human microbiota, our natural competition could be thought of as other companies within the microbiome space. While many others in the microbiome space are still highly focused on environmental changes to the microbiome and correlations between certain microbiota profiles and disease, we believe that our function-driven approach to single strain LBP development using our MicroRx platform is highly differentiated, and this has been evidenced by our significant progress in the clinic across a broad range of therapeutic areas. Additionally, our capability in both manufacturing and intellectual property has provided significant competitive advantages that we expect will continue.

Other companies developing microbiome targeted therapeutics include Seres Therapeutics, Inc., Evelo Biosciences, Inc., Vedanta Biosciences, Inc., Kaleido Biosciences, Inc., Finch Therapeutics Group, Inc., Synlogic, Inc. and BiomX.

Competition in the oncology space, the area in which we are developing lead candidate MRx0518, is high. As is common in the oncology space, we may seek to combine our candidates with those of competitors to provide therapeutic regimens with improved efficacy for patients. Significant players in the oncology arena include MSD, Bristol Myers Squibb, F. Hoffmann-La Roche AG, AstraZeneca plc, Regeneron Pharmaceuticals, Inc, Novartis, Janssen, Merck KGaA and Pfizer Inc.

Several add-on therapies for patients with uncontrolled asthma have been developed and commercialized. These therapies generally target IL-4α or IL-5, and are developed by companies including Astrazeneca plc, Regeneron Pharmaceuticals, Inc, GlaxoSmithKline plc and Teva Pharmaceutical Industries Ltd.

While there are currently no disease modifying therapies for neurodegenerative diseases, many companies have therapies that address the symptoms, or have products in development that seek to address aspects of biology that are implicated in the pathology of neurodegenerative disease. In Parkinson's disease specifically, these companies include F. Hoffmann-La Roche AG, AbbVie, Kyowa Kirin Co., Ltd and UCB.

In the GI space, we are developing Blautix for IBS - a therapeutic that seeks to meet the need of patients with both IBS-C and IBS-D. Patients with these subtypes are treated with therapeutics specific to each subtype that are commercialized by institutions that include AbbVie, Ironwood Pharmaceuticals, Inc and Bausch Health Companies Inc.

In the immune-inflammatory disease space, we are developing candidates for a range of different indications including IBD, MS and RA. These are competitive arenas in which numerous products already exist that are commercialized, including by the following companies:

- ***IBD***: The Takeda Pharmaceutical Company Limited, Johnson & Johnson, Abbvie and Pfizer Inc.
- ***MS***: Biogen Inc., F. Hoffmann-La Roche AG, Merck Serono, Novartis International AG and Sanofi S.A.
- ***RA***: Abbvie, Amgen Inc., Johnson & Johnson, Bristol Myers Squibb and UCB.

Intellectual Property

We continue to prioritize establishing robust intellectual property protection for our candidate therapies and other key assets, while also protecting our industry-leading manufacturing know-how. This approach also enables us to protect our competitive advantage gained from investing in establishing and developing the manufacturing by bringing LBP manufacturing in-house.

Importantly, we have procured granted patents that cover our clinical stage therapeutic products in the United States, and other major territories. As of December 31, 2021, our patent portfolio included approximately 50 issued U.S. patents, approximately 61 pending U.S. provisional or non-provisional patent applications, approximately 1456 foreign patents, and approximately 757 pending foreign patent applications, which patents and patent applications we own. The foreign patents and pending foreign patent applications were filed in countries and jurisdictions that include Australia, Brazil, Canada, Chile, China, Colombia, Eurasia, Hong Kong, India, Israel, Japan, Mexico, New Zealand, Nigeria, Russia, Saudi Arabia, Singapore, South Africa, South Korea, Taiwan, Turkey, United Arab Emirates, and countries within the European Patent Convention, the Eurasian Patent Organization, the African Regional Intellectual Property Organization, and the Organisation Africaine de la Propriété Intellectuelle. The claims of these owned patents and patent applications are directed toward various aspects of our product candidates and research programs. Specifically, the claims of these patents and patent applications include, for example, compositions of matter, methods of use, combination therapies, and methods of manufacture. These patents, and patent applications if issued, are expected to expire between 2022 and 2042, without taking into account any possible patent term adjustments or extensions.

With regard to MRx0518, as of December 31, 2021, we have approximately 5 issued U.S. patents, approximately 9 pending U.S. provisional or non-provisional patent applications, approximately 57 foreign patents, and approximately 166 pending foreign patent applications that include claims directed to MRx0518, such as compositions of matter and methods of use. These patents, and patent applications if issued, are expected to expire between 2036 and 2042, without taking into account any possible patent term adjustments or extensions.

With regard to MRx-4DP0004, as of December 31, 2021, we have approximately 3 issued U.S. patents, approximately 2 pending U.S. provisional or non-provisional patent application, approximately 137 foreign patents, and approximately 48 pending foreign patent applications that include claims directed to MRx-4DP0004, such as compositions of matter and methods of use. These patents, and patent applications if issued, are expected to expire between 2036 and 2039, without taking into account any possible patent term adjustments or extensions

With regard to Blautix, as of December 31, 2021, we have approximately 15 issued U.S. patents, approximately 11 pending U.S. provisional or non-provisional patent applications approximately 244 foreign patents, and approximately 116 pending foreign patent applications that include claims directed to Blautix, such as compositions of matter and methods of use. These patents, and patent applications if issued, are expected to expire between 2022 and 2040, without taking into account any possible patent term adjustments or extensions.

With regard to Thetanix, as of December 31, 2021, we have approximately 2 issued U.S. patent, approximately 3 pending U.S. provisional or non-provisional patent application, approximately 75 foreign patents, and approximately 35 pending foreign patent applications that include claims directed to Thetanix, such as compositions of matter and methods of use. These patents, and patent applications if issued, are expected to expire between 2022 and 2039, without taking into account any possible patent term adjustments or extensions.

We strive to protect the proprietary technology that is important to our business, including seeking and maintaining patents intended to cover both our broad platform and individual therapeutic candidates. We seek to obtain domestic and international patent protection and endeavor to promptly file patent applications for new commercially valuable inventions. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

We have established a comprehensive IP estate among specialist LBP developers and continue to implement our aggressive intellectual property strategy in securing robust, multi-layered protection of our therapeutic candidates.

We plan to continue to expand our intellectual property estate by filing patent applications directed to pharmaceutical compositions, methods of treatment, methods of manufacture, and methods for patient selection created or identified from our ongoing development of our therapeutic candidates, as well as discoveries based on our proprietary platform. Our success will depend on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business, defend and enforce any patents that we may obtain, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know-how and continuing technological innovation to develop and maintain our proprietary position and, in the future, may rely on or leverage in-licensing opportunities.

The patent positions of biopharmaceutical companies like us are generally uncertain and involve complex legal, scientific, and factual questions. In addition, the coverage claimed in a patent may be challenged in courts after issuance. Moreover, many jurisdictions permit third parties to challenge issued patents in administrative proceedings, which may result in narrowing or even cancellation of patent claims. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or at all, whether the claims of any patent applications, should they issue, will cover our therapeutic candidates, or whether the claims of any issued patents will provide sufficient protection from competitors or otherwise provide any competitive advantage, or, if challenged, in courts or administrative proceedings, be determined to be invalid or unenforceable.

Because patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months or potentially even longer, and because publication of discoveries in the scientific or patent literature often lags behind actual discoveries and patent application filings, we cannot be certain of the priority of inventions covered by pending patent applications. Accordingly, we may not have been the first to invent the subject matter disclosed in some of our patent applications or the first to file patent applications covering such subject matter, and we may have to participate in interference proceedings or derivation proceedings declared by the USPTO to determine priority of invention.

Patent Portfolio

We continue to recognize the importance of establishing robust intellectual property protection for our candidate therapies, and protecting the competitive advantage derived from our industry-leading manufacturing know-how. This is essential to capturing the value of our research while sharing the advances we have made among the scientific community. It also enables us to protect the competitive advantage gained by bringing LBP manufacturing in-house.

We have established a comprehensive IP estate among specialist LBP developers and continue to implement our aggressive intellectual property strategy in securing robust, multi-layered protection of our therapeutic candidates. As of December 31, 2021, our patent portfolio includes numerous issued patents and pending applications that cover our therapeutic candidates in the US and other countries internationally.

License and Manufacturing Agreements

We are a party to several license agreements under which we license patents, patent applications and other intellectual property. The licensed intellectual property includes composition of matter and methods of using LBP candidates. In some cases, licenses cover physical material in the form of microbial strains. Certain diligence and financial obligations are tied to these agreements. Additionally, we are a party to manufacturing agreements for committed resources and exclusivity.

Collaborations

Collaboration with University of Texas MD Anderson

In November 2017, we entered into a strategic collaboration agreement with MD Anderson, which was amended on February 24, 2021. This partnership brings together MD Anderson's translational medicine and clinical research capabilities with our expertise in the discovery and development of LBPs in oncology. Under the agreement, we provide funding and in-kind support for pre-clinical and clinical studies in solid tumors and radiation oncology. All data, results, and inventions generated in the conduct of the studies under the agreement are owned by us, and we have the sole right to prepare, file, prosecute and enforce patents covering the same. We granted to MD Anderson a royalty-free non-exclusive license to use such data, results and inventions for MD Anderson's internal research, academic and patient care purposes. To date, we have initiated two studies as part of the collaboration: a Phase I/II study of MRx0518 in combination with Keytruda in solid tumors, and a Phase I study of MRx0518 in combination with hypofractionated radiotherapy in patients with potentially resectable pancreatic cancer. Pursuant to the agreement, we agreed to pay MD Anderson at least $10 million for the performance of the studies and have paid $5 million to date. The agreement expires eight years from the effective date, unless earlier terminated due to a party materially breaching the agreement and failing to cure such breach within 30 days of receiving notice from the non-breaching party.

For the years ended December 31, 2021, 2020 and 2019, we have recognized $1.1 million, $1.7 million and $1.7 million, respectively, in costs from MD Anderson which are included within research and development costs in the consolidated statement of operations and comprehensive loss.

Research Collaboration and Option to License Agreement with Merck

In October 2019, the Company entered into the MSD Collaboration Agreement. The MSD Collaboration Agreement is for the use of the Company's MicroRx discovery platform to discover and develop LBP candidates as vaccines in up to three indications. The Company is responsible for the discovery and engineering of the LBPs.

Under the MSD Collaboration Agreement, the Company received a non-refundable, upfront payment, of $2.5 million, a $5.0 million equity investment, and are eligible to receive up to $347.5 million per indication in option exercise fees and in development, regulatory and sales milestone payments, ranging from low seven figures to high eight figures, plus royalties on sales of any licensed product deriving from the collaboration. Such royalty rates range from low- to high-single digit royalties. The achievement and timing of the milestones depend on the success of development, approval and sales progress, if any, of vaccines in the future.

For the years ended December 31, 2021, 2020 and 2019 we have recognized $0.7 million, $0.7 million and $0.3 million in collaboration revenues, respectively. Associated costs of sale of $1.5 million, $1.3 million and $0.2 million, respectively, are included within research and development costs in the consolidated statements of operations and comprehensive loss. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as a current portion of deferred revenue in the balance sheets in our financial statements included elsewhere in this prospectus. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion. As of December 31, 2021, we have current deferred revenues of $0.9 million.

Government Regulation

Government authorities in the United States, at the federal, state, and local level, and other countries extensively regulate, among other things, the research, development, nonclinical and clinical testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing, and export and import of the biological products we are developing. Generally, before a new biologic drug, or biopharmaceutical, product can be marketed, considerable data must be generated, which demonstrate the product candidate's quality, safety, purity, and potency, or efficacy. Such data must then be organized into a format specific for each regulatory authority, submitted for review and approved by the regulatory authority.

U.S. Biologics Development Process

In the United States, the FDA regulates biopharmaceutical products under the federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require 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, the approval process or after approval may subject an applicant to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, adverse publicity, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

The process required by the FDA before a biopharmaceutical product may be marketed in the United States generally involves the following:

- completion of nonclinical laboratory tests, animal studies, and formulation studies in accordance with FDA's good laboratory practice ("**GLP**") regulations and other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval of the study and informed consent by an independent IRB or ethics committee, either centralized or with respect to each clinical site, before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with GCP requirements to establish the safety and potency, or efficacy, of the proposed product for its intended use;
- submission to the FDA of a Biologics License Application ("**BLA**") after successful completion of all pivotal trials;
- determination by the FDA within 60 days of its receipt of a BLA to accept the filing for substantive review;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with cGMP regulations to ensure that the facilities, methods and controls are adequate to ensure the product's identity, strength, potency, quality, and purity, and of selected clinical investigation sites to assess compliance with GCPs; and
- FDA review and approval of the BLA to permit commercial marketing of the product for a particular indication or indications for use in the United States.

Prior to beginning the first clinical trial with a product candidate in the United States, we must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug or biologic product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical studies. The IND also includes results of animal and *in vitro* studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational product for the indication being studied. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

In 2012 and updated subsequently, FDA has issued an industry guidance on early clinical trials with Live Biotherapeutic products, which sets forth various regulatory considerations and standards on chemistry, manufacturing, and control information, which applicants are expected to submit in an IND, including culture/passage of history of microbial strains, summary of phenotype and genotype of the product strains, identification of cells used to establish the master cell bank, methods used to attenuate virulent strains, description of cell growth and harvesting, measures of potency, purity tests, and tests for microbial bioburden, among other considerations. If the applicant and FDA cannot agree on the proper tests and measures of safety, purity and potency for LBPs, clinical testing and regulatory approval of product candidates may be significant delayed, or may never be approved by FDA.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are performed in accordance with protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. Furthermore, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site and must monitor the study until completed. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the clinical trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which may review data and endpoints at designated check points, make recommendations and/or halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries.

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

- *Phase 1*: The product candidate is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism, and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- *Phase 2*: The product candidate is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages, and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.

- *Phase 3*: The product candidate is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

Post-approval clinical trials, sometimes referred to as Phase 4 studies, may be conducted after initial marketing approval. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of a BLA.

During the development of a new biopharmaceutical product, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before a BLA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach agreement on the next phase of development. Sponsors typically use the meetings at the end of the Phase 2 clinical trial to discuss Phase 2 clinical results and present plans for the pivotal Phase 3 clinical trials that they believe will support approval of the new biopharmaceutical product for a particular indication.

Phase I, Phase II, and Phase III clinical testing may not be completed successfully within a specified period, if at all, and there can be no assurance that the data collected will support FDA approval or licensure of a product candidate. Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product candidate and 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 candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, potency, quality, and purity of the final product. In addition, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its proposed shelf life.

While the IND is active and before approval, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar product, findings from animal or *in vitro* testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure.

We will be required to develop and implement additional clinical trial policies and procedures designed to help protect subjects from the COVID-19 virus. For example, in March 2020, the FDA issued guidance, which the FDA subsequently updated, on conducting clinical trials during the pandemic. This guidance describes a number of considerations for sponsors of clinical trials impacted by the pandemic, including the requirement to include in the clinical trial report contingency measures implemented to manage the clinical trial, and any disruption of the clinical trial as a result of the COVID-19 pandemic; a list of all subjects affected by the COVID-19-pandemic related study disruption by unique subject identifier and by investigational site and a description of how the individual's participation was altered; and analyses and corresponding discussions that address the impact of implemented contingency measures (e.g., participant discontinuation from investigational product and/or study, alternative procedures used to collect critical safety and/or efficacy data) on the safety and efficacy results reported for the clinical trial. Recently, FDA also issued guidance on good manufacturing practice considerations for responding to COVID-19 infection in employees in drug and biological products manufacturing, including recommendations for manufacturing controls to prevent contamination of drugs, a guidance on resuming normal drug and biologics manufacturing operations during the COVID-19 public health emergency, and guidance on revised recommendations for reducing the risk of human immunodeficiency virus transmission by blood and blood products. To the extent we are required to implement additional or to modify existing policies and procedures for our clinical studies and/or manufacturing functions, or if the pandemic significantly impacts recruitment of patients or the conduct of our clinical studies, our anticipated timelines for initiating or completing clinical studies and seeking regulatory approval may be substantially delayed, and we may incur additional costs. The extent to which the COVID-19 pandemic impacts our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence.

BLA Review and Approval Process

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development nonclinical and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the product candidate, proposed labeling and other relevant information are submitted to the FDA as part of a BLA requesting approval to market the product for a particular indication or indications. The submission of a BLA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances. Additionally, no user fees are assessed on BLAs for products designated as orphan products, unless the product also includes a non-orphan indication.

Within 60 days following submission of the application, the FDA reviews a BLA to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. Once a BLA has been filed, the FDA's goal is to review the application within ten months after it accepts the application for filing, or, if the application relates to an unmet medical need in a serious or life-threatening indication, six months after the FDA accepts the application for filing. The review process is often significantly extended by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether a product is safe, pure, potent and effective for the proposed indication(s) and the facility in which it is manufactured, processed, packed or held meets standards designed to assure the product's continued safety, purity, and potency, or efficacy. The FDA may convene an advisory committee to provide clinical insight on application review questions.

Before approving a BLA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities comply with cGMP requirements and are adequate to assure consistent production of the product within required specifications. If applicable, FDA regulations also require tissue establishments to register and list their human cells, tissues, and cellular and tissue-based products with the FDA and to evaluate donors through screening and testing. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with Current Good Clinical Practices ("**CGCP**"). If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission in a Complete Response Letter, and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

The testing and approval process require substantial time, effort and financial resources, and each may take several years to complete. The FDA may not grant approval on a timely basis, or at all, and we may encounter difficulties or unanticipated costs in our efforts to secure necessary governmental approvals, which could delay or preclude us from marketing our product candidates. After the FDA evaluates a BLA and conducts inspections of manufacturing facilities where the investigational product will be produced, the FDA may issue an Approval Letter, a Complete Response Letter, or a Not Approval Letter. An Approval Letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete, and the application is not ready for approval. A Complete Response Letter may request additional information or clarification. The FDA may delay or refuse approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety and potency, or efficacy of a product.

If regulatory approval of a product is granted, such approval will entail limitations on the indicated uses for which such product may be marketed. Additionally, the FDA may approve the BLA with a Risk Evaluation and Mitigation Strategy, or REMS, plan to mitigate risks, which could include medication guides, physician communication plans, or other restrictions to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing regulatory standards is not maintained or if problems occur after the product reaches the marketplace. The FDA may require one or more Phase IV post-market trials and surveillance to further assess and monitor the product's safety and effectiveness after commercialization and may limit further marketing of the product based on the results of these post-marketing studies. In addition, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our product candidates under development.

Expedited Development and Review Programs

A sponsor may seek approval of its product candidate under programs designed to accelerate the FDA's review and approval of new drugs and biological products that meet certain criteria. Specifically, new biologic products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. For a Fast Track product, the FDA may consider sections of the BLA for review on a rolling basis before the complete application is submitted if relevant criteria are met. A Fast Track designated product candidate may also qualify for priority review, under which the FDA sets the target date for FDA action on the BLA at six months after the FDA accepts the application for filing. Priority review is granted when there is evidence that the proposed product would be a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious condition. If criteria are not met for priority review, the application is subject to the standard FDA review period of ten months after the 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.

Under the accelerated approval program, the FDA may approve a BLA on the basis of 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, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Post-marketing studies or completion of ongoing studies after marketing approval are generally required to verify the product's clinical benefit in relationship to the surrogate endpoint or ultimate outcome in relationship to the clinical benefit.

In addition, the Food and Drug Administration Safety and Innovation Act of 2012, or FDASIA, established Breakthrough Therapy designation. A sponsor may seek FDA designation of its product candidate as a Breakthrough Therapy if the product candidate is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the therapy may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Sponsors may request the FDA to designate a Breakthrough Therapy at the time of, or any time after, the submission of an IND, but ideally before an end-of-Phase II meeting with the FDA. 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 product candidate 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 or more efficient clinical trials that require less time to complete and may minimize the number of patients exposed to a potentially less efficacious treatment. Breakthrough Therapy designation also allows the sponsor to file sections of the BLA for review on a rolling basis. We may seek designation as a Breakthrough Therapy for some or all of our product candidates.

Fast Track designation, priority review and Breakthrough Therapy designation do not change the standards for approval but may expedite the development or approval process.

In addition, the Pediatric Research Equity Act ("**PREA**"), requires a sponsor to conduct pediatric clinical trials for certain drugs and biological products, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original BLAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the product candidate is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA will send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

Orphan Drugs

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 individuals in the United States when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested before submitting a BLA or NDA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA.

If a product that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a full BLA or NDA, to market the same biologic or drug product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the BLA application user fee.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for 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.

Post-Approval Requirements

Any products manufactured or distributed by us pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record keeping, reporting of adverse events, periodic reporting, distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data. Biopharmaceutical manufacturers and their subcontractors 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, which impose certain procedural and documentation requirements upon us and any third-party manufacturers that we may decide to use. Changes to the manufacturing process are strictly regulated and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements upon us, and any third-party manufacturers, that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance. We cannot be certain that we or our present or future suppliers will be able to comply with the cGMP regulations and other FDA post approval regulatory requirements. If our present or future suppliers are not able to comply with these requirements, the FDA may, among other things, halt our clinical trials, require us to recall a product from distribution, or withdraw approval of a BLA.

Future FDA and state inspections may identify compliance issues at our facilities or at the facilities of contract manufacturers that may disrupt production or distribution or require substantial resources to correct. In addition, discovery of previously unknown problems with a product or the failure to comply with applicable requirements may result in restrictions on a product, manufacturer or holder of an approved BLA, including withdrawal or recall of the product from the market or other voluntary, FDA-initiated or judicial action that could delay or prohibit further marketing.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events 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 warnings, contraindications and safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution restrictions 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 product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license 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 closely regulates the marketing, labeling, advertising and promotion of biologics and drug products. A company can promote only the safety, purity, and potency, or efficacy, that are approved by the FDA and reflected in the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties, and exclusion from participation in governmental health programs, like Medicare and Medicaid. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products.

Other U.S. Regulatory Matters

Manufacturers of biological products are subject to additional healthcare laws, regulation, and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business. Such laws include, without limitation, U.S. federal anti-kickback, anti-self-referral, false claims, transparency, including the federal Physician Payments Sunshine Act, consumer fraud, pricing reporting, data privacy, data protection, and security laws and regulations as well as similar foreign laws in the jurisdictions outside the U.S. Similar state and local laws and regulations may also restrict business practices in the pharmaceutical industry, such as state anti-kickback and false claims laws, which may apply to business practices, including but not limited to, research, distribution, sales, and marketing arrangements and claims involving healthcare items or services reimbursed by nongovernmental third-party payors, including private insurers, or by patients themselves; 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, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information; state and local laws which require the tracking of gifts and other remuneration and any transfer of value provided to physicians, other healthcare providers and entities; and state and local laws that require the registration of pharmaceutical sales representatives; and state and local laws governing the privacy and security of 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.

The risk of our being found in violation of these or other laws and regulations is increased by the fact that many have not been fully interpreted by the regulatory authorities or the courts and their provisions are open to various interpretations. These laws and regulations are subject to change, which can increase the resources needed for compliance and delay product approval or commercialization. Any action brought against us for violations of these laws or regulations, even successfully defended, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Also, we may be subject to private "qui tam" actions brought by individual whistleblowers on behalf of the federal or state governments. Actual or alleged violation of any such laws or regulations may lead to investigations and other claims and proceedings by regulatory authorities and in certain cases, private actors, and violation of any of such laws or any other governmental regulations that apply may result in penalties, including, without limitation, significant administrative, civil and criminal penalties, damages, fines, 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, the curtailment or restructuring of operations, exclusion from participation in government healthcare programs and imprisonment.

Coverage and Reimbursement

Sales of any pharmaceutical product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state, and foreign government healthcare programs, commercial insurance, and managed healthcare organizations, and the level of reimbursement for such product by third-party payors. Significant uncertainty exists as to the coverage and reimbursement status of any newly approved product. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. One third-party payor's decision to cover a particular product does not ensure that other payors will also provide coverage for the product. As a result, the coverage determination process can require manufacturers to provide scientific details, information on cost-effectiveness, and clinical support for the use of a product to each payor separately. This can be a time-consuming process, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. In addition, third-party payors are increasingly reducing reimbursements for pharmaceutical products and related services. The U.S. government and state legislatures have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Third-party payors are increasingly challenging the prices charged, examining the medical necessity and reviewing the cost effectiveness of pharmaceutical products, in addition to questioning their safety and efficacy. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product.

In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Pharmaceutical products may face competition from lower-priced products in foreign countries that have placed price controls on such products and may also compete with imported foreign products. Furthermore, there is no assurance that a product will be considered medically reasonable and necessary for a specific indication, that it will be considered cost-effective by third-party payors, that an adequate level of reimbursement will be established even if coverage is available, or that the third-party payors' reimbursement policies will not adversely affect the ability for manufacturers to sell products profitably.

Healthcare Reform

In the United States and certain foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system. Third-party payors, whether domestic or foreign, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system that could impact our ability to sell our products profitably. In particular, in 2010, the Patient Protection and Affordable Care Act, or Affordable Care Act ("**ACA**") was enacted, which, among other things, subjected biologic products to potential competition by lower-cost biosimilars, 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, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations, subjected manufacturers to new annual fees and taxes for certain branded prescription drugs, and provided incentives to programs that increase the federal government's comparative effectiveness research.

Since its enactment there have been executive, judicial and Congressional challenges to certain aspects of the ACA. For example, in June 2021 the U.S. Supreme Court held that Texas and other challengers had no legal standing to challenge the ACA, dismissing the case on procedural grounds without specifically ruling on the constitutionality of the ACA. Thus, the ACA will remain in effect in its current form. Further, prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period in 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. This executive order also instructs certain governmental agencies to review existing policies and rules that limit access to health insurance coverage through Medicaid or the ACA, among others. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how any such challenges and healthcare measures promulgated by the Biden administration will impact the ACA. our business, financial condition and results of operations. Complying with any new legislation or reversing changes implemented under the ACA could be time-intensive and expensive, resulting in a material adverse effect on our business. Future legislation, rulemaking, or other regulatory actions or developments under the ACA or otherwise could adversely impact the number of Americans with health insurance and, consequently, prescription drug coverage, which can impact the way we do business. We cannot predict the timing or impact of any future legislative, rulemaking, litigation, or other regulatory actions, but any such action could have a material adverse impact on the results of our operations.

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, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in 2013, and, due to subsequent legislative amendments to the statute, will remain in effect through 2031, with the exception of a temporary suspension implemented under various COVID-19 relief legislation from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester. The American Taxpayer Relief Act of 2012 further reduced Medicare payments to several 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 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. For example, in 2020, HHS and CMS issued various rules that are expected to impact, among others, price reductions from pharmaceutical manufacturers to plan sponsors under Part D, fee arrangements between pharmacy benefit managers and manufacturers, manufacturer price reporting requirements under the Medicaid Drug Rebate Program, including regulations that affect manufacturer-sponsored patient assistance programs subject to pharmacy benefit manager accumulator programs and Best Price reporting related to certain value-based purchasing arrangements. Multiple lawsuits have been brought against the HHS challenging various aspects of the rules implemented during the Trump administration. As a result, the Biden administration and HHS have delayed the implementation or published rules rescinding some of these Trump-era policies.

Under the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs will be eliminated. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than it receives on the sale of products, which could have a material impact on our business. In July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at increasing competition for prescription drugs. In response to this executive order, the HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and potential legislative policies that Congress could pursue to advance these principles. In addition, Congress is considering legislation that, if passed, could have significant impact on prices of prescription drugs covered by Medicare, including limitations on drug price increases. The impact of these legislative, executive, and administrative actions and any future healthcare measures and agency rules implemented by the Biden administration on us and the pharmaceutical industry as a whole is unclear. Any reduction in reimbursement from Medicare or other government programs may result in a reduction in payments from private payors.

There has recently been heightened governmental scrutiny over the manner in which pharmaceutical manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted legislation designed, among other things, to bring more transparency to drug pricing, to reform government program reimbursement methodologies for pharmaceutical products, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures and, in some cases, mechanisms to encourage importation from other countries and bulk purchasing. There has also been increased interest by third party payors and governmental authorities in reference to pricing systems and publication of discounts and list prices, which may adversely affect our revenue and financial condition. Further, at the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological 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. A number of states are considering or have recently enacted state drug price transparency and reporting laws that could substantially increase our compliance burdens and expose us to greater liability under such state laws once we begin commercialization after obtaining regulatory approval for any of our product candidates.

We are unable to predict the future course of federal or state healthcare legislation in the United States directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. These and any further changes in the law or regulatory framework that reduce our revenue or increase our costs could also have a material and adverse effect on our business, financial condition and results of operations. It is also possible that additional governmental action is taken to address the COVID-19 pandemic. 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 our product candidates, if we obtain regulatory approval;
- our ability to receive or set a price that we believe is fair for our products;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, 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 product. 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 our product candidates, if approved.

Foreign Regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our product candidates to the extent we choose to develop or sell any product candidates outside of the United States. The approval process varies from country to country and the time may be longer or shorter than that required to obtain FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

C. Organizational Structure

As at December 31, 2021, 4D Pharma plc had the following wholly-owned direct active subsidiaries:

Name of Subsidiary	Jurisdiction of Organization
4D Pharma Research Ltd	Scotland
4D Pharma Leon S.L.U.	Spain
4D Pharma Cork Ltd	Ireland
4D Pharma Delaware Inc.	Delaware, U.S.
4D Pharma (BVI) Limited	British Virgin Islands

D. Property, Plants and Equipment

Our corporate headquarters are located in Leeds, England, where we currently lease 5,800 square feet of office space that expires in May 2027. We also lease 7,600 square feet of office and laboratory space in Aberdeen, Scotland, that expires on November 30, 2022 with rolling one-year extensions and lease 14,100 square feet of manufacturing facilities in Leòn, Spain that expires in April 2026. We believe our facilities are sufficient to meet our current needs and that suitable space will be available as and when needed.

We have two real estate leases classified as right of use operating leases, one in Spain and one in the UK. No additional right of use operating leases were entered into during the periods.

The UK lease is for our headquarters in Leeds, England. The premises comprise office space and parking and are for a ten-year term which commenced in May 2017. A tenant lease break clause is available in May 2022 which has not been included in the lease calculations as there is no indication that this would be executed. Lease escalation costs have been included on a fixed rate basis as a practical expedient. The lease includes a provision to return the premises to their original condition on exit, as such an asset retirement obligation has been included in other liabilities of $0.2 million at December 31, 2021.

The Spanish lease relates to our manufacturing premises in Leon, Spain. The agreement is for a ten-year term which commenced in April 2016 and includes a tenant lease break clause that can be executed after providing six months' written notice at any point five years from the commencement date, again this break clause has not been included in the lease value as there is no evidence that this will be executed. Lease escalation cost have also been included on a fixed rate basis as a practical expedient. The lease includes the requirement to make certain repairs and as such an asset retirement obligation has been included in other liabilities at $41 thousand at December 31, 2021.

ITEM 4A. UNRESOLVED STAFF COMMENTS

None.

ITEM 5. OPERATING AND FINANCIAL REVIEW AND PROSPECTS

The following discussion and analysis should be read in conjunction with our financial statements and related notes included elsewhere in this 20-F. As discussed in the section titled "Cautionary Statement Regarding Forward-Looking Statements," the following discussion and analysis contains forward looking statements that involve risks and uncertainties, as well as assumptions that, if they never materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward looking statements. Our actual results and the timing of selected events could differ materially from those anticipated in these forward-looking statements as a result of several factors, including those set forth under "Risk Factors" and elsewhere in this 20-F.

A. Operating Results

Overview

4D Pharma was established with the mission of leveraging the deep and varied interactions between the human body and the gut microbiome, the trillions of bacteria that colonize the human gastrointestinal tract, to develop an entirely novel class of drug: Live Biotherapeutics. We are focused on understanding how individual strains of bacteria function and how their interactions with the human host can be exploited to treat particular diseases, from cancer, respiratory, central nervous system, immunological and gastrointestinal diseases and disorders.

To further advance our product pipeline, we have developed MicroRx, our proprietary discovery platform. MicroRx interrogates our proprietary library of bacterial isolates for therapeutic functionality and comprehensively characterizes the bacterial isolates using a range of complementary tools and technologies. By developing a thorough understanding of the functionality and mechanism of action of our therapeutic candidates, we can develop LBPs that target disease pathology rationally and effectively and expand our robust sector-leading patent portfolio with additional patents relating to LBP functionality.

To this end, our key clinical focus areas include immuno-oncology, IBS and respiratory disease, with preclinical candidates targeting CNS and autoimmune conditions. We have completed three clinical trials and currently have five clinical programs ongoing. One of our key focus areas is immuno-oncology, and with our lead immuno-oncology therapeutic candidate, MRx0518, we delivered what we believe to be the first positive proof of-concept data with a LBP in the treatment of cancer. MRx0518 is being evaluated in three ongoing clinical trials, including a Phase I/II clinical trial in solid tumors in combination with Keytruda (supplied under a free of charge supply agreement) in patients with advanced or metastatic NSCLC, RCC and UC who are refractory to prior anti-PD-1/ PD-L1 therapy. Additionally, new cohorts of 10 patients with new tumor types are being enrolled in the study, including patients with TNBC, HNSCC and MSI-H high tumors. We successfully completed Part A of this Phase I/II clinical trial and Part B of the clinical trial is currently enrolling up to an additional 30 patients per tumor type and will assess clinical benefit in addition to safety. We also completed recruitment for Part A of an ongoing Phase I trial of MRx0518 as a monotherapy in patients undergoing surgical resection of solid tumors, which is being conducted at Imperial College London. We are currently redesigning Part B of this Phase I clinical trial after initial data from Part A showed encouraging early biomarker readouts. Our third clinical trial of MRx0518 is a Phase I clinical trial of MRx0518 in patients with potentially resectable pancreatic cancer in combination with hypofractionated radiotherapy, which is part of our strategic collaboration with the University of Texas MD Anderson Cancer Center. We anticipate that in 2022, the first patient will be enrolled as part of a Phase I/II clinical trial to investigate Bavencio (to be supplied under a free of charge supply agreement) in combination with MRx0518 in a first-line maintenance setting for patients with locally advanced or metastatic urothelial carcinoma that has not progressed on first-line platinum-containing chemotherapy.

We are engaged in business development activities with the goal of expanding the development of MRx0518 into new settings and are actively exploring additional collaboration opportunities

A second-generation oncology candidate, MRx1299, is in preclinical development and its ability to enhance the anti-tumor activity of cytotoxic T lymphocytes (CTL) and CAR-T therapies in animal models of cancer, resulting in better tumor clearance, was reported in July 2021.

In our gastro-intestinal disease portfolio, we currently have two LBP candidates that have completed early clinical evaluation, Blautix and Thetanix. Blautix is being developed as the first therapeutic to treat patients with IBS, regardless of clinical subtype. The Phase II clinical trial results for Blautix provide a foundation for the continued development of Blautix as the first therapeutic with the potential to treat both major subtypes of IBS, and this data will advance regulatory engagement around the design of a potential Phase III pivotal program. Thetanix is a single strain human gut commensal bacteria that has an anti-inflammatory mechanism and is currently under investigation for the treatment of IBD. Thetanix has an Orphan Drug Designation for pediatric Crohn's disease from the FDA. We have successfully completed a Phase Ib clinical trial of Thetanix in pediatric Crohn's disease patients, and we are exploring strategic options for Thetanix, including parallel development in pediatric and adult populations in both Crohn's disease and ulcerative colitis, as well as potential partners.

We are also developing therapeutic candidates for our respiratory disease portfolio. MicroRx enabled the discovery of MRx-4DP0004, an immunomodulatory single strain LBP candidate that demonstrated marked effects in preclinical trials of respiratory inflammation, particularly in the lungs. We have successfully completed Part A of a Phase I/II clinical trial of MRx-4DP0004 in partly controlled asthma, with enrollment for 90 patients in Part B to commence shortly. To our knowledge, this is the world's first clinical trial of an LBP in the indication.

We continue to utilize the MicroRx platform to discover promising new LBP candidates for major diseases with significant unmet need. As part of our CNS portfolio, we have identified novel LBP candidates that act upon multiple aspects of the pathology of neurodegenerative diseases in preclinical models, including gut-barrier function, neuroinflammation and protection of neurons critical to healthy CNS function. Accordingly, we are currently planning a first-in-human clinical study for our lead CNS therapeutic candidates, MRx0005 and MRx0029, in Parkinson's disease patients. In February 2022, the U.S. Food and Drug Administration cleared investigational new drug ("**IND**") applications for MRx0005 and MRx0029 for the treatment of Parkinson's disease. As part of our commitment to CNS research and drug development, in December 2020, we became an industry partner of the Parkinson's Progression Markers Initiative, a longitudinal study sponsored by The Michael J. Fox Foundation for Parkinson's Research to better understand Parkinson's disease and accelerate the development of new treatments. In December 2021, our involvement in this project was extended by a further 12 months.

In addition to our internal development programs, we are seeking to realize the value and potential of the MicroRx platform through collaborations in new areas. In 2019, we entered into a research collaboration and option to license agreement with MSD to discover and develop LBPs for vaccines. This collaboration pairs our proprietary MicroRx platform with MSD's expertise in the development and commercialization of novel vaccines, to discover and develop LBPs as vaccines in up to three undisclosed indications. See "Business—Collaborations—Research Collaboration and Option to License Agreement with Merck."

In 2020, the global COVID-19 pandemic hit the United Kingdom, United States and other regions worldwide, affecting almost all aspects of the economy including the pharmaceutical industry in which we operate. In response we have been proactive, putting the safety of staff and patients first. We have made good use of technology to minimize disruption to our operations while protecting our staff. However, as has been seen across the biopharma industry, there have been unavoidable impacts on certain activities, resulting in some potential delays to expected clinical readouts. We continue to monitor the situation closely and will provide updates as and when the expected resolution of the situation becomes clearer.

In light of this unprecedented situation, we have carefully re-evaluated our strategic priorities and near to-mid-term objectives. We have taken measures to streamline the business, including changes to management structure and reducing staffing requirements, primarily relating to manufacturing, research and administrative services. We have also prioritized allocation of capital and resources to key programs, such as oncology and are set to continue to deliver key clinical value drivers for our shareholders in the coming months.

Key Performance Indicators

We track a series of metrics focused primarily on science and product development whilst ensuring that the business maintains both sufficient resources and effective allocation of those resources to achieve our strategic goals. The Board and management of 4D Pharma monitor the following metrics as an indicator of how we are progressing towards the goal of advancing our Live Biotherapeutic programs:

1. Clinical trials are essential in converting the productivity and potential of our MicroRx platform and early-stage research into long-term value. Prior to 2019, we had initiated two Phase I clinical studies and one Phase II study. During 2019 we initiated three clinical studies, including one Phase I study in oncology and two Phase I/II studies, in oncology and asthma. In 2020 we commenced two new clinical trials, of which one Phase I and one Phase II. No new clinical studies were initiated in the year ended 31 December 2021.

2. Successful clinical trials – We are a drug development company and will realize long-term value by successfully progressing its candidates through the clinic to registration and approval. Prior to 2019 we had completed two Phase I clinical trials. No studies were completed in 2019. During 2020, we completed a Phase II trial in IBS, Part A of the Phase I/II clinical study of MRx0518 with Keytruda in oncology, and Part A of a Phase I trial of MRx0518 as a neoadjuvant monotherapy in oncology. The two studies of MRx0518 remain ongoing. For the year ended 31 December 2021, Part A of a Phase I/II trial in asthma was completed and this study remains ongoing.

3. Collaborations enable us to realize the potential of our platform, leveraging the complementary expertise of our partners. Prior to 2019 we had entered into one strategic collaboration, a clinical collaboration with MSD to evaluate MRx0518 in combination with Keytruda, an anti-PD-1 ICI marketed by MSD, in patients with in patients with metastatic solid tumours that are refractory to prior anti-PD-1/PD-L1 therapy. In 2019 we added two new collaborations, a strategic collaboration with the University of Texas MD Anderson Cancer Center to evaluate 4D Pharma's Live Biotherapeutic oncology pipeline across a range of cancer settings, and a research collaboration and option to license agreement with MSD to discover and develop vaccines derived from our proprietary gut microbiome-derived commensal bacteria selected from our culture collection for use in up to three indications, combining our MicroRx platform with MSD's world-leading expertise in vaccine development. In 2020 we became an industry partner of the Parkinson's Progression Markers Initiative (PPMI), a longitudinal study sponsored by The Michael J. Fox Foundation for Parkinson's Research to better understand Parkinson's disease and accelerate the development of new treatments. In the year ended 31 December 2021 we initiated two collaborations. In February 2021 we announced a clinical trial collaboration and supply agreement with Merck KGaA, Darmstadt, Germany and Pfizer Inc. for Bavencio (avelumab), under which we are initiating a clinical trial to evaluate Bavencio in combination with MRx0518 as a first-line maintenance therapy for patients with locally advanced or metastatic urothelial carcinoma that has not progressed with first-line platinum-containing chemotherapy. In April 2021 we announced a collaboration with Parkinson's UK, a non-profit organization focused on advancing the understanding of Parkinson's disease and improving treatments, to establish a Patient Advisory Board (PAB) comprised of people living with Parkinson's. Supported by Parkinson's UK, the PAB provides valuable patient-centric perspective to 4D Pharma as we continue to advance novel Live Biotherapeutics into the clinic to treat neurodegenerative conditions such as Parkinson's, as well as raising awareness of the issues people with Parkinson's face with current treatment options.

4. Intellectual property portfolio – Intellectual property is essential to our strategy and capturing the value of our world-leading research output. We have continued to invest significantly in expanding our intellectual property rights, and by December 31, 2021, had initiated 69 patent families including over 1,000 granted patents providing coverage for our pipeline and clinical-stage candidates, manufacturing innovations and novel diagnostic approaches across major global markets. This is a 3.0% increase over the 67 patent families initiated as of the year ended December 31, 2020

5. Cash and equivalents – We continue to invest capital from our shareholders and partners into supporting research and clinical development programs, to generate the critical data to advance this novel modality. See "Liquidity and Capital Resources" section below for additional information.

6. Research and development spend – Investment in research and development ("**R&D**") is central to our progress and returning long-term value. For the year ended December 31, 2021, our R&D spend was $21.6 million compared to $23.4 million for the year ended December 31, 2020. While maintaining our strategy to invest in our clinical development programs on a long-term basis, the decrease reflects both the periodic nature of expenditure on clinical trials and the effects which COVID-19 has had on both patient recruitment and managements resulting actions to reduce costs.

Critical Accounting Policies

We describe our significant accounting policies more fully in Note 2 to our consolidated financial statements included elsewhere in this 20-F. We believe that the accounting policies described below and in Note 2 are critical in order to fully understand and evaluate our financial condition and results of operations.

We prepare our financial statements in accordance with U.S. GAAP. At the time of the preparation of the consolidated financial statements. Management is required to use estimates, evaluations, and assumptions which affect the application of the accounting policy and the amounts reported for assets, obligations, income, and expenses. Any estimates and assumptions are continually reviewed. The changes to the accounting estimates are credited during the period in which the change to the estimate is made.

Revenue Recognition

For the year ended December 31, 2021, 2020 and 2019, we recognized revenue from our research collaboration and option agreement. The balance of the upfront payment has been deferred. Our research collaboration and option agreement with MSD is for the development of novel vaccines (the "**MSD Collaboration Agreement**"). The MSD Collaboration Agreement is within the scope of ASC 606, "*Revenue from Contract with Customer"* ("**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 receive 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, management 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 in the context of the contract; (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) we satisfy each performance obligation. We only apply the five-step model to contracts when it is probable that the entity will collect consideration it is 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, management 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 to or dependent on other goods or services in the contract.

We measure the transaction price based on the amount of consideration to which it expects to be entitled in exchange for transferring the promised goods and/or services to the customer. We utilize the "most likely amount" method to estimate the amount of variable consideration, to predict the amount of consideration to which it will be entitled for its one open contract. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved. At the inception of each arrangement that includes development and regulatory milestone payments, management evaluates whether the associated event is considered probable of achievement and estimates the amount to be included in the transaction price using the most likely amount method. Currently, we have one contract with an option to acquire exclusive licenses for identified targets for development product candidates which it evaluated and determined that it was not a material right related to the MSD Agreement.

We allocate the transaction price based on the estimated stand-alone selling price of each of the performance obligations. We must develop assumptions that require judgment to determine the stand-alone selling price for each performance obligation identified in a contract with a customer. We utilize key assumptions to determine the stand-alone selling price for service obligations, which may include other comparable transactions, pricing considered in negotiating the transaction and the estimated costs. Additionally, in determining the standalone selling price for material rights, we may reference comparable transactions, clinical trial success probabilities, and develop estimates of option exercise likelihood. Any variable consideration is allocated specifically to one or more performance obligations in a contract when the terms of the variable consideration relate to the satisfaction of the performance obligation and the resulting amounts allocated are consistent with the amount we would expect to receive for the satisfaction of each performance obligation.

The consideration allocated to each performance obligation is recognized as revenue when control is transferred for the related goods or services. 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. Management evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Development and regulatory milestone payments are assessed under the most likely amount method and constrained if it is probable that a significant revenue reversal would occur. Milestone payments that are not within our control or the licensee's control, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. At the end of each reporting period, management re-evaluates the probability of achievement of such development milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect license revenues in the period of adjustment.

For revenue related to sales-based royalties received from licensees, including milestone payments based on the level of sales, where the license is deemed to be the predominant item to which the royalties relate, we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, we have not recognized any consideration related to sales-based royalty revenue resulting from our MSD Collaboration Agreement.

To the extent we receive payments, including non-refundable payments, in excess of the recognized revenue, such excess is recorded as deferred revenue until we perform our obligations under these arrangements. Amounts are recorded as accounts receivable when our right to consideration is unconditional.

Functional and Reporting Currency

Our functional currency, and that of our subsidiaries (other than the non-UK subsidiaries mentioned below), is the GBP. The operations of two foreign subsidiaries are conducted in EUR and one is in USD. Balances denominated in, or linked to, foreign currencies are stated on the basis of the exchange rates prevailing at the balance sheet date. For foreign currency transactions included in the statement of operations and comprehensive loss, the exchange rates applicable to the relevant transaction dates are used. Transaction gains or losses arising from changes in the exchange rates used in the remeasurement of such balances are carried to financing income or expenses. Assets and liabilities of the two EUR subsidiaries and that of our USD subsidiary are translated from their functional currency to GBP at the balance sheet date exchange rates. Income and expense items are translated at the average rates of exchange prevailing during the year. Translation adjustments are reflected in the consolidated balance sheets as a component of accumulated other comprehensive income or loss.

Our group reporting currency is the USD and these consolidated financial statements are presented in USD. Dollar amounts included herein are in thousands, except per share data. Stockholders' equity is translated into USD from GBP at historical exchange rates. Assets and liabilities are translated at the exchange rates as of the balance sheet date. Income and expenses are translated at the average exchange rates prevailing during the reporting period. Adjustments resulting from translating the financial statements into USD are recorded as a separate component of Accumulated Other Comprehensive Loss in stockholders' equity.

Goodwill and Indefinite Assets

Goodwill represents the excess of the purchase price over the fair value of identifiable net assets off an acquired business. Our acquired research and development is an indefinite lived asset. These assets are accounted for under FASB ASC Topic 350, "Goodwill and Other Intangibles", under which these assets are not amortized but instead are reviewed annually, or more frequently as a result of an event or change in circumstances, for possible impairment with impaired assets written down to fair value. Management's judgments regarding the existence of impairment indicators, on an interim or annual basis, are based on various factors, including market conditions and operational performance of our business. As of December 31, 2021, 2020 and 2019, we had $13.0 million, $13.5 million and $12.7 million of goodwill accounting for 22%, 27% and 31% of our total assets, respectively, and $6.1 million, $6.3 million and $5.9 million of research and development intellectual property, respectively. We test our goodwill and indefinite lived assets for impairment at least annually. This test is conducted in December of each year in connection with the annual budgeting and forecast process. Also, on a quarterly basis, we evaluate whether events or changes in circumstances have occurred that would negatively impact the realizable value of our intangibles or goodwill.

We completed our annual goodwill and indefinite lives assets impairment analysis as of December 31, 2021, for our singular reporting unit. Our assessment concluded that there was no impairment of goodwill. Our analysis employed the use of both a market and income approach, with each method given equal weighting. Significant assumptions used in the income approach include growth and discount rates, profit margins and our weighted average cost of capital. We used historical performance and management estimates (based on comparable product market data) to assess the future performance and determine profit margins and growth rates. Our weighted average cost of capital was based on market data for similar stage companies. The fair value was evaluated as being in excess of the goodwill carrying value. Considerable management judgment is necessary to evaluate the impact of operating changes and to estimate future cash flows. Changes in our actual results and/or estimates or any of our other assumptions used in our analysis could result in a different conclusion.

Research and Development Expenses

We have entered into various research and development-related contracts with research institutions, CROs, contract manufacturers and other companies. These agreements are generally cancellable, and related payments are recorded as research and development expenses as incurred. Costs of certain development activities, such as manufacturing, pre-clinical and clinical trial expenses, are recognized based on an evaluation of the progress to completion of specific tasks. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the consolidated financial statements as prepaid or accrued research and development costs. Non-refundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed. Costs incurred in obtaining technology licenses are charged to research and development expense as acquired in-process research and development if the technology licensed has not reached technological feasibility and has no alternative future use.

Share-based Compensation

Equity settled share-based payment transactions are measured with reference to the fair value of equity awards at the date of grant, and are recognized on a straight-line basis over the vesting period, based on our estimate of shares that will eventually vest. Fair value is measured using a suitable option pricing model, which takes into account any market conditions.

At each reporting date before vesting, the cumulative expense is calculated, representing both the extent to which the vesting period has expired and management’s best estimate of the achievement or otherwise of non-market conditions. This calculation determines the number of equity instruments that will ultimately vest with the movement in cumulative expense since the previous reporting date recognized in the Consolidated Statements of Operations and Other Comprehensive Loss, with a corresponding entry in equity.

When share-based payments have lapsed due to a failure to meet performance criteria, no expense is recognized and any previously recognized expense is reversed when the lapse occurs. Where share-based payments fail to vest as a result of market-based vesting criteria, the fair value of the award is expensed and included in the Consolidated Statements of Operations and Comprehensive Loss as an expense until the fair value is recognized in full.

Income Taxation

We account for income taxes under an asset and liability approach for financial accounting and reporting for income taxes. Accordingly, we recognize deferred tax assets and liabilities for the expected impact of differences between the financial statements and the tax basis of assets and liabilities.

We account for uncertainties in income tax law under a comprehensive model for the financial statement recognition, measurement, presentation and disclosure of uncertain tax positions taken or expected to be taken in income tax returns as prescribed by GAAP. The tax effects of a position are recognized only if it is "more-likely-than-not" to be sustained by the taxing authority as of the reporting date. If the tax position is not considered "more-likely-than-not" to be sustained, then no benefits of the position are recognized.

We record a valuation allowance to reduce its deferred tax assets to the amount that is more likely than not to be realized. In the event we were to determine that we would be able to realize our deferred tax assets in the future in excess of the recorded amount, an adjustment to the deferred tax assets would be credited to operations in the period such determination was made. Likewise, should we determine that we would not be able to realize all or part of our deferred tax assets in the future, an adjustment to the deferred tax assets would be charged to operations in the period such determination was made. As of December 31, 2021, we had a valuation allowance of $27.0 million.

Significant Contracts and Agreements Related to Research and Development Activities

Collaboration Agreements

MSD Collaboration Agreement

In October 2019, the Company entered into the MSD Collaboration Agreement. The MSD Collaboration Agreement is for the use of the Company's MicroRx discovery platform to discover and develop LBP candidates as vaccines in up to three indications. The Company is responsible for the discovery and engineering of the LBPs.

Under the MSD Collaboration Agreement, the Company received a non-refundable, upfront payment, of $2.5 million, a $5.0 million equity investment, and are eligible to receive up to $347.5 million per indication in option exercise fees and in development, regulatory and sales milestone payments, ranging from low seven figures to high eight figures, plus royalties on sales of any licensed product deriving from the collaboration. Such royalty rates range from low- to high-single digit royalties. The achievement and timing of the milestones depend on the success of development, approval and sales progress, if any, of vaccines in the future.

For the years ended December 31, 2021, 2020 and 2019 we recognized $0.7 million, $0.7 million and $0.3 million in collaboration revenues, respectively. Associated costs of sale of $1.5 million, $1.3 million and $0.2 million, respectively, are included within research and development costs in the consolidated statements of operations and comprehensive loss. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as a current portion of deferred revenue in the balance sheets in our financial statements included elsewhere in this prospectus. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion. As of December 31, 2021, we have current deferred revenues of $0.9 million and long-term deferred revenues of Nil million, which will be recognized as the research and development costs and labor effort are incurred. Company related activities expected to complete by the end of 2022.

MD Anderson Collaboration Agreement

In November 2017, we entered into a strategic collaboration agreement with MD Anderson, which was amended on February 24, 2021. This partnership brings together MD Anderson's translational medicine and clinical research capabilities with our expertise in the discovery and development of LBPs in oncology. Under the agreement, we provide funding and in-kind support for pre-clinical and clinical studies in solid tumors and radiation oncology. All data, results, and inventions generated in the conduct of the studies under the agreement are owned by us, and we have the sole right to prepare, file, prosecute and enforce patents covering the same. We granted to MD Anderson a royalty-free non-exclusive license to use such data, results and inventions for MD Anderson's internal research, academic and patient care purposes. To date, we have initiated two studies as part of the collaboration: a Phase I/II study of MRx0518 in combination with Keytruda in solid tumors, and a Phase I study of MRx0518 in combination with hypofractionated radiotherapy in patients with potentially resectable pancreatic cancer. Pursuant to the agreement, we agreed to pay MD Anderson at least$10 million for the performance of the studies and have paid $5 million to date. The agreement expires eight years from the effective date, unless earlier terminated due to a party materially breaching the agreement and failing to cure such breach within 30 days of receiving notice from the non-breaching party.

For the years ended December 31, 2021, 2020 and 2019, we have recognized $1.1 million, $1.7 million and $1.7 million, respectively, in costs from MD Anderson which are included within research and development costs in the consolidated statement of operations and comprehensive loss.

Results of Operations

Revenues

We have not generated commercial revenues from product sales. To date, we have generated revenues from the collaboration agreement with MSD Collaboration Agreement.

Operating Expenses

We recognize operating expenses as they are incurred in two general categories, general and administrative expenses and research and development expenses. Our operating expenses also include non-cash components related to depreciation and amortization of property and equipment, intangibles, and stock-based compensation, which are allocated, as appropriate to general and administrative expenses and research and development expenses.

General and administrative expenses consist of salaries and related expenses for executive, legal, finance and administrative personnel, as well as professional fees, insurance costs, and other general corporate expenses. Management expects general and administrative expenses to increase in future periods as we add personnel and incur additional expenses related to an expansion of our research and development activities and our operation as a public company listed on two markets, including higher legal, accounting, insurance, compliance, compensation and other expenses.

Patent spend has increased slightly since 2020, increasing by $0.5 million, as we continued to add to our significant patent portfolio whilst also reducing the incremental costs to do so.

Staff costs remained relatively consistent in 2021 and 2020. The remaining effects of the staff the cost cutting exercise implemented by management during the COVID-19 pandemic reduced average staff numbers and overall payroll costs by $0.3 million though this was offset by additional costs associated with the share options scheme implemented in the year and currency fluctuations resulting in a reported overall increase in $0.2 million.

Our research and development expenses consist primarily of salaries and related personnel expenses, contractual commitments, depreciation, amortization, and other expenses. We charge research and development expenses to operations as they are incurred. Costs are not directly tied to a specific product candidate until such product candidate reaches the clinical trial stage. Product candidates often have more than one associated clinical trial related to different therapeutic areas or clinical indications. Once a product candidate enters a clinical trial, we track costs of such clinical trial but do not track other costs associated with specific clinical indications which are pooled.

The following table discloses the breakdown of research and development expenses:

(in thousands)	For the Year Ended December 31, 2021	2020	2019
Contractual commitments	$ 7,918	$ 12,080	$ 16,190
Staff costs	6,034	5,823	6,414
Depreciation and amortization	1,023	1,278	1,171
Other MRx research costs	3,856	3,032	1,572
Other MDx research costs	-	79	658
Other manufacturing research and development costs	2,801	1,092	3,187
Total	$ 21,632	$ 23,384	$ 29,192

Over the last year we have continued to lead the development of Live Biotherapeutics, further expanding our clinical development activities: generating clinical data in multiple indications while launching new trials. Meanwhile, we continued to progress promising new LBP candidates in exciting new areas like Parkinson's disease. While we continue to rapidly progress our proprietary development candidates into and through the clinic, we are also leveraging the MicroRx platform to generate value through partnerships, such as our research collaboration with MSD in the vaccines space which serves as an example of the potential of the platform and provides a valuable endorsement from an industry leading partner.

In 2021 we continued to make good progress across our clinical-stage pipeline, with new clinical readouts as well as clinical biomarker data to further develop our understanding of the mechanisms of action of our Live Biotherapeutics.

After successfully completing Part A of the ongoing Phase I/II study of MRx0518 with Keytruda in patients with RCC or NSCLC refractory to prior ICI therapy, in February we announced the first signals of anti-tumor activity for the combination in bladder cancer in Part B. In addition, we presented biomarker data from this study at ESMO 2021 which identified tumor biomarkers at baseline which were associated with clinical benefit in patients treated with the combination of MRx0518 and Keytruda compared to patients who experienced progressive disease. At ESMO we also presented further data from another study of MRx0518, as a neoadjuvant monotherapy for solid tumors, showing that MRx0518 treatment for just two to four weeks was associated with significant gene and metagene signature changes in solid tumors associated with increases in anti-tumor immune activity. Furthermore, in February 2021 the Company announced a second clinical trial collaboration involving MRx0518, this with Merck KGaA, Darmstadt, Germany and Pfizer Inc. for Bavencio (avelumab), the first and only immunotherapy approved as a first-line maintenance treatment for patients with locally advanced or metastatic urothelial carcinoma. Under the collaboration, 4D Pharma is conducting a clinical trial to evaluate Bavencio in combination with MRx0518 as a first-line maintenance therapy for patients with locally advanced or metastatic urothelial carcinoma that has not progressed with first-line platinum-containing chemotherapy. This study is expected to commence in 2022.

Beyond oncology, in December 2021 we announced positive topline results from Part A of the clinical trial. Part A met the primary endpoint, the safety and tolerability profile of MRx-4DP0004 was comparable to placebo and no serious adverse events (SAEs) related to treatment were reported. In addition, MRx-4DP0004 generated encouraging signals of clinical activity in a number of key secondary endpoints of efficacy, which support progression into Part B of the study.

Following positive topline results for the Blautix Phase II trial in IBS-C and IBS-D first announced in late 2020, in May 2021 we presented additional positive data from the Phase II study at Digestive Disease Week (DDW). Further analysis of the clinical data revealed particularly strong efficacy in the key symptom of bowel habit, a potential approvable primary endpoint per FDA guidelines, which was statistically significant in IBS-D (Blautix 62.0% vs placebo 47.4%, p=0.042), and nearing significance in IBS-C (Blautix 53.8% vs placebo 39.3%, p=0.054). Post-hoc analysis of the data by geographical region shows that earlier topline results were impacted by an unusually high placebo response in patients in the UK and Ireland, and enhanced positive signals were seen in the larger US population. In addition, in December 2021, we presented new fecal microbiome analyses from the Phase II trial at Gastro 2021. Treatment with Blautix led to structural changes in the gut microbiota of patients with both IBS-C or IBS-D. These changes did not occur in placebo treatment groups.

The completion of the Blautix trial in the early part of 2020 resulted in reduced comparable costs in 2021. These were partly offset by the uptick in patient recruitment as the effects of COVID-19 started to ease in 2021, helping to accelerate commitments on the Asthma (MRx-4DP004) and Cancer (MRx-0518) reducing overall contractual commitments from $12.1 million in 2020 to $7.9 million in 2021, a decrease of $4.2 million. The easing of COVID-19 related restrictions during 2021, which had resulted in management scaling back costs and operation in 2020, allowed an element of operational normalization during 2021, albeit at a reduced starting cost base in some areas. Staff costs in 2021 remained lower than the previous year by $0.2 million (on a normalized basis) due to reduced average staffing levels established the previous year though reported costs actually increased by $0.2 overall as a result of currency value fluctuations from $5.8 million in 2020 to $6.0 million in 2021. A lack of further investment in new assets reduced depreciation and amortization by $0.3 million. Investment in our MRx platform increased as we manufactured product for the Asthma trial in 2021 but offset costs against annual supplier cost negotiated during COVID reduced our trial costs for MRx-0518, generating an overall increase from $3.0 million in 2020 to $3.9 million in 2021, an increase in costs of $0.9 million. Manufacturing, research and development costs increased by $1.7 million between 2020 and 2021 as we invested in developing the manufacturing process for our Parkinson's drugs MRx0005 and MRx0029.

Results of Operations

The following table sets forth selected consolidated statements of operations data for each of the periods indicated:

	For the Year Ended December 31,		
	2021	**2020**	**2019**
Revenues	$ 718	$ 690	$ 269
Operating expenses:			
Research and development	21,632	23,384	29,193
General and administrative expenses	15,888	13,015	10,380
Foreign currency losses (gains)	459	(699)	957
Total operating expenses	37,979	35,700	40,530
Operating loss	(37,261)	(35,010)	(40,261)
Other income (expense), net			
Interest income	1	6	78
Interest expense	(581)		
Other income	4,847	4,496	6,883
Loss on issuance of securities in recapitalization transaction	(17,744)		
Change in fair value of derivative liabilities	18,778		
Change in fair value of contingent consideration payable	-	-	2,967
Total other income, net	5,301	4,502	9,928
Net loss before income tax benefit —	(31,960)	(30,508)	(30,333)
Income tax benefit	22	13	-
Net loss	$ (31,938)	$ (30,495)	$ (30,333)

Comparison of the Year Ended December 31, 2021 to the Year Ended December 31, 2020

Revenues

We have not generated commercial revenues from product sales. To date, we have generated revenues from the collaboration agreement with MSD Collaboration Agreement. Our revenues from our MSD Collaboration Agreement totaled $0.7 million for each of the years ended December 31, 2021 and 2020. There were no other revenues for the years ended December 31, 2021 and 2020.

Research and Development Expenses

Our research and development expenses were $21.6 million for the year ended December 31, 2021, representing a decrease of $1.8 million, or 8%, compared to $23.4 million for the year ended December 31, 2020. The easing of COVID-19 restrictions in 2021 allowed more testing centers to open which led to the completion of part A of the Asthma trial in 2021. This resulted in an increase in costs of $3.9 million to $5.8 million to December 31, 2021 as compared to costs of $1.9 million to setup the trial in the year to December 31, 2020. While there were supplier savings of $0.2 million overall on MRx-0518 in 2021, the majority of the decrease in research and development expense was related to the completion of the Blautix Ph II clinical trial in 2020. This resulted in a $6.2 million decrease as compared to costs of $7.7 million in 2020. The remaining balance of $0.7 million of increased costs arose over the equivalent expenditure in 2020 through a mixture of foreign currency fluctuations, net additional costs across staff, contractual commitments and manufacturing, research and development costs

General and Administrative Expenses

Our general and administrative expenses were $15.9 million for the year ended December 31, 2021, representing an increase of $2.9 million, or 22%, compared to $13.0 million for the year ended December 31, 2020. The single largest component of the change being attributable increased insurance costs which increased from $0.1 million to $1.8 million, an increase of $1.7 million This increase is due to the addition of Director's and Officer's Liability Insurance as result of the company being listed on the NASDAQ Exchange. While payroll costs went down overall, total staff remuneration costs increased by $0.3 million in recognition of the costs associated with the employee share option plan. An additional $0.2 million was incurred in 2021 as compared to 2020 due to an increase in expenses related to corporate communications and investor relations. Other administrative expenses and foreign currency fluctuations accounted for the remaining increase of $0.6 million.

Foreign currency losses (gains)

For foreign currency transactions included in the statement of operations and comprehensive loss, the exchange rates applicable to the relevant transaction dates are used. Transaction gains or losses arising from changes in the exchange rates used in the translation of such balances are carried to financing income or expenses. We recognized foreign currency loss of $0.5 million for the year ended December 31, 2021, compared to foreign currency gains of $0.7 million for the year ended December 31, 2020. The foreign currency losses and gains are due to the change in the exchange rates.

Operating Loss

As a result of the foregoing, our operating loss totaled $37.3 million for the year ended December 31, 2021, representing an increase of $2.3 million, or 6%, compared to $35.0 million for the year ended December 31, 2020.

Interest Income

Interest income consists of interest earned on our short-term investments. We recognized $1 thousand of interest income for the year ended December 31, 2021, representing a decrease of $5 thousand, or 83%, compared to $6 thousand for the year ended December 31, 2020. The decrease was primarily attributable to the reduction in short-term investments during the year ended December 31, 2020.

Interest Expense

Interest Expense consists of loan interest paid on the credit facility with Oxford Finance S.A.R.L. Interest expense was $0.6 million for the year ended December 31, 2021. There was no corresponding interest expense for the year ended December 31, 2020. This increase is due to the interest paid on the first tranche of $12.5 million loan drawn in July 2021.

Other Income

Other income consists of UK, Irish and Spanish tax credit refunds based on a portion of our research and development expenses. This refund is treated as a governmental grant. Other income was $4.9 million for the year ended December 31, 2021, representing an increase of $0.4 million, or 8%, compared to $4.5 million for the year ended December 31, 2020. The increase was due to the increase in grant-based research and development expenses over the prior year.

Loss on Issuance of securities in Recapitalization Transaction

As part of the recapitalization transaction on March 22, 2021, we issued common stock, warrants and representative units and after allocating the proceeds received to the full fair value of warrants that were determined to be liabilities, the remaining proceeds were less than the total transaction costs, which included the full fair value of backstop warrants issued as part of the transaction costs. The excess transaction costs were recorded as a loss of $17.7 million on the statement of operations and comprehensive loss for the year ended December 31, 2021.

Change in Fair Value of Derivative Liabilities

In accordance with FASB ASC 470, "*Debt – Debt with Conversion and Other Options"* ("ASC Topic 470") and FASB ASC 820, *Fair Value Measurements and Disclosures* ("ASC Topic 820"), we measured the fair value of our warrants and representative units that were recorded at their fair value and recognized as liabilities as of December 31. 2021, and recorded $18.8 million in other income for the year ended December 31. 2021.

Net Loss

As a result of the foregoing, our net loss was $32.0 million for the year ended December 31, 2021, representing an increase of $1.5 million, or 5%, compared to $30.5 million for the year ended December 31, 2020.

Comparison of the Year Ended December 31, 2020 to the Year Ended December 31, 2019

Revenues

We have not generated commercial revenues from product sales. To date, we have generated revenues from the collaboration agreement with MSD Collaboration Agreement. Our revenues from our MSD Collaboration Agreement totaled $0.7 million and $0.3 million for the years ended December 31, 2020 and 2019, respectively. There were no other revenues for the years ended December 31, 2020 and 2019.

Research and Development Expenses

Our research and development expenses totaled $23.4 million for the year ended December 31, 2020, representing a decrease of $5.8 million, or 19.9%, compared to $29.2 million for the year ended December 31, 2019. Although costs for the running of our cancer trials increased by $1.2 million the completion of the Blautix Ph II clinical trial in the first half of the year meant that there were no significant second half costs when compared to 2019, this created an overall reduction in costs when compared to the full year for 2019 equating to $2.5 million. Furthermore, the cumulative effect of COVID-19, which both slowed recruitment for our Asthma trails and triggered a number of costs reduction exercises to extend the cash runway, resulted in an overall decrease in costs in other areas of $3.3 million when compared to 2019.

General and Administrative Expenses

Our general and administrative expenses totaled $13.0 million for the year ended December 31, 2020, representing an increase of $2.6 million, or 25.0%, compared to $10.4 million for the year ended December 31, 2019. The increase was related to the exploration of funding options, Nasdaq readiness, restructuring costs and increased patent costs, which were offset, in part, by reductions on staff costs and travel expenses as a result of COVID-19. General and administrative expenses are mainly attributed to staff costs, contractual commitments, legal and professional expenses patent costs, depreciation and amortization.

Foreign currency losses (gains)

For foreign currency transactions included in the statement of operations and comprehensive loss, the exchange rates applicable to the relevant transaction dates are used. Transaction gains or losses arising from changes in the exchange rates used in the translation of such balances are carried to financing income or expenses. We recognized foreign currency gains of $0.7 million for the year ended December 31, 2020, compared to foreign currency losses of $1.0 million for the year ended December 31, 2019. The change is due to the changes in the exchange rates.

Operating Loss

As a result of the foregoing, our operating loss totaled $35.0 million for the year ended December 31, 2020, representing a decrease of $5.3 million, or 13.2%, compared to $40.3 million for the year ended December 31, 2019.

Interest Income

Interest income consists of interest earned on our short-term investments. We recognized interest income of $6 thousand for the year ended December 31, 2020, representing a decrease of $72 thousand, or 92.3%, compared to $78 thousand for the year ended December 31, 2019. The decrease was primarily attributable to the reduction in short-term investments during the year ended December 31, 2019.

Other Income

Other income consists of UK and Irish tax credit refunds based on a portion of our research and development expenses. This refund is treated as a governmental grant. Other income was $4.5 million for the year ended December 31, 2020, representing a decrease of $2.4 million, or 34.7%, compared to $6.9 million for the year ended December 31, 2019. The decrease was due to the decrease in research and development expenses over the prior year.

Change in Fair Value of Contingent Consideration Payable

The change in fair value of contingent consideration payable relates to payment milestones for the MDx platform achievable on the recruitment of a certain number of patients and on regulatory approval of a medical device following the recruitment. There was no change in the fair value of the contingent consideration payable at December 31, 2020 as the milestones had failed or the probability of failure was effectively established based on progress relative to the time-based recognition endpoints. Based on the failure of completing these milestones within the required timeframes, we reduced the fair value of the contingent consideration payable to $0 at December 31, 2019, which triggered a change in the fair value of contingent consideration income of $3.0 million for the year ended December 31, 2019.

Net Loss

As a result of the foregoing, our net loss was $30.5 million for the year ended December 31, 2020, representing an increase of $0.2 million, or 0.1%, compared to $30.3 million for the year ended December 31, 2019.

B. Liquidity and Capital Resources

Overview

Since our inception through December 31, 2020, we have funded our operations principally from the sales of our common shares and the MSD Collaboration Agreement. As of December 31, 2021, we had $21.0 million in cash and cash equivalents.

The table below presents our cash flows for the periods indicated:

	For the Year Ended December 31,		
(in thousands)	**2021**	**2020**	**2019**
Cash used in operating activities	$ (37,916)	$ (27,270)	$ (28,683)
Cash (used in) provided by investing activities	(279)	(230)	12,283
Cash provided by (used in) financing activities	46,418	34,467	(14)
Effect of exchange rate changes on cash and cash equivalents	760	(8)	1,000
Net increase (decrease) in cash and cash equivalents	$ 8,983	$ 6,959	$ (15,414)

Operating Activities

Net cash used in operating activities of $37.9 million during the year ended December 31, 2021, was primarily related to $14.3 million for clinical trials and research including other third-party expenses and an aggregate of $7.3 million in salary and other staff costs, a further $5.6 million is attributable to patent spend and $11.0 million attributable to general and administrative costs. These expenses were offset by the $0.2 million in research and development tax credits and foreign currency fluctuations of £0.1 million.

Net cash used in operating activities of $27.2 million during the year ended December 31, 2020, was primarily related to $18.4 million for clinical trials and research including other third-party expenses and an aggregate of $8.4 million in salary and other staff costs, a further $5.4 million is attributable to patent spend. These expenses were offset by the $6.9 million in research and development tax credits.

Net cash used in operating activities of $28.7 million during the year ended December 31, 2019, was primarily related to $22.0 million for clinical trials and research including other third-party expenses and an aggregate of $9.0 million in salary and other staff costs, a further $5.0 million is attributable to patent spend. These expenses were offset by the receipt of the $2.5 million upfront payment related to the MSD Collaboration Agreement and $6.0 million in research and development tax credits.

Investing Activities

Net cash used in investing activities of $0.3 million and $0.2 million during the years ended December 31, 2021 and 2020, respectively, was due to the purchases of property and equipment and software. Net cash provided by investing activities of $12.3 million during the year ended December 31, 2019, was due to the maturities of short-term investments of $13.0 million, offset, in part, by purchases of property and equipment and software of $0.8 million.

Financing Activities

Net cash provided by financing activities of $48.9 million during the year ended December 31, 2021 was primarily related to the issuance of ordinary shares of $24.8 million, $11.5 million from the recapitalization transaction and $12.5 million from the issuance of debt. Net cash provided by financing activities of $34.5 million during the year ended December 31, 2020 was primarily related to the issuance of ordinary shares, which may be represented by ADSs, of $32.9 million, issuance of warrants of $3.4 million and warrant exercises of $0.1 million, offset in part by $1.9 million of deferred merger costs. Net cash used in financing activities in the year ended December 31, 2019 consisted of $14 thousand in lease payments.

On March 22, 2021 the Company completed its recapitalization with Longevity and received $11.5 million ($7.7 million net of transaction costs) through the issuance of 31 million ordinary shares, which may be represented by ADSs, at £1.10 ($1.51) per share. Additionally, the Company also issued 4.3 million warrants to purchase 16.3 million shares of ordinary shares, which may be represented by ADSs, at £1.10 ($1.51) per ordinary share and assumed 240,000 units to purchase the Company's ordinary shares, which may be represented by ADSs, and warrants.

On March 22, 2021, concurrently with the merger with Longevity, the Company raised $25.0 million ($23.0 million net of transaction costs) through the issuance of 16.4 million ordinary shares, which may be represented by ADSs, at a share price of £1.10 ($1.51) per share.

On April 16, 2021, the directors who were unable to participate in the March 2021 financing, purchased 1.3 million shares of ordinary shares, which may be represented by ADSs, at the same terms as the March 2021 financing, for a total of approximately £1.4 million ($2.0 million).

Current Outlook

We have historically financed our operations primarily through the sale of ordinary shares. We intend to continue to raise additional capital through sales of ordinary shares and ADSs, but there can be no assurance that these funds will be available or that they are readily available at terms acceptable to us or in an amount sufficient to enable us to continue its development and commercialization of its products or sustain operations in the future.

We have incurred losses and generated negative cash flows from operations since inception. To date we have not generated significant revenue, and we do not expect to generate significant revenues from the sale of our product candidates in the near future. In order to capture the potential of the platform and maximize value creation, we are actively pursuing additional research collaborations, pairing our expertise in LBP discovery and development and access to our library of well characterized bacterial isolates with the disease-specific expertise of partners. The amounts that we actually spend for any specific purpose may vary significantly and will depend on a number of factors, including, but not limited to, our research and development activities and programs, clinical testing, regulatory approval, market conditions, and changes in or revisions to our business strategy and technology development plans. Investors will be relying on the judgment of our management regarding the application of the proceeds from the sale of our ordinary shares.

In July 2021, we entered into an agreement with Oxford Finance Luxembourg S.À.R.L. providing for a term loan facility maturing on July 1, 2026 in an aggregate principal amount of up to $30.0 million. $12.5 million of such term loan was available and borrowed on the closing date. $7.5 million of such term loan is available upon the achievement of certain milestones. The remaining $10 million of such term loan is uncommitted and available at the discretion of the Lenders and each drawdown attracts a 2% charge, to be issued in warrants, and attracts interest on the balance. The proceeds of the term loans may be used for general corporate purposes.

The Loan also the includes restrictive covenants that limit the Group's ability to undertake certain functions that may affect recoverability and include a clause that require the Group to always maintain a cash balance of $7.5 million if it does not generate at least $45 million of capital through the issue of shares and partnering arrangements before April 1, 2022. These transactions are not included in the financial statements as they did not include a constructive obligation on December 31, 2021.

The restrictive covenants may have a significant effect on our current and future business by limiting the availability of cash provided by the loan, or by limiting our ability to perform certain transactions. It is not unreasonable that this could have a short- or longer-term effect on our financial condition, changes in financial condition, expenses, results of operations, liquidity, capital expenditures or capital resources in a manner that is material to investors.

As of December 31, 2021, our cash and cash equivalents were $21.0 million. We expect that our existing cash and cash equivalents, will be sufficient to fund our operations into the fourth quarter of 2022. For further information, see the notes to our consolidated financial statements included elsewhere in this Annual Report.

We currently anticipate that we will require approximately $27.6 million for research and development activities over the course of the next 18 months based on the execution of existing programs but also dependent on exchange rates. We also anticipate that we will require approximately $18.3 million for general and administrative costs over such 18-month period, which consists primarily of expenditures for staff costs, legal professional and insurance fees, patent costs and other administrative expenses. We also estimate receiving approximately $9.7 million in cash for research and development tax credit refunds over this 18-month period. We anticipate making $2.3 million of payments towards loans and interest during this period.

In addition, our operating plans may change as a result of many factors that may currently be unknown to us, and we may need to seek additional funds sooner than planned. Our future capital requirements will depend on many factors, including:

- the length of the COVID-19 pandemic and its impact on our planned clinical trials, operations and financial condition;
- the progress and costs of our pre-clinical studies, clinical trials and other research and development activities;
- the scope, prioritization and number of our clinical trials and other research and development programs;
- any cost that we may incur under in- and out-licensing arrangements relating to our therapeutic candidates that we may enter into in the future;
- the costs and timing of obtaining regulatory approval for our therapeutic candidates;
- the costs of filing, prosecuting, enforcing and defending patent claims and other intellectual property rights;
- the costs of scaling our manufacturing capabilities for production of sufficient clinical and commercial quantities of our therapeutic candidates;
- the potential costs of contracting with third parties to provide marketing and distribution services for us or for building such capacities internally;
- the costs of acquiring or undertaking the development and commercialization efforts for additional, future therapeutic applications of our product candidates and the magnitude of our general and administrative expenses;
- the timing of payment and changes to tax regimes relate to our research and development tax credits;
- changes in the value and taxable position of our warrants and units;
- the costs of operating as a public company; and
- adverse trial results that would invalidate further investment in a product or products.

Until we can generate significant revenues, if ever, we expect to satisfy our future cash needs through our existing cash, cash equivalents and short-term deposits, the net proceeds from equity financings, or by out-licensing applications of our product candidates. We cannot be certain that additional funding will be available to us on acceptable terms, if at all. If funds are not available, we may be required to delay, reduce the scope of, or eliminate research or development plans for, or commercialization efforts with respect to, one or more applications of our product candidates.

Off-balance sheet arrangements

The only off-balance sheet arrangements pertaining to the Group were related to short term operating leases that did not meet the requirements under ASC 842 and were not included as a right-of-use asset and associated lease liability.

Principal Commitments

Leased Facilities

We have two real estate leases classified as operating leases, one on Spain and one in the UK. No additional leases were entered into during the periods.

The UK lease was for our headquarters in Leeds, England. The premises comprise office space and parking and are for a ten-year term which commenced in May 2017. A tenant lease break clause is available in May 2022 which has not been included in the lease calculations as there is no indication that this would be executed. Lease escalation costs have been included on a fixed rate basis as a practical expedient. The lease includes a provision to return the premises to their original condition on exit, as such an asset retirement obligation has been included in other liabilities of $0.2 million at December 31, 2021.

The Spanish lease relates to our manufacturing premises in Leon, Spain. The agreement is for a ten-year term which commenced in April 2016 and includes a tenant lease break clause that can be executed after providing six months' written notice at any point five years from the commencement date, again this break clause has not been included in the lease value as there is no evidence that this will be executed. Lease escalation cost have also been included on a fixed rate basis as a practical expedient. The lease includes the requirement to make certain repairs and as such an asset retirement obligation has been included in other liabilities at $37 thousand at December 31, 2021.

JOBS Act Accounting Election

Section 102(b)(1) of the JOBS Act exempts emerging growth companies from being required to comply with new or revised financial accounting standards until private companies (that is, those that have not had a Securities Act registration statement declared effective or do not have a class of securities registered under the Exchange Act) are required to comply with the new or revised financial accounting standards. The JOBS Act provides that an emerging growth company can elect to opt out of the extended transition period and comply with the requirements that apply to non-emerging growth companies but any such an election to opt out is irrevocable. We have elected to use the extended transition period to enable us to comply with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date we (i) are no longer an emerging growth company and (ii) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

We will remain an emerging growth company until the earliest to occur of: (i) the last day of the fiscal year in which we have more than $1.07 billion in annual revenue; (ii) the date we qualify as a "large accelerated filer," with at least $700.0 million of equity securities held by non-affiliates; (iii) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period; and (iv) the last day of the fiscal year following the fifth anniversary of the completion of the Merger.

This may make comparison of our financial statement with another public company that is neither an emerging growth company nor an emerging growth company that has opted out of using the extended transition period difficult or impossible because of the potential differences in accounting standards.

C. Research and Development Expenses

For a description of our research and development policies for the last three years see "Item 5. Operating and Financial Review and Prospects—A. Operating Results—Critical Accounting Policies—Research and Development Expenses." For a description of our intellectual property, see "Item 4. Information on the Company—B. Business Overview—Intellectual Property."

D. Trend Information

We are currently in the development stage and we expect to remain in that stage for the upcoming year, and therefore trends relating to production, sales, inventory, backlog and selling prices are not applicable. See "—A. Operating Results."

E. Critical Accounting Estimates

The following table sets forth certain information concerning our estimated fixed obligations and commitments to make future payments under existing contracts at December 31, 2021.

	Payments Due by Period			
Description	Total	Less Than One Year	1 – 3 Years	3 – 5 Years
Operating lease obligations	$ 1,556	$ 310	$ 985	$ 261
Supplier contracts	$ 6,820	$ 2,567	$ 4,253	$ -
Total	$ 8,376	$ 2,877	$ 5,238	$ 261

ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

A. Directors and Senior Management

Set forth below are the name, age, principal position and a biographical description of each of our directors and executive officers:

Name	Age	Position
Executive Officers		
Duncan Peyton	52	Chief Executive Officer, and Director
Dr. Alexander Stevenson	51	Director and Chief Scientific Officer
John Doyle	44	Chief Financial Officer
Non-Executive Directors		
Prof. Axel Glasmacher	61	Non-Executive Director Chairman
Dr. Edgardo (Ed) Baracchini	62	Non-Executive Director
Dr. Alexander (Sandy) Macrae	59	Non-Executive Director
Dr. Katrin Rupalla	54	Non-Executive Director
Paul Maier	74	Non-Executive Director

There are no known family relationships between any of our officers and directors. To the best knowledge of our knowledge, there are no arrangements or understandings with any major shareholders, customers, suppliers or others, pursuant to which any of our officers and directors was selected as a director or member of senior management.

Executive Officers

Duncan Peyton co-founded 4D Pharma and has served as our Chief Executive Officer and as a member of our board of directors since February 2014. Mr. Peyton also founded and serves as a director of Aquarius Equity, a life sciences investment firm, since August 2004. Mr. Peyton holds a B.Sc. in Biotechnology from the University of Sunderland and a CPE and LPC at Northumbria College of Law.

Alexander Stevenson co-founded 4D Pharma and has served as our Chief Scientific Officer and as a member of our board of directors since June 2014. Dr. Stevenson also serves as a director of Aquarius Equity, a life sciences investment firm, since May 2008. Prior to joining Aquarius Equity, Alex served as Chief Operating Officer of Modern Biosciences plc (a subsidiary of IP Group plc), from 2006 to 2008.Dr. Stevenson currently serves on the board of directors of C4X Discovery PLC. Dr. Stevenson holds a B.Sc. (Hons) in Microbiology, a Ph.D. in Microbiology, and an MBA from the University of Leeds.

John Doyle was appointed as our Chief Financial Officer in January 2022. Prior to joining us, Mr. Doyle served as Chief Financial Officer of Chiasma Inc., a biopharmaceutical company acquired by Amryt Pharma, from January 2021 to August 2021. Mr. Doyle also served as Vice President, Finance and Investor Relations and previously as Senior Director Financial Planning Analysis at Verastem Oncology, Inc. from February 2018 to December 2020. Prior to joining Verastem, Mr. Doyle also served as Head of Financial Planning and Analysis at SimpliVity, later acquired by Hewlett Packard Enterprises from May 2016 to February 2018. Before that, Mr. Doyle was Director of Business Unit Financial Planning & Analysis, Early Phase Division of Parexel International from January 2015 to April 2016. Mr. Doyle holds a B.S. in Finance from the University of Massachusetts.

Non-Executive Directors

Prof. Dr. Axel Glasmacher joined our board of directors in January 2019, and he has served as our Chairman since April 2020. Prof. Glasmacher currently serves as the Owner of AG Life Science Consulting GmbH & Co. KG since March 2018. Previously, Prof. Glasmacher served as Senior Vice President, Global Clinical Research & Development at Celgene, from April 2016 to February 2018, as Corporate Vice President, Clinical Research and Development from January 2015 to April 2016 and as Vice-President of Medical Affairs for Europe, Middle East, and Africa from April 2012 to December 2014. Prior to Celgene, Professor Glasmacher worked within the field of haematology-oncology at the University Hospital in Bonn from August 1988 to April 2006. Prof. Glasmacher currently serves on the board of Active Biotech AB, a Nasdaq listed company, Ryvu Therapeutics S.A. and Avencell Therapeutics Inc. Prof. Glasmacher holds a Medical Doctorate from the University of Bonn.

Dr. Edgardo (Ed) Baracchini joined our board of directors in January 2019. Dr. Baracchini currently serves as the Principal of Baracchini Consulting since January 2019. Prior to that, Dr. Baracchini served as Chief Business Officer of Imago BioSciences, Inc., from April 2020 to February 2021, and Chief Business Officer at Xencor Inc, from January 2010 to September 2018. Dr. Baracchini has also served as the SVP, Business Development for Metabasis Therapeutics (which was acquired by Ligand Pharmaceuticals, Inc.) from May 2002 to November 2009. Dr. Baracchini currently serves on the board of CoImmune, Inc. and INmune Bio, Inc., a Nasdaq listed company. Dr. Baracchini holds a B.S. in Microbiology from University of Notre Dame, a Ph.D. in Molecular and Cell Biology from the University of Texas at Dallas, and an MBA from the University of California, Irvine — Paul Merage School of Business.

Dr. Alexander (Sandy) Macrae joined our board of directors in August 2019. Since June 2016, Dr. Macrae serves as the President and Chief Executive Officer of Sangamo Therapeutics, Inc., a biotechnology company. Dr. Macrae previously served as Global Medical Officer at Takeda Pharmaceuticals, from 2012 to March 2016. Dr. Macrae holds a B.Sc. and Bachelor of Medicine and Bachelor of Surgery degrees from the University of Glasgow and a Ph.D. in Molecular Genomics from the King's College, Cambridge.

Dr. Katrin Rupalla joined our board of directors in August 2020. Dr. Rupalla currently serves as the Chief Executive Officer of Ymmunobio AG since December 2021. Prior to that, Dr. Rupalla served as SVP, Head Regulatory, MedDoc, R&D Quality at Lundbeck from October 2019 to December 2021, VP, Regulatory Oncology Head from April 2018 to July 2019, VP, China Head Development from November 2015 to September 2018, and VP, EU Regulatory Sciences from May 2012 to December 2015 at Bristol-Myers Squibb. Dr. Rupalla currently serves on the board of Ambrx, Inc. and Ymmunobio AG. Dr. Rupalla holds a M.Sc. in Pharmacy and a Ph.D. in CNS Pharmacology from the Philipps-University Marburg and an MBA in Project Management from Jones International University.

Paul Maier joined our board of directors in March 2021. Mr. Maier currently serves as a board member of Eton Pharmaceuticals, Inc, a life science company, since September 2017, and as a board member of International Stem Cell Corporation, a life science company, since July 2007. Previously, Mr. Maier was the Chief Financial Officer at Sequenom Inc. from November 2009 to June 2014. Mr. Maier also served as Senior Vice President and Chief Financial Officer of Ligand Pharmaceuticals from October 1992 to January 2007, and as independent financial consultant to certain life sciences companies. Mr. Maier holds an MBA from Harvard University and a BS in Business Logistics from the Pennsylvania State University.

B. Compensation

Compensation of Executive Officers

The following table sets forth the approximate remuneration paid to our executive officers for the year ended December 31, 2021.

Name	Salary ($)	Bonus ($)[1]	All Other Compensation ($)[2]	Total ($)[3]
Duncan Peyton	251	-	3	254
Alexander Stevenson	215	-	3	218
John Beck(4)	104	-	2	106
John Doyle(5)	-	-	-	-

(1) Amount shown reflects cash bonuses awarded for achievement of performance goals. See "—D. Share Ownership—Equity Compensation Arrangements."
(2) Amount shown represents health benefit payments and pension contributions made by us.
(3) Total compensation set out in this table does not include the value of options to acquire our ordinary shares or awards granted to or held by current senior management, which is described in "—Equity Compensation Arrangements."
(4) Appointed between March 2021 and July 2021.
(5) Appointed in January 2022.

Executive Officer Employment and Consultancy Agreements

Service Agreement of Duncan Peyton

Duncan Peyton is currently engaged as our Chief Executive Officer under a service agreement entered into on February 10, 2014. In 2019, 2020 and the first half of 2021, he received a base salary of £100,000 ($137,436) per annum. Effective as of July 1, 2021, his base salary was increased to £264,500 ($363,519) per annum. In addition to the base salary, he is entitled to participate in private health care scheme and a bonus scheme, which may be paid from time to time at the discretion of the Remuneration Committee.

The agreement may be terminated by either party on one year's written notice or, immediately by us, in the event of default, which includes, but is not limited to circumstances in which, Mr. Peyton is disqualified from acting as a director, convicted of a criminal offence, declared bankrupt, found guilty of fraud or conducting gross misconduct. In the event of early termination not caused by an event of default, we may exercise our discretion to make a payment in lieu of notice to Mr. Peyton. The agreement includes certain restrictive covenants, and, upon termination, Mr. Peyton is restricted from becoming involved, directly or indirectly, with any business which is similar to or competitive with us, for a period of 12 months.

Service Agreement of Alex Stevenson

Alexander Stevenson is currently engaged as our Chief Scientific Officer under a service agreement entered into on February 10, 2014 In 2019, 2020 and the first half of 2021, he received a base salary of £100,000 ($137,436) per annum. Effective as of July 1, 2021, his base salary was increased to £212,600 ($292,189)per annum. In addition to the base salary, he is entitled to participate private health care scheme and in a bonus scheme, which may be paid from time to time at the discretion of the Remuneration Committee.

The agreement may be terminated by either party on one year's written notice or, immediately by us, in the event of default, which includes, but is not limited to circumstances in which, Dr. Stevenson is disqualified from acting as a director, convicted of a criminal offence, declared bankrupt, found guilty of fraud or conducting gross misconduct. In the event of early termination not caused by an event of default, we may exercise our discretion to make a payment in lieu of notice to Dr. Stevenson. The agreement includes certain restrictive covenants, and, upon termination, Dr. Stevenson is restricted from becoming involved, directly or indirectly, with any business which is similar to or competitive with us, for a period of 12 months.

Service Agreement of John Beck

John Beck was engaged as our Chief Financial Officer under a service agreement entered into on March 1, 2021. He was entitled to a base salary of $330,000 per annum. In addition to the base salary, he was entitled to participate in a bonus scheme, which may be paid from time to time at the discretion of the Remuneration Committee. He served as our Chief Financial Officer until July 2021, when he sadly passed away.

The agreement may be terminated by either party on one year's written notice or, immediately by us, in the event of default, which includes, but is not limited to circumstances in which, Mr. Beck is disqualified from acting as a director, convicted of a criminal offence, declared bankrupt, found guilty of fraud or conducting gross misconduct. In the event of early termination not caused by an event of default, we may exercise our discretion to make a payment in lieu of notice to Mr. Beck. The agreement includes certain restrictive covenants, and, upon termination, Mr. Beck is restricted from becoming involved, directly or indirectly, with any business which is similar to or competitive with us, for a period of 12 months.

Service Agreement of John Doyle

John Doyle is currently engaged as our Chief Financial Officer under a service agreement entered into on January 3, 2022. He is entitled to a base salary of $385,000 per annum. In addition to the base salary, he is entitled to participate in a bonus scheme, which may be paid from time to time at the discretion of the Remuneration Committee.

The agreement may be terminated by either party on three month's written notice or, immediately by us, in the event of default, which includes, but is not limited to circumstances in which, Mr. Doyle is disqualified from acting as a director, convicted of a criminal offence, declared bankrupt, found guilty of fraud or conducting gross misconduct. In the event of early termination not caused by an event of default, we may exercise our discretion to make a payment in lieu of notice to Mr. Doyle. The agreement includes certain restrictive covenants, and, upon termination, Mr. Doyle is restricted from becoming involved, directly or indirectly, with any business which is similar to or competitive with us, for a period of 12 months.

Non-Employee Director Compensation

The following table sets forth the remuneration paid during 2021 to the current non-employee directors, all of which was in the form of annual fees:

Name	Base Salary ($ in thousands)
Prof. Axel Glasmacher (1)	103
Dr. Edgardo (Ed) Baracchini	69
Dr. Alexander (Sandy) Macrae (2)	74
Dr. Katrin Rupalla	69
Paul Maier(3)(4)	67

(1) Prof. Glasmacher's base salary was increased from £50,000 ($68,718) to £100,000 ($137,436), effective July 1, 2021.
(2) Dr Macrae's base salary was increased from £50,000 ($68,718) to £57,300 ($78,751), effective July 1, 2021.
(3) Mr. Maier was appointed as a member of our board of directors March 1, 2021.
(4) Mr Maier's base salary was increased from £50,000 ($68,718) to £61,000 ($83,836), effective July 1, 2021.

Non-executive Director Letters of Appointment

We have entered into letters of appointment with each of our non-executive directors which provides each director with cash compensation of £50 ($69) per annum for service on our board of directors. Effective as of July 1, 2021, the base salary of Dr Glasmacher was increased to £100 ($137), the base salary or Dr Macrae was increased to £57 ($79) and the base salary of Mr Maier was increased to £61 ($84). The appointment of our non-executive directors can be terminated by either us or the director upon three calendar months' written notice, or by us in our absolute discretion at any time with immediate effect on payment of money in lieu of notice.

Under the non-executive director appointment letters, we may also terminate each appointment with immediate effect if the non-executive director: (i) commits a material breach of his or her obligations under the letter of appointment; (ii) commits a serious or repeated breach or non-observance of his or her obligations to us; (iii) has been guilty of any fraud or dishonesty or acts in any manner which, in our opinion, brings or is likely to bring us into disrepute or is materially adverse to our interests; (iv) is incompetent or guilty of gross misconduct and/or any serious or persistent negligence or misconduct in respect of his or her obligations under the letter of appointment; (v) is convicted of an arrestable criminal offence other than a road traffic offence for which a fine or non-custodial penalty is imposed; (vi) is declared bankrupt or makes an arrangement with or for the benefit of his creditors, or suffers comparable proceedings in another jurisdiction; (vii) is disqualified from acting as a director in any jurisdiction; (viii) accepts a position with another company, without our prior agreement, which in the reasonable opinion of our board of directors may give rise to a conflict of interest between his position as a director of our company and his interest in such other company; or (ix) commits any offence under the U.K. Bribery Act 2010.

Equity Compensation Awards to Directors and Executive Officers

The following table summarizes: (i) the outstanding number of options and awards under the equity incentive plans; and (ii) the number of shares granted to directors, executive officers, and non-executive directors, as of December 31, 2021:

Name	Ordinary Shares Outstanding (including those represented by ADS	Ordinary Shares Underlying Options	Exercise Price Per Ordinary Share($)	ADSs Underlying Options	Exercise Price Per ADS($)	Grant Date	Expiration Date
Executive Officers:							
Duncan Peyton	—	—	—	—	—	—	
Alexander Stevenson	—	—	—	—	—	—	
John Beck(1)	—	—	—	—	—	—	
John Doyle(2)	—	—	—	—	—	—	
Non-Executive Directors							
Prof. Axel Glasmacher	—	—	—	—	—	—	
Dr. Edgardo (Ed) Barachini	—	—	—	—	—	—	
Dr. Alexander (Sandy) Macrae	—	—	—	—	—	—	
Dr. Katrin Rupalla(3)	—	—	—	—	—	—	
Paul Maier(4)	—	—	—	—	—	—	

(1) Mr. Beck was appointed as Chief Financial Officer on March 1, 2021 and served until July 26, 2021.
(2) Mr. Doyle was appointed as Chief Financial Officer on January 3, 2022.
(3) Dr. Rupalla was appointed as a member of our board of directors on September 23, 2020.
(4) Mr. Maier was appointed as a member of our board of directors March 1, 2021

Equity Incentive Arrangements

We operated the 2015 Long Term Incentive Plan (the "**2015 LTIP**"), which was the primary mechanism for attracting and retaining selected key employees through the grant of stock options. In 2021, the rules of the LTIP were updated (the "**2021 LTIP**"). All of our employees are eligible to participate in the LTIP and receive stock options, under the 2021 LTIP.

The 2015 and 2021 LTIPs are administered by the remuneration committee and may be amended on a forward-looking basis in any respect at its discretion.

Stock options granted under the 2015 LTIP will ordinarily vest and become capable of exercise on (or shortly after) the third anniversary of their grant, subject to the extent to which individual performance criteria applicable to the stock options have been met by the company and/or the relevant option holder over the preceding three years.

Under the 2021 LTIP, 25% of awarded stock options will ordinarily vest and become capable of exercise on (or shortly after) the first anniversary of their grant. Thereafter the remainder of the awarded stock options will ordinarily vest and become capable of exercise monthly thereafter over a period of 36 months.

Once vested, stock options may be exercised at any point up until the tenth anniversary of their grant. Stock options may only be exercised on payment of the associated exercise price. Under the 2015 LTIP, the associated exercise price is ordinarily an amount equal to the aggregate nominal value of the stock that may be acquired on exercise. Under the 2021 LTIP, the associated exercise price is ordinarily the closing market price on the date of grant of the award.

Stock options will ordinarily lapse on cessation of the option holder's employment with us, unless the option holder falls into a prescribed category of "good leaver" (e.g. cessation due to their death, ill-health, disability, to recognize exceptional performance during their time with the company) or have otherwise been determined by the remuneration committee to be permitted to retain their stock options on a discretionary basis. Where performance conditions apply, the extent to which such stock options may be exercised shall be subject to the extent to which the applicable performance criteria are determined to have been met and (ordinarily) to a time pro-rata reduction in the number of shares that may be acquired on exercise to reflect the reduced period of time spent in employment relative to the normal three-year vesting period.

To the extent not already exercisable, stock options will become exercisable in connection with any change of control or on a winding-up. In such circumstances, stock options will become exercisable for a limited period after the occurrence of the change of control or winding-up, subject to the extent to which the applicable performance criteria are determined by the remuneration committee to have been met at that date and (ordinarily) to time pro-rating. The remuneration committee retains the right to assess the performance criteria on any modified basis it considers appropriate taking into account the curtailed vesting period.

Alternatively, the remuneration committee may (subject to having obtained consent of the acquiring company) specify that stock options will not become exercisable in connection with a change of control and will instead be exchanged for equivalent awards over shares in the acquiring company.

If any variation in our share capital (e.g. a capitalization, rights issue, consolidation, sub-division or reduction of capital) occurs, then the number of shares held under any stock options (or the exercise price) may be adjusted to ensure that the value of the stock option in the hands of the relevant option holder is not impacted by the variation in share capital.

Stock options granted under the LTIP are not subject to any ongoing clawback provisions.

Stock options granted under the 2015 LTIP are non-transferrable (except, on death, to the option holder's personal representatives) and may not be assigned or charged. This obligation does not apply to the 2021 LTIP.

No stock options may be granted under the 2015 LTIP in any single financial year over stock having an aggregate market value in excess of 200% of the option holder's annual basic salary for the year. This obligation only applies to option grants made under the 2021 LTIP while the company remains listed on AIM.

Furthermore, no stock option may be granted under the LTIP if the grant of that stock option, when aggregated with all stock options granted under the LTIP and any awards granted under any other employee stock plans in the preceding 10 years, would cause the total number of shares falling to be issued in connection with such options or awards to exceed 10% of our issued ordinary share capital. This obligation only applies to option grants made under the 2021 LTIP while the company remains listed on AIM.

C. Board Practices

Composition of our Board of Directors

Our board of directors is currently composed of seven members, consisting of Mr. Peyton, Dr. Stevenson and five non-executive directors. Our board of directors has determined that for the purposes of the Corporate Governance Code published by the Quoted Companies Alliance, which is the corporate governance code that we apply in the United Kingdom, all of our non-executive directors are independent. Additionally, our board of directors has determined that none of our directors, other than Mr. Peyton and Dr. Stevenson, who are executive officers of the company, has a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of director and that each of these four directors is "independent" as that term is defined under Nasdaq rules. There are no family relationships among any of our executive officers or directors.

In accordance with our articles of association, any director who served as a director at each of the preceding two annual general meetings of shareholders and who was not appointed or re-appointed by the shareholders at a general meeting at, or since, either such meeting shall retire from office at the next annual general meeting of shareholders. Retiring directors are eligible for re-election. See "Item 10. Additional Information—B. Memorandum and Articles of Association—Directors."

Insurance and Indemnification

To the extent permitted by the U.K. Companies Act, we are empowered to indemnify our directors and executive officers against any liability they incur by reason of their directorship or work with the company. We maintain directors' and officers' insurance to insure such persons against certain liabilities. Insofar as indemnification of liabilities arising under the Securities Act may be permitted to our board, executive officers or persons controlling us pursuant to the foregoing provisions, we have been informed that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Committees of our Board of Directors

Our board of directors has two standing committees: an audit and risk committee and a remuneration committee.

Audit and Risk Committee

Our audit and risk committee, which consists of Dr. Rupalla, Dr. Baracchini and Mr. Maier, assists the board of directors in overseeing our accounting and financial reporting processes and the audits of our financial statements. Mr. Maier serves as chairman of the audit and risk committee. The audit and risk committee consists exclusively of members of our board who are financially literate, and Mr. Maier is considered an "audit committee financial expert" as defined by applicable SEC rules and has the requisite financial sophistication as defined under applicable Nasdaq rules. Our board of directors has determined that all of the members of the audit and risk committee satisfy the "independence" requirements set forth in Rule 10A-3 under the Exchange Act. We have also adopted a charter governing the audit and risk committee that complies with the rules of Nasdaq.

The audit and risk committee's responsibilities include:

- monitoring the integrity of our financial and narrative reporting, preliminary announcements and any other formal announcements relating to our financial performance;
- advise the Board on whether, taken as a whole, the Annual Report and Accounts is fair, balanced and understandable reviewing the appropriateness and completeness of our risk management and internal controls;
- considering annually whether we should have an internal audit function;
- overseeing our relationship with the external auditors and assessing the effectiveness of the external audit process, including in relation to appointment and tendering, remuneration and other terms of engagement, and appropriate planning ahead of each annual audit cycle;
- maintaining regular, timely, open and honest communication with the external auditors, ensuring the external auditors report to the committee on all relevant matters to enable the committee to carry out its oversight responsibilities; and
- monitoring risk.

Remuneration Committee

Our remuneration committee, which consists of Prof. Glasmacher and Dr. Macrae, assists the board of directors in determining executive officer compensation. Dr. Macrae serves as chairman of the remuneration committee.

The remuneration committee's responsibilities include:

- setting a remuneration policy that is designed to promote our long-term success;
- ensuring that the remuneration of executive directors and other senior executives reflects both their individual performance and their contribution to our overall results;
- determining the terms of employment and remuneration of executive directors and other senior executives, including recruitment and retention terms;
- approving the design and performance targets of any annual incentive schemes that include the executive directors and other senior executives;
- agreeing upon the design and performance targets, where applicable, of all share incentive plans;
- gathering and analyzing appropriate data from comparator companies in the biotechnology sector; and
- the selection and appointment of external advisers to the remuneration committee, if any, to provide independent remuneration advice where necessary.

D. EMPLOYEES

As of December 31, 2021, we had 106 employees, including 45 employees in the United Kingdom and four employees in the United States. Of these employees, 90 were engaged in research and development activities and 16 were engaged in administrative activities. We also engage contractors and consultants. To the company's knowledge, none of our employees outside of Spain are represented by a labor union or covered under a collective bargaining agreement. Our staff based in Spain are covered by a sector-wide collective bargaining agreement. They are also represented by a union-backed staff representative. We have not experienced any work stoppages due to employee disputes, and we consider our relationship with our employees to be good.

E. Share Ownership

The following table sets forth information relating to the beneficial ownership of our ordinary shares as of March 25, 2022 by each member of our board of directors and each of our other executive officers. The percentage of beneficial ownership in the table below is based upon a total of 180,300,967 ordinary shares.

The number of our ordinary shares beneficially owned by each board member or executive officer is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any shares over which the individual has sole or shared voting power or investment power as well as any shares that the individual has the right to acquire within 60 days of March 25, 2022 through the exercise of any option, warrant or other right. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all ordinary shares held by that person.

	Amount and Nature of Share Ownership	
Name of Principal Stockholder	**Number of Shares(1)**	**Percentage Owned (%)**
Duncan Peyton(2)	10,181,437	5.6%
Alexander Stevenson(3)	10,025,130	5.5%
Axel Glasmacher(4)	30,000	*%
John Doyle	—	*%
Edgardo Baracchini	—	*%
Katrin Rupalla	—	*%
Sandy Macrae	—	*%
Paul Maier	—	*%

* Represents beneficial ownership of less than one percent (1%) of the outstanding ordinary shares.

(1) Ordinary shares figures include ordinary shares represented by ADSs.

(2) Consists of (i) 9,018,675 shares held of record, (ii) 666,666 warrants issued pursuant to the February 2020 fundraise and exercisable for £1.00 per share at any time for 5 years after issuance on March 9, 2020 by Mr. Peyton and (iii) 496,096 shares issued to Mr. Peyton pursuant to a commitment to provide financial backing to Longevity in the event of redemptions by shareholders of Longevity pursuant to a certain backstop arrangement.

(3) Consists of (i) 8,976,736 shares held of record, (ii) 666,666 warrants issued pursuant to the March 9, 2020 fundraise and exercisable for £1.00 per share at any time for 5 years after issuance by Dr. Stevenson and (iii) 381,728 shares issued to Dr. Stevenson pursuant to a commitment to provide financial backing to Longevity in the event of redemptions by shareholders of Longevity pursuant to a certain backstop arrangement.

(4) Consists of 30,000 shares held of record by Prof. Glasmacher.

For further information regarding options issued to our executive officers and directors see “Item 6. Director, Senior Management, Employees—B. Compensation—Equity Compensation Awards to Directors and Executive Officers.” For further information regarding arrangements involving the issue or grant of options or shares or securities of the company see “Item 6. Director, Senior Management, Employees—B. Compensation—Equity Incentive Arrangements.”

ITEM 7. MAJOR SHAREHOLDERS AND RELATED PARTY TRANSACTIONS

A. Major Shareholders

The following table sets forth certain information regarding the beneficial ownership of 4D Pharma's ordinary shares as of March 25, 2022 by each person known by us to be the beneficial owner of more than 5% of our outstanding ordinary shares. The percentage of beneficial ownership in the table below is based upon a total of 180,300,967 ordinary shares.

The number of our ordinary shares beneficially owned by each board member or executive officer is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any shares over which the individual has sole or shared voting power or investment power as well as any shares that the individual has the right to acquire within 60 days of March 25, 2022 through the exercise of any option, warrant or other right. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all ordinary shares held by that person.

	Amount and Nature of Share Ownership	
Name of Principal Stockholder	**Number of Shares(1)**	**Percentage Owned (%)**
Merck & Co.[(1)]	12,145,523	6.6%
Duncan Peyton[(2)]	10,181,437	5.6%
Alexander Stevenson[(3)]	10,025,130	5.5%

(1) Consists of 8,315,023 shares of record and 3,830,500 warrants issued on March 9, 2020 exercisable for £1.00 per share at any time for 5 years after issuance held by Merck & Co. The address for these entities is 2000 Galloping Hill Road Kenilworth NJ 07033.

(2) Consists of (i) 9,018,675 shares held of record, (ii) 666,666 warrants issued on March 9, 2020 exercisable for £1.00 per share at any time for 5 years after issuance by Mr. Peyton and (iii) 496,096 shares issued to Mr. Peyton pursuant to a commitment to provide financial backing to Longevity in the event of redemptions by shareholders of Longevity pursuant to a certain backstop arrangement.

(3) Consists of (i) 8,976,736 shares held of record, (ii) 666,666 warrants issued on March 9, 2020 exercisable for £1.00 per share at any time for 5 years after issuance by Dr. Stevenson and (iii) 381,728 shares issued to Dr. Stevenson pursuant to a commitment to provide financial backing to Longevity in the event of redemptions by shareholders of Longevity pursuant to a certain backstop arrangement.

As of March 25, 2022, to the best of the Company's knowledge, approximately 72% of our issued share capital was held in the U.K. (approximately 64% including warrants) and approximately 25 % of our share capital was held in the United States (approximately 33% including warrants) with the remainder being held elsewhere.

As of March 24, 2022, entities affiliated with Steven Oliveira hold 8,600,000 ordinary shares, a decrease of approximately 10% in ownership since March 23, 2021, which is the date that our ordinary shares underlying the ADSs listed on The Nasdaq Global Market were authorized. Since March 23, 2021, which is the date that our ordinary shares underlying the ADSs listed on The Nasdaq Global Market were authorized, there has been no significant change in the percentage ownership held by any other major shareholder.

In the past three years, the following issuances of securities have impacted the percentage ownership held by the major shareholders listed above:

On July 29, 2021, we issued warrants equating to 212,568 shares, exercisable at $1.18 per share to Oxford Finance Luxembourg S À R L.

On March 23, 2021, we issued 31,048,192 ordinary shares. Additionally, we also issued new warrants convertible into ordinary shares comprising (i) 4,320,000 outstanding warrants that were previously issued by Longevity to holders of Longevity ordinary shares at the time of the Longevity initial public offering and which will be converted into warrants to purchase up to 16,268,040 of our ordinary shares, payable in ADSs, (ii) warrants to acquire up to 7,530,000 of our ordinary shares issued pursuant to certain backstop arrangements, and (iii) an option to acquire up to 2,892,096 of our ordinary shares to Cantor Fitzgerald, in its capacity as underwriter to Longevity at the time of the Longevity initial public offering. If all of the New Warrants are exercised for cash, we will receive approximately $29 million of capital.

On March 23, 2021, we issued 16,367,332 ordinary shares in connection with the private placement to raise approximately $25.0 million (£18.0 million).

In July 2020, we raised £7.7 million ($9.7 million) (£7.1 million ($9.0 million) net of transaction costs) through the issuance of 21,898,400 ordinary shares at a share price of 35 pence ($0.44) per share.

In February 2020, we raised £22 million ($28.6 million) (£20.9 million ($27.2 million) net of transaction costs) through the issuance of 44 million ordinary shares at a share price of 50 pence ($0.65) per share. A warrant was also issued on the basis of one share for every two ordinary shares issued and have an exercise price of 100 pence ($1.30) per share and is exercisable for five years from the date of issuance.

We have also exercised our right to cause MSD to purchase $5 million of new ordinary shares at the same price as other investors in the February 2020 fundraising pursuant to the terms of a subscription agreement.

Change in Control Arrangements

None.

B. Related Party Transactions

Agreements with Our Executive Officers and Directors

A director in one of our subsidiaries, 4D Pharma León S.L.U., Antonio Fernandez, is also a director of Biomar Microbial Technologies ("**Biomar**"), which charged rent and building service costs to the Company of $131 thousand, $153 thousand and $51 thousand for the years ended December 31, 2021, 2020 and 2019, respectively. We charged Biomar $38 thousand, $41 thousand and $35 thousand for services as of December 31, 2021, 2020 and 2019, respectively. As of December 31, 2021, 2020 and 2019, $15 thousand, $4 thousand and $54 thousand, respectively, was due from Biomar for these services.

We have entered into service contracts with our executive officers and appointment letters with our non-executive directors. These agreements contain customary provisions and representations, including confidentiality, non-competition, non-solicitation and inventions assignment undertakings by the executive officers. However, the enforceability of the non-competition provisions may be limited under applicable law.

Agreements with Collaborators

MSD purchased 7,661,000 shares of the Company's ordinary shares in February 2020, a further 654,023 were added during the March 22, 2021 fundraise, with MSD currently holding 4.6% of the Company's total outstanding ordinary shares. The Company entered into the MSD Agreement with MSD in October 2019. See "Item 4. Information on the Company—B. Business Overview—Collaborations—Research Collaboration and Option to License Agreement with Merck" for further information. Additionally, the Company also has an ongoing clinical trial evaluating MRx0518 in the combination with Keytruda in patients with solid tumors who progresses on prior PD-1 inhibitor therapy. Under the terms of the agreement MSD will provide Keytruda free of charge to the trial.

Indemnification Agreements

We have entered into a deed of indemnity with each of our directors and executive officers. The deeds of indemnity and our articles of association require us to indemnify our directors and executive officers to the fullest extent permitted by law. See "Item 6. Directors, Senior Management and Employees—C. Board practices—Composition of our Board—Insurance and

Related Party Transaction Policy

Our Board has adopted a written related person transaction policy, which sets forth the policies and procedures for the review and approval or ratification of related person transactions. This policy covers any transaction or proposed transactions between us and a related person that are material to us or the related person. In reviewing and approving any such transactions, our audit and risk committee is tasked to consider all relevant facts and circumstances, including, but not limited to, whether the transaction is on terms comparable to those that could be obtained in an arm's length transaction and the extent of the related person's interest in the transaction. The related party transaction policy also covers related party transactions under the AIM Rules for Companies published by the London Stock Exchange.

C. Interests of Experts and Counsel

Not applicable.

ITEM 8. FINANCIAL INFORMATION

A. Consolidated Statements and Other Financial Information

See "Item 17. Financial Statements." For a discussion of our results see "Item 5. Operating and Financial Review."

Legal Proceedings

From time to time, we may become involved in legal proceedings or be subject to claims arising in the ordinary course of our business. We are not currently a party to any material legal proceedings. Regardless of outcome, such proceedings or claims can have an adverse impact on us because of defense and settlement costs, diversion of resources and other factors, and there can be no assurances that favorable outcomes will be obtained.

Dividend Policy

We have never declared or paid any cash dividends on our shares and we do not anticipate paying any cash dividends on our shares in the foreseeable future. We intend to retain all available funds and any future earnings to fund the development and expansion of our business. Under English law, among other things, we may only pay dividends if we have sufficient distributable reserves (on a non-consolidated basis), which are calculated as our accumulated realized profits that have not been previously distributed or capitalized less its accumulated realized losses, so far as such losses have not been previously written off in a reduction or reorganization of capital.

B. Significant Changes

No significant changes have occurred since December 31, 2021, except as otherwise disclosed in this annual report.

ITEM 9. LISTINGS

A. Offer and Listing Details

ADSs

Our ADSs, each representing eight ordinary shares of ours, with a £0.0025 per share nominal value each, have been listed on Nasdaq since March 22, 2021. Our ADSs trade on the Nasdaq Global Market under the symbol "LBPS." Prior to that date, there was no public trading market for our ADSs.

Ordinary shares

Our ordinary shares have traded on AIM under the symbol "DDDD" since February 18, 2014. No trading market currently exists for our ordinary shares in the United States.

New Warrants

Certain of our warrants, which we assumed in connection with the Merger, have been listed on Nasdaq since March 23, 2021. These warrants trade on the Nasdaq Global Market under the symbol "LBPSW." Prior to that date, these warrants traded on the Nasdaq Capital Market under the symbol "LOACW."

B. Plan of Distribution

Not applicable

C. Markets

Our ordinary shares have traded on AIM under the symbol "DDDD" since February 18, 2014. Our ADSs have traded on the Nasdaq Global Market under the symbol "LBPS" since March 22, 2021. Our warrants have traded on the Nasdaq Global Market under the symbol "LBPSW" since March 23, 2021.

D. Selling Shareholders

Not applicable.

E. Dilution

Not applicable.

F. Expense of the Issue

Not applicable.

ITEM 10. ADDITIONAL INFORMATION

A. Share Capital

Not applicable.

B. Memorandum and Articles of Association

This section summarizes certain material provisions of our Articles of Association and relevant U.K. corporate law. The following summary does not purport to be complete and is qualified in its entirety by reference to our articles of association.

Share rights

Subject to the U.K. Companies Act, the articles and to any rights for the time being attached to any existing share, ordinary shares may be issued with such rights or restrictions as we may from time to time by ordinary resolution determine, or, if we have not so determined, as our board of directors may determine.

Subject to the U.K. Companies Act, any share may be issued which is to be redeemed or is to be liable to be redeemed at the option of 4D Pharma or the holder, on such terms, conditions and in such manner as our board of directors may determine.

Voting rights

Subject to any rights or restrictions attached to any shares from time to time, the 4D Pharma shareholders, their duly appointed proxies shall have voting rights as provided in the U.K. Companies Act, except that on a vote on a resolution on a show of hands at a meeting, a proxy has one vote for and one vote against the resolution if the proxy has been duly appointed by more than one member entitled to vote on the resolution and either:

- the proxy has been instructed by one or more of those members to vote in one way and has been instructed by one or more other of those members to vote in the other way; or
- the proxy has been instructed by one or more of those members to vote in one way and is given discretion as to how to vote by one or more other of those members and wishes to use that discretion to vote in the other way.

At any general meeting a resolution put to the vote of the meeting shall be decided on a show of hands unless a poll is (before or on the declaration of the result of the show of hands) demanded. Subject to the provisions of the Companies Act, a poll may be demanded by:

- the chairman of the meeting;
- not less than five members present in person having the right to vote on the resolution;
- a member or members present in person representing in aggregate not less than one tenth of the total voting rights of all the members having the right to vote at the meeting; or
- a member or members present in person holding shares in the Company conferring a right to vote at the meeting, being shares on which an aggregate sum has been paid up equal to not less than one tenth of the total sum paid up on all the shares conferring that right.

Restrictions on Voting

No shareholder shall, unless the directors otherwise determine, be entitled to vote, either in person or by proxy, at any general meeting or at any separate class meeting in respect of any share held by such shareholder unless all calls or other sums payable by such shareholder in respect of that share have been paid.

Our board of directors may from time to time make calls upon the shareholders in respect of any money unpaid on their shares and each shareholder shall (subject to us serving on such shareholder at least 14 days' notice specifying the time or times and place of payment) pay at the time or times so specified the amount called on such holder's shares.

Variation of Rights

The rights attached to any class of shares may be varied or abrogated, in accordance with the provisions of the U.K. Companies Act and with either the written consent of the holders of not less than three-fourths in nominal value of the issued shares of that class (calculated excluding any shares held as treasury shares), or with the sanction of a special resolution (being a 75% majority of 4D Pharma shareholders, present at a general meeting in person or by proxy) passed at a separate meeting of the holders of those shares. At every such separate general meeting (except an adjourned meeting) the quorum must be two or more persons holding or representing by proxy not less than one-third in nominal value of the issued shares of the class (calculated excluding any shares held as treasury shares).

The rights conferred upon the holders of any shares are not, unless otherwise expressly provided in the rights attaching to those shares, deemed to be varied by the creation or issue of further shares ranking equally with them.

Share transfers

The ordinary shares are in registered form. Any ordinary shares may be held in uncertificated form.

A member may transfer certificated shares to another person by a written instrument of transfer in any usual form (or any other form approved by our board of directors) executed by or on behalf of the member and, in the case of a share which is not fully paid, by or on behalf of that person. Our board of directors may refuse to register the transfer of a certificated share which is in respect of a partly paid share provided that any refusal does not prevent open and proper dealings of any class of shares which are admitted to trading on AIM. Our board of directors may also refuse to register the transfer of a certificated share unless the transfer is in respect of only one class of share, is duly stamped (or certified as not chargeable to stamp duty) and is deposited to our registered office or any place that our board of directors may determine and is accompanied by the relevant share certificate or such other evidence our board of directors may reasonably require.

The transferor of an ordinary share is deemed to remain the holder until the transferee's name is entered in the share register.

Subject to the provisions of our articles of association, title to uncertificated shares may be transferred in accordance with the Uncertificated Securities Regulations 2001. Our board of directors is required to register a transfer of any uncertificated share in accordance with those regulations. Our board of directors may refuse to register any such transfer which is in favor of more than four persons jointly or in any other circumstance permitted by those regulations. Provisions of the articles of association do not apply to any uncertificated shares to the extent that such provisions are inconsistent with the holding of shares in uncertificated form or with the transfer of shares by means of a relevant system.

Our board of directors can decline to register any transfer of any share which is not a fully paid share or any transfer of any share on which we have a lien.

Dividends

Subject to it having sufficient distributable reserves, we may by ordinary resolution (being a resolution passed by a 50% majority of 4D shareholders in person or by proxy) from time to time declare dividends not exceeding the amount recommended by our board of directors. Our board of directors may pay interim dividends, and also any fixed rate dividend, whenever our financial position, in the opinion of our board of directors, justifies its payment.

All dividends on shares are to be paid according to the amounts paid up on their nominal value, or otherwise in accordance with the terms concerning entitlement to dividends on which shares were issued.

All unclaimed dividends may be made use of by our board of directors for our benefit until claimed. Any dividend unclaimed for a period of 12 years from the date when it was declared or became due for payment shall revert to 4D Pharma.

Our board of directors can be claimed by way of scrip dividend instead of cash in respect of any dividend.

Shareholder meetings

Our board of directors is required to convene annual general meetings in accordance with the U.K. Companies Act. The U.K. Companies Act provides that a general meeting (other than an adjourned meeting) must be called by notice of at least 21 days' in the case of an annual general meeting (unless shareholders approve a notice period of 14 days' by special resolution (being a resolution passed by a 75% majority of 4D Pharma shareholders present at a general meeting in person or by proxy) and at least 14 days' in any other case). Our board of directors may convene a general meeting which is not an annual general meeting whenever it thinks fit.

We are required to give notice of a general meeting to each member (other than a person who, under our articles of association or pursuant to any restrictions imposed on any shares, is not entitled to receive such a notice or to whom we, in accordance with applicable law, have not sent and are not required to send our latest annual report and accounts), to our directors and to our auditors. For these purposes "members" are the persons registered in our register of members as being holders of shares at any particular time on any particular record date fixed by our board of directors that (in accordance with the Uncertificated Securities Regulations 2001) is not more than 21 days before the sending out of the notice convening the meeting. The notice of a general meeting may specify a time by which a person must be entered on our register of members in order to have the right to attend or vote at the meeting.

A member who is entitled to attend and vote at a general meeting is entitled to appoint another person, or two or more persons in respect of different shares held by him, as his proxy to exercise all or any of his rights to attend and to speak and to vote at the meeting.

Every member who is present at a general meeting (whether physical or electronic) in person or by proxy is entitled to one vote on a resolution put to the meeting on a show of hands and to one vote for every share of which he is the holder on a resolution put to the meeting on a poll.

Alteration of share capital

We may alter its share capital in any way permitted by the U.K. Companies Act and applicable law and confer any preference or other advantage on one or more of the shares resulting from any division or sub- division of its share capital. We may, by special resolution (being a resolution passed by a 75% majority of 4D Pharma shareholders present at a general meeting in person or by proxy), reduce its share capital, share premium account, capital redemption reserve or any other undistributable reserves.

Change of Control

There is no specific provision in the articles of association that would have the effect of delaying, deferring or preventing a change of control.

Distributions on Winding Up

On a winding up, the liquidator may, with the sanction of a special resolution of shareholders and any other sanctions required by law, divide amongst the shareholders (excluding the company itself to the extent it is a shareholder by virtue only of its holding of shares as treasury shares) in specie or in kind the whole or any part of our assets (whether they shall consist of property of the same kind or not) and may set such values and may determine how such division shall be carried out as between the shareholders or different classes of shareholder. The liquidator may, with the sanction of a special resolution of the shareholders and any other sanctions required by law, vest the whole or any part of such assets in trustees upon such trusts for the benefit of the shareholders as the liquidator shall think fit, but no shareholder shall be compelled to accept any shares or other assets upon which there is any liability.

CREST

To be traded on AIM, securities must be able to be transferred and settled through the CREST system. CREST is a computerized paperless share transfer and settlement system which allows securities to be transferred by electronic means, without the need for a written instrument of transfer. The articles of association are consistent with CREST membership and, amongst other things, allow for the holding, evidencing and transferring of shares through CREST in uncertificated form.

Directors

Number of Directors

Unless and until otherwise determined by an ordinary resolution of shareholders, we may not have less than two directors and no more than ten directors on our board of directors.

Appointment of Directors

Subject to the provisions of the articles of association we may, by ordinary resolution of the shareholders, elect any person who is willing to act to be a director, either to fill a casual vacancy or as an addition to the existing board. No person that is not a director retiring from the existing board is eligible for appointment as a director unless recommended by the board of directors, or unless not less than seven and not more than 42 days before the date appointed for the meeting a notice is given to the company by a member expressing an intention to propose such person for appointment as a director, and such notice has also been signed by that person expressing a willingness to be elected.

Without prejudice to the power to appoint any person to be a director by shareholder resolution, the board has power to appoint any person to be a director, either to fill a casual vacancy or as an addition to the existing board but so that the total number of directors does not exceed any maximum number fixed by or in accordance with the Articles.

Any director appointed by the board will hold office only until the following annual general meeting. Such a director is eligible for re-appointment at that meeting.

Rotation of Directors

At every annual general meeting, there shall retire from office at least one third of the directors. A retiring director shall be eligible for re-appointment. A director retiring at a meeting shall, if he or she is not re- appointed at such meeting, retain office until the meeting appoints someone in his or her place, or if it does not do so, until the conclusion of such meeting.

Directors' Interests

The directors may authorize, to the fullest extent permitted by law, any matter proposed to them which would otherwise result in a director infringing his or her duty to avoid a situation in which he or she has, or can have, a direct or indirect interest that conflicts, or possibly may conflict, with our interests. A director shall not, save as otherwise agreed by him or her, be accountable to us for any benefit which he or she derives from any matter authorized by the directors and any contract, transaction or arrangement relating thereto shall not be liable to be avoided on the grounds of any such benefit.

Subject to the requirements under sections 175, 177 and 182 of the Companies Act, a director who is any way, whether directly or indirectly, interested in a proposed or existing transaction or arrangement with us shall declare the nature of his interest at a meeting of the directors.

A director shall not vote in respect of any contract, arrangement or transaction whatsoever in which he or she has an interest which is to his or her knowledge a material interest otherwise than by virtue of interests in shares or debentures or other securities of or otherwise in or through our company. A director shall not be counted in the quorum at a meeting in relation to any resolution on which he or she is debarred from voting.

A director shall be entitled to vote (and be counted in the quorum) in respect of any resolution concerning any of the following matters:

- the giving of any guarantee, security or indemnity in respect of (i) money lent or obligations incurred by him or any other person at the request of, or for the benefit of, the Company or any of its subsidiary undertakings, or (ii) a debt or obligation of the of the Company or any of its subsidiary undertakings for which he himself has assumed responsibility under a guarantee or indemnity or by the giving of security;

- any contract concerning the subscription of or purchase of shares, debentures or other securities of the Company by him under an offer to members;

- any contract concerning any issue or offer of shares or debentures or other securities of or by the Company or any of its subsidiary undertakings for subscription or purchase, in respect of which he is or may be entitled to participate in his capacity as a holder of any such securities or as an underwriter or sub-underwriter;

- any contract concerning another company in which he is interested, directly or indirectly, and whether as an officer or member or otherwise, provided that he does not hold an interest representing one per cent or more of any class of the equity share capital of such company (or of any third company through which his interest is derived and calculated exclusive of any shares of that class in that company held as treasury shares) or of the voting rights available to members of the relevant company (any such interest being deemed for the purposes of this article to be a material interest in all circumstances);

- any contract for the benefit of employees of the Company or of any of its subsidiary undertakings which does not accord to him any privilege or benefit not generally accorded to the employees to whom the contract or arrangement relates;

- any contract concerning the purchase or maintenance of insurance either for or for the benefit of any director or for persons who include directors; and

- any proposal for the Company (i) to provide him with an indemnity permitted by the Statutes, (ii) to provide him with funds in circumstances permitted by the Statutes to meet his defense expenditure in respect of any civil or criminal proceedings or regulatory investigation or other regulatory action or in connection with any application for any category of relief permitted by the Statutes, or (iii) to do anything to enable him to avoid incurring any such expenditure.

If a question arises at a meeting of the board or of a committee of the board as to the right of a director to vote or be counted in the quorum, and such question is not resolved by his or her voluntarily agreeing to abstain from voting or not to be counted in the quorum, the question shall be determined by the chairman and his or her ruling in relation to any director other than himself or herself shall be final and conclusive except in a case where the nature or extent of the interest of the director concerned has not been fairly disclosed.

Directors' Fees and Remuneration

Each of the non-executive directors shall be paid a fee in such sums as may from time to time be determined by the directors provided that the aggregate of all such fees so paid to a director shall not exceed £0.6 million per annum, or such higher amount as may from time to time be determined by ordinary resolution of shareholders.

Each director may be paid all proper and reasonable expenses incurred in attending and returning from meetings of the directors or committees of the directors or general meetings of the company or separate meetings of the holders of any class of shares or debentures of the company or otherwise in connection with the business of our Company.

Any director who is appointed to any executive office or who serves on any committee or who devotes special attention to the business of our company, or who otherwise performs services which in the opinion of the 4D Pharma Board are outside the scope of the ordinary duties of a director, may be paid such extra remuneration by way of salary, percentage of profits or otherwise as the 4D Pharma Board may determine.

Borrowing Powers

Our board of directors may exercise all the powers to borrow money and to mortgage or charge all or any part of our undertaking, property, assets (present or future) and uncalled capital and to issue debentures, debenture stock and other securities, whether outright or as collateral security for any debt, liability or obligation of us or of any third party, subject to and in accordance with the U.K. Companies Act.

Our board of directors must restrict our borrowings and exercise all voting and other rights or powers of control exercisable by us in relation to its subsidiaries so as to secure that the aggregate principal amount of all borrowings by the Group outstanding at any time shall not, without the previous sanction of an ordinary resolution of the shareholders, exceed a sum equal to three times the aggregate of:

- the amount paid up on our issued share capital and on any share capital that has been unconditionally allotted but not issued; and
- the amounts standing to the credit of our reserves (including any share premium account, capital redemption reserve and revaluation reserve) after adding any credit balance or deducting any debit balance on the profit and loss account;

all as shown in the latest audited consolidated balance sheet, subject to certain adjustments.

Indemnity

Every one of our directors or other officers shall be indemnified out of our funds against all costs, charges, expenses, losses and liabilities sustained or incurred by him or her for negligence, default, breach of duty or breach of trust or otherwise in relation to our affairs or the affairs of an associated company, or in connection with our activities, or the activities of an associated company.

Other English Law Considerations

Notification of Voting Rights

A shareholder in a public company incorporated in the United Kingdom whose shares are admitted to trading on AIM is required pursuant to Rule 5 of the Disclosure Guidance and Transparency Rules of the U.K. Financial Conduct Authority to notify us of the percentage of his, her or its voting rights if the percentage of voting rights which he, she or it holds as a shareholder or through his, her or its direct or indirect holding of financial instruments (or a combination of such holdings) reaches, exceeds or falls below 3%, 4%, 5%, and each 1% threshold thereafter up to 100% as a result of an acquisition or disposal of shares or financial instruments.

Mandatory Purchases and Acquisitions

Pursuant to Sections 979 to 991 of the U.K. Companies Act, where a takeover offer has been made for us and the offeror has acquired or unconditionally contracted to acquire not less than 90% in value of the shares to which the offer relates and not less than 90% of the voting rights carried by those shares, the offeror may give notice to the holder of any shares to which the offer relates which the offeror has not acquired or unconditionally contracted to acquire that he, she or it wishes to acquire, and is entitled to so acquire, those shares on the same terms as the general offer. The offeror would do so by sending a notice to the outstanding minority shareholders telling them that it will compulsorily acquire their shares.

Such notice must be sent within three months of the last day on which the offer can be accepted in the prescribed manner. The squeeze-out of the minority shareholders can be completed at the end of six weeks from the date the notice has been given, subject to the minority shareholders failing to successfully lodge an application to the court to prevent such squeeze-out any time prior to the end of those six weeks following which the offeror can execute a transfer of the outstanding shares in its favor and pay the consideration to us, which would hold the consideration on trust for the outstanding minority shareholders. The consideration offered to the outstanding minority shareholders whose shares are compulsorily acquired under the U.K. Companies Act must, in general, be the same as the consideration that was available under the takeover offer.

Sell Out

The U.K. Companies Act also gives our minority shareholders a right to be bought out in certain circumstances by an offeror who has made a takeover offer for all of our shares. The holder of shares to which the offer relates, and who has not otherwise accepted the offer, may require the offeror to acquire his, her or its shares if, prior to the expiry of the acceptance period for such offer, (i) the offeror has acquired or unconditionally agreed to acquire not less than 90% in value of the voting shares, and (ii) not less than 90% of the voting rights carried by those shares. The offeror may impose a time limit on the rights of minority shareholders to be bought out that is not less than three months after the end of the acceptance period. If a shareholder exercises his, her or its rights to be bought out, the offeror is required to acquire those shares on the terms of this offer or on such other terms as may be agreed.

Disclosure of Interest in Shares

Pursuant to Part 22 of the U.K. Companies Act, we are empowered by notice in writing to any person whom we know or have reasonable cause to believe to be interested in our shares, or at any time during the three years immediately preceding the date on which the notice is issued has been so interested, within a reasonable time to disclose to us particulars of that person’s interest and (so far as is within such person’s knowledge) particulars of any other interest that subsists or subsisted in those shares.

Under the articles of association, if a person defaults in supplying us with the required particulars in relation to the shares in question, or default shares, within the prescribed period of 14 days from the date of the service of notice, the directors may by notice direct that:

- in respect of the default shares, the relevant shareholder shall not be entitled to vote (either in person or by proxy) at any general meeting or to exercise any other right conferred by a shareholding in relation to general meetings; and

- where the default shares represent at least 0.25% of their class, (i) any dividend or other money payable in respect of the default shares shall be retained by us without liability to pay interest and/or (ii) no transfers by the relevant shareholder of any default shares may be registered (unless the shareholder is not in default and the shareholder provides a certificate, in a form satisfactory to the directors, to the effect that after due and careful enquiry the shareholder is satisfied that none of the shares to be transferred are default shares).

Purchase of Own Shares

Under the laws of England and Wales, a limited company may only purchase its own shares out of the distributable profits of the company or the proceeds of a fresh issue of shares made for the purpose of financing the purchase, provided that they are not restricted from doing so by their articles of association.

A limited company may not purchase its own shares if, as a result of the purchase, there would no longer be any issued shares of the company other than redeemable shares or shares held as treasury shares. Shares must be fully paid in order to be repurchased.

Subject to the above, we may purchase our own shares in the manner prescribed below. We may make an "on-market" purchase of our own fully paid shares pursuant to an ordinary resolution of shareholders. The resolution authorizing an on-market purchase must:

- specify the maximum number of shares authorized to be acquired;
- determine the maximum and minimum prices that may be paid for the shares; and
- specify a date, not being later than five years after the passing of the resolution, on which the authority to purchase is to expire.

We may purchase our own fully paid shares in an "off-market" purchase otherwise than on a recognized investment exchange pursuant to a purchase contract authorized by resolution of shareholders before the purchase takes place. Any authority will not be effective if any shareholder from whom we propose to purchase shares votes on the resolution and the resolution would not have been passed if he, she or it had not done so. The resolution authorizing the purchase must specify a date, not being later than five years after the passing of the resolution, on which the authority to purchase is to expire.

For these purposes, on-market purchases can only be made on AIM. Any purchase of our ADSs through Nasdaq would be an off-market purchase.

Distributions and Dividends

Under the U.K. Companies Act, before a company can lawfully make a distribution or dividend, it must ensure that it has sufficient distributable reserves (on a non-consolidated basis). The basic rule is that a company's profits available for the purpose of making a distribution are its accumulated, realized profits, so far as not previously utilized by distribution or capitalization, less its accumulated, realized losses, so far as not previously written off in a reduction or reorganization of capital duly made. The requirement to have sufficient distributable reserves before a distribution or dividend can be paid applies to us and to each of our subsidiaries that has been incorporated under the laws of England and Wales.

It is not sufficient that we, as a public company, have made a distributable profit for the purpose of making a distribution. An additional capital maintenance requirement is imposed on us to ensure that the net worth of the company is at least equal to the amount of its capital. A public company can only make a distribution:

- if, at the time that the distribution is made, the amount of its net assets (that is, the total excess of assets over liabilities) is not less than the total of its called up share capital and undistributable reserves; and
- if, and to the extent that, the distribution itself, at the time that it is made, does not reduce the amount of the net assets to less than that total.

City Code on Takeovers and Mergers

As a public company incorporated in England and Wales with our registered office in England and Wales which has shares admitted to AIM, we are subject to the U.K. Takeover Code, which is issued and administered by the U.K. Panel on Takeovers and Mergers, or the Takeover Panel. The U.K. Takeover Code provides a framework within which takeovers of companies subject to it are conducted. In particular, the U.K. Takeover Code contains certain rules in respect of mandatory offers. Under Rule 9 of the U.K. Takeover Code, if a person:

- acquires an interest in our shares which, when taken together with shares in which he or she or persons acting in concert with him or her are interested, carries 30% or more of the voting rights of our shares; or

- who, together with persons acting in concert with him or her, is interested in shares that in the aggregate carry not less than 30% and not more than 50% of the voting rights of our shares, and such persons, or any person acting in concert with him or her, acquires additional interests in shares that increase the percentage of shares carrying voting rights in which that person is interested, the acquirer and depending on the circumstances, its concert parties, would be required (except with the consent of the Takeover Panel) to make a cash offer for our outstanding shares at a price not less than the highest price paid for any interests in the shares by the acquirer or its concert parties during the previous twelve months.

Corporate Governance Code

The AIM Rules for Companies published by the London Stock Exchange require us to include on our website details of a recognized corporate governance code that our board of directors has decided to apply, how we comply with that code and, where we depart from our chosen corporate governance code, an explanation of the reasons for doing so.

Since 2015, our board of directors has sought to apply The QCA Corporate Governance Code (2018 edition). Our board of directors views this as an appropriate corporate governance framework for our company and consideration has been given to each of the ten principles set out in the code.

C. Material Contracts

The following are summaries of existing agreements and are qualified in their entirety by reference to the complete text of each of agreement, copies of each of which are included as exhibits to this Annual Report on Form 20-F.

Merger Agreement

On October 21, 2020, we entered into an agreement and plan of merger (the "**Merger Agreement**") with Longevity and Merger Sub, pursuant to which, among other things, Longevity would merge with and into Merger Sub, with Merger Sub continuing as the surviving entity and a wholly-owned subsidiary of 4D Pharma. Pursuant to the Merger Agreement, the obligations of each party to complete the Merger depended on the satisfaction (or, to the extent permitted by applicable law, waiver) of the certain closing conditions, including, among others, approvals of the Merger by all requisite regulatory authorities; absence of a material adverse effect, which had not been appropriately cured; compliance by each of Longevity and 4D Pharma with their respective material obligations set forth in the Merger Agreement; and the representations and warranties made by Longevity and 4D Pharma in the Merger Agreement being true and accurate, in all material aspects. The Merger was consummated on March 22, 2021.

At closing, Longevity merged with and into Dolphin Merger Sub Limited ("**Merger Sub**"), our new wholly owned subsidiary, with Merger Sub continuing as the surviving company. Each of Longevity's common shares issued and outstanding prior to the effective time of the merger (excluding shares held by the Company and Longevity and dissenting shares, if any) was automatically converted into the right to receive certain per share merger consideration (as defined below), and each warrant to purchase Longevity's ordinary shares and right to receive Longevity's ordinary shares that was outstanding immediately prior to the effective time of the merger was assumed by us and automatically converted into a warrant to purchase our ordinary shares and a right to receive our ordinary shares, payable in our ADSs, respectively. The per share merger consideration consisted of 7.5315 ordinary shares, payable in ADSs (each ADS representing 8 ordinary shares), for each issued and outstanding ordinary share of Longevity. Longevity had $11.6 million at the time of the merger after paying all of its debtors.

PIPE Subscription Agreement

On March 16, 2021, we entered into subscription agreements (the "**Subscription Agreements**") with certain accredited investors (collectively, the "**PIPE Investors**") pursuant to, and on the terms and subject to the conditions of which, the PIPE Investors collectively subscribed for 16,367,332 ordinary shares at a share price of £1.10 ($1.53) per share for an aggregate investment amount equal to £18.0 million ($25.0 million) (the "**PIPE Investment**"). On April 16, 2021, a further £1.4 million ($2.0 million) was raised through the issuance of 1,317,680 ordinary shares at a share price of £1.10 ($1.52) per share to Duncan Peyton and Alexander Stevenson, the Company's CEO and CSO, respectively.

The Subscription Agreements for the PIPE Investors provide for certain registration rights. In particular, we were required to no later than 30 calendar days following the consummation of the Merger (the "**Filing Deadline**"), submit to or file with the SEC a registration statement registering the resale of the shares sold pursuant to the Subscription Agreements. Additionally, we were required to use commercially reasonable efforts to have the registration statement declared effective as soon as practicable after the filing thereof, but no later than the earlier of (i) the 60th calendar day (or 90th calendar day if the SEC notifies us that it will "review" the registration statement) following the Filing Deadline and (ii) the 10th business day after the date 4D Pharma is notified (orally or in writing, whichever is earlier) by the SEC that the registration statement will not be "reviewed" or will not be subject to further review. We must use commercially reasonable efforts to keep the registration statement effective until the earliest of: (a) the date on which the registrable shares held by the PIPE Investors may be resold without volume or manner of sale limitations pursuant to Rule 144 promulgated under the Securities Act of 1933, as amended, and without the requirement for us to be in compliance with the current public information required under Rule 144(c)(2) (or Rule 144(i)(2), if applicable), (b) the date on which all registrable shares have actually been sold and (c) the date which is three years after the closing of the Merger. The Subscription Agreement contains customary indemnification provisions with respect to the registration statement.

The Subscription Agreements would terminate with no further force and effect upon the earliest to occur of: (a) such time as we notified the PIPE Investors in writing, or publicly disclosed, that we did not intend to consummate the Merger or the PIPE Investment, (b) such date and time as the Merger Agreement was terminated in accordance with its terms without the Merger being consummated, (c) upon the mutual written agreement of 4D Pharma and each of the PIPE Investors to terminate the Subscription Agreements or (d) April 29, 2021 if the Merger had not been completed on or before such date.

Loan Agreement

In July 2021, we entered into an agreement with Oxford Finance Luxembourg S.À.R.L. providing for a term loan facility maturing on July 1, 2026 in an aggregate principal amount of up to $30.0 million. $12.5 million of such term loan was available and borrowed on the closing date. $7.5 million of such term loan is available upon the achievement of certain milestones. The remaining $10 million of such term loan is uncommitted and available at the discretion of the Lenders. The proceeds of the term loans may be used for general corporate purposes.

Collaboration Agreements

For a description of our material collaboration agreements, please see "Item 4. Information on the Company—B. Business Overview—Collaborations."

D. Exchange Controls

There are no governmental laws, decrees, regulations or other legislation in the United Kingdom that may affect the import or export of capital, including the availability of cash and cash equivalents for use by us, or that may affect the remittance of dividends, interest, or other payments by us to non-resident holders of our ordinary shares or ADSs, other than withholding tax requirements. There is no limitation imposed by English law or in the Articles on the right of non-residents to hold or vote shares.

E. TAXATION

U.S. Federal Income Taxes

The following is a summary of the material U.S. federal income tax consequences to U.S. Holders (as defined below) of purchasing, owing and disposing of the ADSs, ordinary shares or warrants. This discussion is included for general informational purposes only, does not purport to consider all aspects of U.S. federal income taxation that might be relevant to a U.S. Holder, and does not constitute, and is not, a tax opinion for or tax advice to any particular U.S. Holder ADS, ordinary shares or warrants. The summary does not address any U.S. tax matters other than those specifically discussed. The summary is based on the provisions of the Code, existing, temporary and proposed Treasury Regulations issued thereunder, judicial decisions and administrative rulings and pronouncements and other legal authorities, all as of the date hereof and all of which are subject to change, possibly with retroactive effect. Any such change could alter the tax consequences described herein.

The discussion below applies only to U.S Holders as capital assets within the meaning of Section 1221 of the Code (generally, property held for investment), and does not address the tax consequences that may be relevant to U.S. Holders who, in light of their particular circumstances, may be subject to special tax rules, including without limitation:

- insurance companies, tax-exempt organizations, regulated investment companies, real estate investment trusts, brokers or dealers in securities or foreign currencies, banks and other financial institutions, mutual funds, retirement plans, traders in securities that elect to mark to market, certain former U.S. citizens or long-term residents;
- U.S. Holders that are classified for U.S. federal income tax purposes as partnerships and other pass-through entities and investors therein;
- U.S. Holders who hold ADSs, ordinary shares or warrants as part of a hedge, straddle, constructive sale, conversion, or other integrated or risk-reduction transaction, as "qualified small business stock," within the meaning of Section 1202 of the Code or as Section 1244 stock for purposes of the Code;
- U.S. Holders who hold ADSs, ordinary shares or warrants through individual retirement or other tax-deferred accounts;
- U.S. Holders that have a functional currency other than the U.S. dollar;
- U.S. Holders who are subject to the alternative minimum tax provisions of the Code or the tax on net investment income imposed by Section 1411 of the Code;

- U.S. Holders who acquire their ADSs, ordinary shares or warrants pursuant to any employee share option or otherwise as compensation;

- U.S. Holders required to accelerate the recognition of any item of gross income with respect to their ADSs, ordinary shares or warrants as a result of such income being recognized on an applicable financial statement; or

- U.S. Holders who hold or held, directly or indirectly, or are treated as holding or having held under applicable constructive attribution rules, 10% or more of the stock of 4D Pharma, measured by voting power or value.

  Any such U.S. Holders should consult their own tax advisors.

For purposes of this discussion, a "U.S. Holder" means a holder of ADS, ordinary shares or warrants that is or is treated as, for U.S. federal income tax purposes, (i) an individual citizen or resident of the United States, (ii) a corporation (or other entity taxable as a corporation for U.S. federal income tax purposes) created or organized in or under the laws of the United States, any State thereof or the District of Columbia or any entity treated as such for U.S. federal income tax purposes, (iii) an estate the income of which is subject to U.S. federal income taxation regardless of its source, or (iv) a trust (A) the administration over which a U.S. court exercises primary supervision and all of the substantial decisions of which one or more U.S. persons have the authority to control, or (B) that has a valid election in effect under the applicable Treasury Regulations to be treated as a U.S. person under the Code.

If a partnership or other pass-through entity (including any entity or arrangement treated as such for purposes of U.S. federal income tax law) holds ADS, ordinary shares or warrants, the tax treatment of a partner of such partnership or member of such entity will generally depend upon the status of the partner and the activities of the partnership. Partnerships and other pass-through entities holding ADS, ordinary shares or warrants, and any person who is a partner or member of such entities should consult their own tax advisors regarding the tax consequences of purchasing, owning and disposing of the ADSs, ordinary shares or warrants.

Passive Foreign Investment Company Considerations

A non-U.S. corporation, such as 4D Pharma, will be classified as a PFIC for U.S. federal income tax purposes, if, in the case of any particular taxable year, either (i) 75% or more of its gross income for such taxable year consists of certain types of "passive" income or (ii) 50% or more of the value of its assets (based on an average of the quarterly values of the assets) during such taxable year is attributable to assets that produce or are held for the production of passive income. For this purpose, cash is categorized as a passive asset and the company's unbooked intangibles associated with active business activities may generally be classified as active assets. Passive income generally includes, among other things, dividends, interest, rents, royalties, and gains from the disposition of passive assets. For this purpose, a foreign corporation will be treated as owning its proportionate share of the assets and earning its proportionate share of the income of any other non-U.S. corporation in which it owns, directly or indirectly, more than 25% (by value) of the stock.

Based upon its current income and assets and projections as to the value of the ADSs and ordinary shares, it is not presently expected that 4D Pharma will be classified as a PFIC for the 2022 taxable year or the foreseeable future.

The determination of whether 4D Pharma will be or become a PFIC will depend upon the composition of its income (which may differ from 4D Pharma's historical results and current projections) and assets and the value of its assets from time to time, including, in particular the value of its goodwill and other unbooked intangibles (which may depend upon the market value of the ADSs or ordinary shares from time to time and may be volatile). Among other matters, if our market capitalization is less than anticipated or subsequently declines, we may be classified as a PFIC for the taxable year in which the Merger occurs or future taxable years. It is also possible that the IRS may challenge the classification or valuation of 4D Pharma's assets, including its goodwill and other unbooked intangibles, or the classification of certain amounts received by 4D Pharma, including from JPMorgan, as depositary, which may result in 4D Pharma being, or becoming classified as, a PFIC for the taxable year in 2021 or future taxable years.

The determination of whether 4D Pharma will be or become a PFIC may also depend, in part, on how, and how quickly, it uses liquid assets and the cash acquired from Longevity in the Merger or otherwise. If 4D Pharma were to retain significant amounts of liquid assets, including cash, the risk of 4D Pharma being classified as a PFIC may substantially increase. Because there are uncertainties in the application of the relevant rules and PFIC status is a factual determination made annually after the close of each taxable year, there can be no assurance that 4D Pharma will not be a PFIC for the 2021 taxable year or any future taxable year, and no opinion of counsel has or will be provided regarding the classification of 4D Pharma as a PFIC. If 4D Pharma were classified as a PFIC for any year during which a holder held 4D Pharma ADSs or ordinary shares, it generally would continue to be treated as a PFIC for all succeeding years during which such holder held the ADSs or ordinary shares.

The discussion below under "—Dividends Paid on ADSs or Ordinary Shares" and "—Sale or Other Disposition of ADSs or Ordinary Shares" is written on the basis that 4D Pharma will not be classified as a PFIC for U.S. federal income tax purposes.

Dividends Paid on ADSs or Ordinary Shares

Subject to the PFIC rules described below, any cash distributions (including constructive distributions) paid on the ADSs or ordinary shares out of 4D Pharma's current or accumulated earnings and profits, as determined under U.S. federal income tax principles, will generally be includible in the gross income of a U.S. Holder as dividend income on the day actually or constructively received by the U.S. Holder, in the case of ordinary shares, or by the depositary bank, in the case of ADSs. Because 4D Pharma does not intend to determine its earnings and profits on the basis of U.S. federal income tax principles, any distribution will generally be treated as a "dividend" for U.S. federal income tax purposes. Under current law, a non-corporate recipient of a dividend from a "qualified foreign corporation" will generally be subject to tax on the dividend income at the lower applicable net capital gains rate rather than the marginal tax rates generally applicable to ordinary income provided that certain holding period and other requirements are met.

A non-U.S. corporation (other than a corporation that is classified as a PFIC for the taxable year in which the dividend is paid or the preceding taxable year) will generally be considered to be a qualified foreign corporation (i) if it is eligible for the benefits of a comprehensive tax treaty with the United States which the Secretary of Treasury of the United States determines is satisfactory for purposes of this provision and which includes an exchange of information program, or (ii) with respect to any dividend it pays on stock (or ADSs in respect of such stock) which is readily tradable on an established securities market in the United States. 4D Pharma believes it is eligible for the benefits of the Convention Between the Government of the United States of America and the Government of the United Kingdom of Great Britain and Northern Ireland for the Avoidance of Double Taxation and the Prevention of Fiscal Evasion with Respect to Taxes on Income and On Capital Gains, or the United States-United Kingdom income tax treaty (which the Secretary of the Treasury of the United States has determined is satisfactory for this purpose and includes an exchange of information program), in which case it would be treated as a qualified foreign corporation with respect to dividends paid on the ordinary shares or ADSs. U.S. Holders are urged to consult their tax advisors regarding the availability of the reduced tax rate on dividends in their particular circumstances. Dividends received on the ADSs or ordinary shares will not be eligible for the dividends received deduction allowed to corporations.

Constructive Distributions on 4D Pharma Warrants

The terms of each 4D Pharma warrant provide for an adjustment to the number of ADSs for which the warrant may be exercised or to the exercise price of the warrant in certain events. An adjustment which has the effect of preventing dilution generally is not taxable. However, a U.S. Holder of a 4D Pharma warrant would be treated as receiving a constructive distribution from 4D Pharma if, for example, the adjustment increases the U.S. Holder's proportionate interest in 4D Pharma's assets or earnings and profits (e.g., through an increase in the number of ordinary shares that would be obtained upon exercise) as a result of a distribution of cash to the holders of 4D Pharma's ADSs or ordinary shares which is taxable to the holders of such ADSs or ordinary shares as described under "-Dividends Paid on ADSs or Ordinary Shares" above. Such constructive distribution would be subject to tax as described under that section in the same manner as if the U.S. Holder of a 4D Pharma warrant received a cash distribution from us equal to the fair market value of such increased interest. For certain information reporting purposes, 4D Pharma is required to determine the date and amount of any such constructive distributions. Proposed Treasury regulations, which 4D Pharma may rely on prior to the issuance of final regulations, specify how the date and amount of constructive distributions are determined.

Sale or Other Disposition of ADSs or Ordinary Shares

Subject to the PFIC rules discussed below, a U.S. Holder of 4D Pharma ADSs or ordinary shares will generally recognize capital gain or loss, if any, upon the sale or other disposition of ADSs or ordinary shares in an amount equal to the difference between the amount realized upon the disposition and the U.S. Holder's adjusted tax basis in such ADSs or ordinary shares. Any capital gain or loss will be long-term capital gain or loss if the ADSs or ordinary shares have been held for more than one year and will generally be United States source capital gain or loss for United States foreign tax credit purposes. Long-term capital gains of non-corporate taxpayers are currently eligible for reduced rates of taxation.

Acquisition of 4D Pharma ADSs or Ordinary Shares Pursuant to a 4D Pharma Warrant

Subject to the PFIC rules discussed below, a U.S. Holder of a 4D Pharma warrant generally will not recognize gain or loss upon the exercise of a warrant for cash. An ADS or ordinary share acquired pursuant to the exercise of a 4D Pharma warrant for cash generally will have a tax basis equal to the U.S. Holder's tax basis in the warrant, increased by the amount paid to exercise the warrant. If a 4D Pharma warrant is allowed to lapse unexercised, a U.S. Holder of a warrant generally will recognize a capital loss equal to such holder's tax basis in the warrant.

Although not entirely clear, a cashless exercise of a 4D Pharma warrant should be treated as a tax-free recapitalization for U.S. federal income tax purposes. In that case, a U.S. Holder's tax basis in the ADSs or ordinary shares received generally would equal the U.S. Holder's tax basis in the 4D Pharma warrants and the holding period of the ADS or ordinary shares would include the holding period in the warrants.

U.S. Holders of 4D Pharma warrants should consult their tax advisors regarding the tax consequences of a cashless exercise.

Passive Foreign Investment Company Rules

If 4D Pharma is classified as a PFIC for any taxable year during which a U.S. Holder holds the 4D Pharma ADSs, ordinary shares or warrants, unless the holder makes a mark-to-market election (as described below), the holder will, except as discussed below, be subject to special tax rules that have a penalizing effect, regardless of whether 4D Pharma remains a PFIC, on (i) any excess distribution that 4D Pharma make to the holder (which generally means any distribution paid during a taxable year to a holder that is greater than 125% of the average annual distributions paid in the three preceding taxable years or, if shorter, the holder's holding period for the ADSs or ordinary shares), and (ii) any gain realized on the sale or other disposition, including, under certain circumstances, a pledge, of 4D Pharma ADSs, ordinary shares or warrants. Under the PFIC rules:

- The excess distribution and/or gain will be allocated ratably over the U.S. Holder's holding period for the ADSs, ordinary shares or warrants;
- The amount of the excess distribution or gain allocated to the taxable year of the distribution or disposition and any taxable years in the U.S. Holder's holding period prior to the first taxable year in which 4D Pharma is classified as a PFIC, or a pre-PFIC year, will be taxable as ordinary income; and
- The amount of the excess distribution or gain allocated to each taxable year other than the taxable year of the distribution or disposition or a pre-PFIC year, will be subject to tax at the highest tax rate in effect applicable to the individuals or corporations, and the interest charge generally applicable to underpayments of tax will be imposed on the resulting tax attributable to each such year.

If 4D Pharma is a PFIC for any taxable year during which a U.S. Holder holds the 4D Pharma ADSs, ordinary shares or warrants and any of its non-United States subsidiaries is also a PFIC, such holder would be treated as owning a proportionate amount (by value) of the shares of the lower-tier PFIC for purposes of the application of these rules. Each U.S. Holder is advised to consult its tax advisors regarding the application of the PFIC rules to any of 4D Pharma's subsidiaries.

As an alternative to the foregoing rules, a U.S. Holder of "marketable stock" in a PFIC may make a mark-to-market election with respect to such stock. The ADSs are expected to be treated as "marketable stock" for this purpose, provided that the ADSs are "regularly traded" (as specially defined under the Code) on The Nasdaq Global Market. No assurances may be given regarding whether the ADSs will qualify, or will continue to be qualified, as being regularly traded in this regard. If a mark-to-market election is made, the U.S. Holder will generally (i) include as ordinary income for each taxable year that 4D Pharma is a PFIC the excess, if any, of the fair market value of ADSs held at the end of the taxable year over the adjusted tax basis of such ADSs and (ii) deduct as an ordinary loss the excess, if any, of the adjusted tax basis of the ADSs over the fair market value of such ADSs held at the end of the taxable year, but only to the extent of the net amount previously included in income as a result of the mark-to-market election. The U.S. Holder's adjusted tax basis in the ADSs would be adjusted to reflect any income or loss resulting from the mark-to-market election. If a U.S. Holder makes an effective mark-to-market election, in each year that 4D Pharma is a PFIC any gain recognized upon the sale or other disposition of the ADSs will be treated as ordinary income and loss will be treated as ordinary loss, but only to the extent of the net amount previously included in income as a result of the mark-to-market election. U.S. Holders of 4D Pharma's ordinary shares should consult their tax advisors regarding the availability of a mark-to-market election with respect to such ordinary shares.

If a U.S. Holder makes a mark-to-market election in respect of a corporation classified as a PFIC and such corporation ceases to be classified as a PFIC, the holder will not be required to take into account the mark-to-market gain or loss described above during any period that such corporation is not classified as a PFIC.

Because a mark-to-market election cannot be made for any lower-tier PFICs that a PFIC may own, a U.S. Holder who makes a mark-to-market election with respect to the ADSs may continue to be subject to the general PFIC rules with respect to such holder's indirect interest in any of 4D Pharma's non-United States subsidiaries that is classified as a PFIC.

4D Pharma does not intend to provide information necessary for U.S. Holders to make qualified electing fund elections, which, if available, would result in tax treatment different from the general tax treatment for PFICs described above. However, as described above under "Passive Foreign Investment Company Considerations-PFIC Classification of 4D Pharma," it is not presently expected that 4D Pharma will be classified as a PFIC for the 2022 taxable year or the foreseeable future.

As discussed above under "*Dividends Paid on ADSs or Ordinary Shares*", dividends that 4D Pharma pays on the ADSs or ordinary shares will not be eligible for the reduced tax rate that applies to qualified dividend income if 4D Pharma is classified as a PFIC for the taxable year in which the dividend is paid or the preceding taxable year. In addition, if a U.S. Holder owns the ADSs or ordinary shares during any taxable year that 4D Pharma is a PFIC, the holder must file an annual information return with the IRS. Each holder is urged to consult its tax advisor concerning the U.S. federal income tax consequences of purchasing, holding, and disposing ADSs or ordinary shares if 4D Pharma is or become a PFIC, including the possibility of making a mark-to-market election and the unavailability of the qualified electing fund election.

Information reporting and backup withholding

Certain U.S. Holders are required to report information to the IRS relating to an interest in "specified foreign financial assets," including shares and warrants issued by a non-U.S. corporation, for any year in which the aggregate value of all specified foreign financial assets exceeds $50.0 thousand (or a higher U.S. dollar amount prescribed by the IRS), subject to certain exceptions (including an exception for shares held in custodial accounts maintained with a United States financial institution). These rules also impose penalties if a holder is required to submit such information to the IRS and fails to do so.

In addition, U.S. Holders may be subject to information reporting to the IRS and backup withholding with respect to dividends on and proceeds from the sale or other disposition of the 4D Pharma's ADSs, ordinary shares or warrants. Information reporting will apply to payments of dividends on, and to proceeds from the sale or other disposition of, 4D Pharma's ADSs, ordinary shares or warrants by a paying agent within the United States to a holder, other than holders that are exempt from information reporting and properly certify their exemption. A paying agent within the United States will be required to withhold at the applicable statutory rate, currently 24%, in respect of any payments of dividends on, and the proceeds from the disposition of, 4D Pharma's ADSs, ordinary shares or warrants within the U.S. to a U.S. Holder (other than holders that are exempt from backup withholding and properly certify their exemption) if the holder fails to furnish its correct taxpayer identification number or otherwise fails to comply with applicable backup withholding requirements. U.S. Holders who are required to establish their exempt status generally must provide a properly completed IRS Form W-9.

Backup withholding is not an additional tax. Amounts withheld as backup withholding may be credited against a holder's U.S. federal income tax liability. A U.S. Holder generally may obtain a refund of any amounts withheld under the backup withholding rules by filing the appropriate claim for refund with the IRS in a timely manner and furnishing any required information. Each U.S. Holder is advised to consult with its tax advisor regarding the application of the United States information reporting rules to their particular circumstances.

Material United Kingdom Tax Considerations

The following is a description of the material U.K. tax considerations relating primarily to the ownership and disposal of our ADSs by the U.S. Holders described above. The U.K. tax comments set out below are based on current U.K. tax law as applied in England and Wales, and HMRC practice (which may not be binding on HMRC) as at the date of this summary, both of which are subject to change, possibly with retrospective effect. They are intended as a general guide and, save where otherwise stated, only apply to you if you are not resident in the U.K. for U.K. tax purposes and do not hold our ADSs for the purposes of a trade, profession or vocation that you carry on in the U.K. through a branch, agency or permanent establishment in the U.K. and if you hold our ADSs as an investment for U.K. tax purposes and are not subject to special rules.

This summary does not address all possible tax consequences relating to an investment in our ADSs. In particular it does not cover the U.K. inheritance tax consequences of holding our ADSs. It assumes that DTC has not made an election under section 97A(1) of the Finance Act 1986. It assumes that we do not (and will not at any time) derive 75% or more of our qualifying asset value, directly or indirectly, from U.K. land, and that we are and remain solely resident in the U.K. for tax purposes. 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 holder. Holders of our ADSs are strongly urged to consult their tax advisers in connection with the U.K. tax consequences of their investment in our ADSs.

U.K. Taxation of Dividends

We will not be required to withhold amounts for or on account of U.K. tax at source when paying a dividend in respect of our ordinary shares.

Holders who hold our ADSs as an investment, who are not resident in the U.K. for U.K. tax purposes and who do not hold their ADSs in connection with any trade, profession or vocation carried on by them in the U.K. through a branch, agency or permanent establishment in the U.K. should not be subject to U.K. tax in respect of any dividends on our ordinary shares.

U.K. Taxation of Capital Gains

An individual holder who is not resident in the U.K. for U.K. tax purposes should not be liable to U.K. capital gains tax on capital gains realized on the disposal of their ADSs unless such holder carries on a trade, profession or vocation in the U.K. through a branch or agency in the U.K. to which our ADSs are attributable.

Any such individual holder of our ADSs who is temporarily non-resident for U.K. tax purposes will, in certain circumstances, become liable to U.K. tax on capital gains in respect of gains realized while they were not resident in the U.K.

A corporate holder of our ADSs which is not resident in the U.K. for U.K. tax purposes should not be liable for U.K. corporation tax on chargeable gains realized on the disposal of our ADSs unless it carries on a trade in the U.K. through a permanent establishment in the U.K. to which our ADSs are attributable.

Stamp Duty and Stamp Duty Reserve Tax

The following statements apply to all holders, regardless of their jurisdiction of tax residence.

It is assumed for the purposes of the following statements that all transfers of, or agreements to transfer, our ordinary shares are only made at times when (i) our ordinary shares are admitted to trading on AIM but are not listed on any market (with the term "listed" being construed in accordance with section 99A of the Finance Act 1986); and (ii) AIM continues to be accepted as a "recognized growth market" (as construed in accordance with section 99A of the Finance Act 1986). Holders of our ADSs who propose to transfer, or agree to transfer, our ordinary shares during such time as these conditions are not met (including during any period between the creation and issue of our ADSs and the admission to trading of our ordinary shares on AIM) are strongly urged to obtain their own advice.

No stamp duty is payable on the issue of our ordinary shares into a depositary receipt system (such as, we understand, that operated by JPMorgan) or a clearance service (such as, we understand, DTC). No stamp duty reserve tax ("**SDRT**") should be payable on the issue of our ordinary shares into a depositary receipt system or a clearance service. Accordingly, no stamp duty or SDRT should be payable on the creation and issue of our ADSs pursuant to the issue of our ordinary shares to JPMorgan's custodian.

No stamp duty or SDRT should be payable on transfers of, or agreements to transfer, our ordinary shares into a depositary receipt system or a clearance service.

No SDRT or stamp duty should be payable on paperless transfers of, or agreements to transfer, our ADSs through the facilities of DTC.

No stamp duty should be payable on a written instrument transferring, or a written agreement to transfer, our ADSs provided the instrument or agreement is executed and remains at all times outside the U.K. No SDRT should be payable in respect of agreements to transfer our ADSs.

No stamp duty or SDRT should be payable on transfers of, or agreements to transfer, our ordinary shares outside of a depositary receipt system or a clearance service.

F. Dividend and Paying Agents

Not applicable.

G. Statement by Experts

Not applicable.

H. Documents on display

We are subject to certain of the information reporting requirements of the Exchange Act. As a foreign private issuer, we are exempt from the rules and regulations under the Exchange Act prescribing the furnishing and content of proxy statements, and our officers, directors and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act, with respect to their purchase and sale of our shares. In addition, we are not required to file reports and financial statements with the SEC as frequently or as promptly as U.S. companies whose securities are registered under the Exchange Act. However, we are required to file with the SEC, within four months after the end of each fiscal year, an annual report on Form 20-F containing financial statements audited by an independent accounting firm. We publish unaudited interim financial information every half year and furnish this half yearly information to the SEC under cover of a Form 6-K .

This annual report and the exhibits hereto and any other document we file pursuant to the Securities Act or the Exchange Act may be inspected without charge and copied at prescribed rates at the following Securities and Exchange Commission public reference rooms: 100 F Street, N.E., Room 1580, Washington, D.C. 20549; and on the Securities and Exchange Commission Internet site (http://www.sec.gov). You may obtain information on the operation of the Securities and Exchange Commission's public reference room in Washington, D.C. by calling the Securities and Exchange Commission at 1-800-SEC-0330 or by visiting the Securities and Exchange Commission's website at http://www.sec.gov, and may obtain copies of our filings from the public reference room by calling 1-800-SEC-0330. The Exchange Act file number for our Securities and Exchange Commission filings is 001-40106.

I. Subsidiary information

Not applicable.

ITEM 11. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are exposed to market risks in the ordinary course of our business. Market risk represents the risk of loss that may impact our financial position due to adverse changes in financial market prices and rates. Market risk arises from our exposure to fluctuation in interest rates and currency exchange rates. These risks are managed by maintaining an appropriate mix of cash deposits in the main currencies we operate in, placed with a variety of financial institutions for varying periods according to expected liquidity requirements.

Interest Rate Risk

As of December 31, 2021, we had cash, cash equivalents and short-term deposits of $21.0 million. Our current investment policy is to invest available cash in bank deposits with banks that have a credit rating of at least BBB. During the year ended December 31, 2021, we have not entered into investments for trading or speculative purposes. Accordingly, available longer-term cash and cash equivalents balances are held in deposits that bear interest. Given the current low rates of interest we receive, we will not be adversely affected if such rates are reduced.

As of July 29, 2021 we entered into a loan agreement with Oxford Finance S.A.R.L. and drew down $12.5 million of a facility for up to $30 million payable in three tranches. The loan includes an interest only period until either September 1, 2023 or September 1, 2024, if certain criteria are met to extend the period. Interest is payable on the loan at 8.15% plus the higher of a) 0.1% and b) the US dollar 30-day LIBOR rate, accordingly a 0.1% increase in the rate of interest (based on the shorter period noted) would result in an increase of $39 thousand over the remaining term of the loan ending in July 2026.

Foreign Currency Exchange Risk

Our market risk exposure is primarily a result of foreign currency exchange rates, which is discussed in detail in the following paragraph.

Our results of operations and cash flow are subject to fluctuations due to changes in foreign currency exchange rates. As discussed above, our liquid assets are held in a mixture of GBP, Euros and USD. Certain purchases are denominated in currencies other than GBP, such as Euros and USD. With certain subsidiaries operating in Euros and, to a lesser degree USD, there remains an underlying currency exposure. However, the historical currency differences may not be indicative of future exposure, as the business adjusts the nature and location of clinical trials and other activities.

We do not hedge our foreign currency exchange risk. In the future, we may enter into formal currency hedging transactions to decrease the risk of financial exposure from fluctuations in the exchange rates of our principal operating currencies. These measures, however, may not adequately protect us from the material adverse effects of such fluctuations.

Credit and Liquidity Risk

Our cash, cash equivalents and short-term deposits are on deposit with financial institutions with a credit rating equivalent to, or above, the main U.K. clearing banks. We invest our liquid resources based on the expected timing of expenditures to be made in the ordinary course of our activities. All financial liabilities are payable in the short term, meaning no more than three months, and we maintain adequate bank balances in either instant access or short-term deposits to meet those liabilities as they fall due. We did not have any material trade receivables as of December 31, 2021.

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 Depository Shares

JPMorgan Chase Bank, N.A. ("**JPMorgan**") is the depositary for our ADSs. Each ADS will represent an ownership interest in eight ordinary shares which we will deposit with the custodian, as agent of the depositary, under the deposit agreement among ourselves, the depositary, yourself as an ADR holder and all other ADR holders, and all beneficial owners of an interest in the ADSs evidenced by ADRs from time to time. In the future, each ADS will also represent any securities, cash or other property deposited with the depositary but which they have not distributed directly to you. Unless certificated ADRs are specifically requested by you, all ADSs will be issued on the books of our depositary in book-entry form and periodic statements will be mailed to you which reflect your ownership interest in such ADSs. In our description, references to American depositary receipts or ADRs shall include the statements you will receive which reflect your ownership of ADSs.

The depositary's office is located at 383 Madison Avenue, Floor 11, New York, NY 10179.

Fees and Expenses

The depositary may charge each person to whom ADSs are issued, including, without limitation, issuances against deposits of shares, issuances in respect of share distributions, rights and other distributions, issuances pursuant to a stock dividend or stock split declared by us or issuances pursuant to a merger, exchange of securities or any other transaction or event affecting the ADSs or deposited securities, and each person surrendering ADSs for withdrawal of deposited securities or whose ADSs are cancelled or reduced for any other reason, $5.00 for each 100 ADSs (or any portion thereof) issued, delivered, reduced, cancelled or surrendered, or upon which a share distribution or elective distribution is made or offered, as the case may be. The depositary may sell (by public or private sale) sufficient securities and property received in respect of a share distribution, rights and/or other distribution prior to such deposit to pay such charge. Notwithstanding the foregoing, the depositary has agreed to waive the issuance fee in respect of ADSs issued pursuant to the merger.

The following additional charges shall also be incurred by the ADR holders and beneficial owners of ADSs, by any party depositing or withdrawing shares or by any party surrendering ADSs and/or to whom ADSs are issued (including, without limitation, issuance pursuant to a stock dividend or stock split declared by us or an exchange of stock regarding the ADSs or the deposited securities or a distribution of ADSs), whichever is applicable:

- a fee of U.S.$1.50 per ADR or ADRs for transfers of certificated or direct registration ADRs;
- a fee of up to U.S.$0.05 per ADS held upon which any cash distribution made pursuant to the deposit agreement or in the case of an elective cash/stock dividend, upon which a cash distribution or an issuance of additional ADSs is made as a result of such elective dividend;

- an aggregate fee of up to U.S.$0.05 per ADS per calendar year (or portion thereof) for services performed by the depositary in administering the ADRs (which fee may be charged on a periodic basis during each calendar year and shall be assessed against ADR holders as of the record date or record dates set by the depositary during each calendar year and shall be payable in the manner described in the next succeeding provision);

- a fee for the reimbursement of such fees, charges and expenses as are incurred by the depositary and/or any of its agents (including, without limitation, the custodian and expenses incurred on behalf of ADR holders in connection with compliance with foreign exchange control regulations or any law, rule or regulation relating to foreign investment) in connection with the servicing of the shares or other deposited securities, the sale of securities (including, without limitation, deposited securities), the delivery of deposited securities or otherwise in connection with the depositary's or its custodian's compliance with applicable law, rule or regulation (which fees and charges shall be assessed on a proportionate basis against ADR holders as of the record date or dates set by the depositary and shall be payable at the sole discretion of the depositary by billing such ADR holders or by deducting such charge from one or more cash dividends or other cash distributions);

- a fee for the distribution of securities (or the sale of securities in connection with a distribution), such fee being in an amount equal to the $0.05 per ADS issuance fee for the execution and delivery of ADSs which would have been charged as a result of the deposit of such securities (treating all such securities as if they were shares) but which securities or the net cash proceeds from the sale thereof are instead distributed by the depositary to those ADR holders entitled thereto;

- stock transfer or other taxes and other governmental charges;

- SWIFT, cable, telex and facsimile transmission and delivery charges incurred at your request in connection with the deposit or delivery of shares, ADRs or deposited securities;

- transfer or registration fees for the registration of transfer of deposited securities on any applicable register in connection with the deposit or withdrawal of deposited securities; and

- fees of any division, branch or affiliate of the depositary utilized by the depositary to direct, manage and/or execute any public and/or private sale of securities under the deposit agreement.

To facilitate the administration of various depositary receipt transactions, including disbursement of dividends or other cash distributions and other corporate actions, the depositary may engage the foreign exchange desk within JPMorgan Chase Bank, N.A. (the "**Bank**") and/or its affiliates in order to enter into spot foreign exchange transactions to convert foreign currency into U.S. dollars ("**FX Transactions**"). For certain currencies, FX Transactions are entered into with the Bank or an affiliate, as the case may be, acting in a principal capacity. For other currencies, FX Transactions are routed directly to and managed by an unaffiliated local custodian (or other third-party local liquidity provider), and neither the Bank nor any of its affiliates is a party to such FX Transactions.

The foreign exchange rate applied to an FX Transaction will be either (i) a published benchmark rate, or (ii) a rate determined by a third-party local liquidity provider, in each case plus or minus a spread, as applicable. The depositary will disclose which foreign exchange rate and spread, if any, apply to such currency on the "Disclosure" page (or Successor page) of www.adr.com (as updated by the depositary from time to time, "**ADR.com**"). Such applicable foreign exchange rate and spread may (and neither the depositary, the Bank nor any of their affiliates is under any obligation to ensure that such rate does not) differ from rates and spreads at which comparable transactions are entered into with other customers or the range of foreign exchange rates and spreads at which the Bank or any of its affiliates enters into foreign exchange transactions in the relevant currency pair on the date of the FX Transaction. Additionally, the timing of execution of an FX Transaction varies according to local market dynamics, which may include regulatory requirements, market hours and liquidity in the foreign exchange market or other factors. Furthermore, the Bank and its affiliates may manage the associated risks of their position in the market in a manner they deem appropriate without regard to the impact of such activities on us, the depositary, ADR holders or beneficial owners of ADSs. The spread applied does not reflect any gains or losses that may be earned or incurred by the Bank and its affiliates as a result of risk management or other hedging related activity. Notwithstanding the foregoing, to the extent we provide U.S. dollars to the depositary, neither the Bank nor any of its affiliates will execute an FX Transaction as set forth herein. In such case, the depositary will distribute the U.S. dollars received from us.

Further details relating to the applicable foreign exchange rate, the applicable spread and the execution of FX Transactions will be provided by the depositary on ADR.com. We and by holding an ADS or an interest therein, ADR holders and beneficial owners of ADSs will each be acknowledging and agreeing that the terms applicable to FX Transactions disclosed from time to time on ADR.com will apply to any FX Transaction executed pursuant to the deposit agreement.

We will pay all other charges and expenses of the depositary and any agent of the depositary (except the custodian) pursuant to agreements from time to time between us and the depositary.

The fees and charges you may be required to pay may vary over time and may be changed by us and by the depositary. ADR holders will receive prior notice of the increase in any such fees and charges. The right of the depositary to charge and receive payment of fees, charges and expenses as provided above shall survive the termination of the deposit agreement.

The depositary may make available to us a set amount or a portion of the depositary fees charged in respect of the ADR program or otherwise upon such terms and conditions as we and the depositary may agree from time to time. The depositary collects its fees for issuance and cancellation of ADSs directly from investors depositing shares or surrendering ADSs for the purpose of withdrawal or from intermediaries acting for them. The depositary collects fees for making distributions to investors by deducting those fees from the amounts distributed or by selling a portion of distributable property to pay the fees. The depositary may collect its annual fee for depositary services by deduction from cash distributions, or by directly billing investors, or by charging the book-entry system accounts of participants acting for them. The depositary will generally set off the amounts owing from distributions made to ADR holders. If, however, no distribution exists and payment owing is not timely received by the depositary, the depositary may refuse to provide any further services to ADR holders that have not paid those fees and expenses owing until such fees and expenses have been paid. At the discretion of the depositary, all fees and charges owing under the deposit agreement are due in advance and/or when declared owing by the depositary.

PART II

ITEM 13. DEFAULTS, DIVIDEND ARREARAGES AND DELINQUENCIES

None.

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

None.

ITEM 15. CONTROLS AND PROCEDURES

A. Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act and regulations promulgated thereunder) 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 effective in recording, processing, summarizing and reporting, on a timely basis, information required to be included in periodic filings under the Exchange Act and that such information is accumulated and communicated to management, including our Chief Executive Officer and Chief Financial Officer, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure.

In connection with the annual review of our accounts, management and the Audit Committee, with the assistance of independent advisors, began an investigation of certain accounting matters related to the Company's previously issued interim financial statements. On February 18, 2022, we issued a restatement of our Unaudited Condensed Consolidated Interim Financial Statements as of June 30, 2021 and for the six-months ended June 30, 2021. We also evaluated the findings identified by this investigation and concluded that material weaknesses existed as of June 30, 2021 related to the control environment, including an insufficient complement of personnel, and information and communication. We immediately took action to remediate such material weakness including implementing additional, timelier, review procedures within its accounting and finance department and hiring additional accounting resources and consulting with more specialist technical experts. In part as a result of the measures we implemented, during the evaluation of the effectiveness of our disclosure controls and procedures carried out as of the end of the period covered by this Annual Report, as described above, our Chief Executive Officer and Chief Financial Officer have concluded that, as of December 31, 2021, our disclosure controls and procedures were effective.

B. Management's Annual Report on Internal Control over Financial Reporting

Our management are responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act as a process designed by, or under the supervision of, a company's principal executive officer and principal financial officer, or persons performing similar functions, and effected by a company's board of directors, management, and other personnel, 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 and includes those policies and procedures that:

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of a company's assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that a company's receipts and expenditures are being made only in accordance with authorizations of the company's management and directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our 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. 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.

Under the supervision of and with the participation of our principal executive officer and principal financial officer, our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2021 based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control—Integrated Framework (2013). Based on this assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2021.

C. Attestation Report of the Registered Public Accounting Firm

This annual report does not include an attestation report of our independent registered public accounting firm regarding internal control over financial reporting due to an exemption for EGCs provided in the JOBS Act.

D. Changes in Internal Control Over Financial Reporting

We have strengthened our internal and financial reporting controls through the appointment, in March 2021, of Paul Maier as a non-executive director and independent "audit committee financial expert". Also in March 2021 appointed John Beck as our CFO before his passing in in June 2021. In January 2022 we appointed John Doyle as our CFO.

ITEM 16.

[Reserved]

ITEM 16A. AUDIT COMMITTEE FINANCIAL EXPERT

Our board has determined that Mr. Paul Maier qualifies to serve as an "audit committee financial expert" as defined under the SEC rules, and has the requisite financial sophistication as defined under the applicable Nasdaq rules and regulations. Mr. Paul Maier also qualifies as an independent director under the corporate governance standards of the Nasdaq listing requirements and the audit committee independence requirements of Rule 10A-3 of the Exchange Act. For more information see "Item 6. Directors, Senior Management and Employees—C. Board Practices—Committees—Audit and Risk Committee."

ITEM 16B. CODE OF ETHICS

Code of Business Conduct and Ethics and Anti-Bribery and Anti-Corruption Policy

We have adopted a Code of Business Conduct and Ethics applicable to all of our directors, executive officers and employees, including our Chief Executive Officer, Chief Financial Officer, controller or principal accounting officer, or other persons performing similar functions, which is a code of ethics as defined in Item 16B of Form 20-F promulgated by the SEC. The full text of the Code of Business Conduct can be found on our website at www.4dpharmaplc.com. Information contained on, or that can be accessed through, our website does not constitute a part of this report and is not incorporated by reference herein. If we make any amendment to the Code of Business Conduct and Ethics or grant any waivers, including any implicit waiver, from a provision of such Code of Business Conduct and Ethics, we will disclose the nature of such amendment or waiver on our website to the extent required by the rules and regulations of the SEC. Under Item 16B of Form 20-F, if a waiver or amendment of the Code of Business Conduct and Ethics applies to our principal executive officer, principal financial officer, principal accounting officer or controller and relates to standards promoting any of the values described in Item 16B(b) of Form 20-F, we are required to disclose such waiver or amendment on our website in accordance with the requirements of Instruction 4 to such Item 16B.

ITEM 16C. PRINCIPAL ACCOUNTING FEES AND SERVICES

Our consolidated financial statements have been prepared in accordance with GAAP and were audited by RSM US LLP, an independent registered public accounting firm registered with the Public Company Accounting Oversight Board in the United States.

RSM US LLP, has served as our independent registered public accounting firm for the three years ended December 31, 2021, 2020 and 2019, for which audited financial statements appear in this annual report.

The following table provides information regarding fees paid by us to RSM US LLP for all services, for the years ended December 31, 2019, 2020 and 2021:

	Year Ended December 31,		
	2019(1)	2020	2021
	(in thousands of dollars)		
Audit fees(2)	$ 375	$ 170	$ 282
Audit related fees(3)	205	-	85
Other fees	5	-	-
Audit and other fees of affiliated entities(4)	$ 73	$ 80	$ 94
Total fees	$ 658	$ 250	$ 461

(1) 2019 audit fees included those incurred for the U.S. GAAP audit of the 2018 accounts
(2) Includes professional services rendered in connection with the audit of our annual financial statements, review of our interim financial statements and audits of our subsidiary accounts for 2018 and 2019.
(3) Includes professional services rendered in connection with the Merger and the planned equity fundraising.
(4) Includes fees in relation to the audit of the annual financial statements under International Financial Reporting Standards (IFRS) by RSM UK.

Pre-approval policies

The Audit and Risk Committee assesses and pre-approves all audit and non-audit services provided by the statutory auditors. The pre-approval includes the type of service and a fee budget.

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

None.

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

None.

ITEM 16F. CHANGE IN REGISTRANT'S CERTIFYING ACCOUNTANT.

None.

ITEM 16G. CORPORATE GOVERNANCE.

Foreign Private Issuer Exemption

As a foreign private issuer and as permitted by the listing requirements of Nasdaq, we rely on certain home country corporate governance practices rather than the corporate governance requirements of Nasdaq.

We qualify as a foreign private issuer and our ADSs are listed on Nasdaq. As a result, in accordance with the listing requirements of Nasdaq, we rely on home country governance requirements and certain exemptions thereunder rather than relying on the corporate governance requirements of Nasdaq. 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 intend to file quarterly reports filed with the SEC, we are not required to file such reports with the SEC as frequently or as promptly as U.S. public companies and are not required to file quarterly reports on Form 10-Q or current reports on Form 8-K that a domestic company would be required to file under the Exchange Act. Accordingly, there may be less publicly available information concerning our company than there would be if we were not a foreign private issuer.

In addition, the Listing Rules for the Nasdaq Stock Market (the "**Nasdaq Listing Rules**"), for domestic U.S. issuers require listed companies to have, among other things, a majority of their board members be independent, and to have independent director oversight of executive compensation, nomination of board members and corporate governance matters. While we currently comply, and intend to continue to comply, with these requirements, we are permitted to follow home country practice in lieu of the above requirements. Our board may in the future not include, or include fewer, independent directors than would be required if we were subject to the Nasdaq Listing Rules, or our board may decide that it is in our interest to have our committees governed by practices that would not comply with the Nasdaq Listing Rules.

We follow home country practice with regard to, among other things, quorum requirements generally applicable to general meetings of shareholders as such quorum requirements are not required under English law. In addition, our shareholders have and may authorize our board of directors to issue securities, including in connection with certain events such as the acquisition of shares or assets of another company, the establishment of or amendments to equity-based compensation plans for employees, certain private placements and directed issues at or above market price. To this extent, our practice varies from the requirements of Nasdaq Listing Rule 5635, which generally requires an issuer to obtain shareholder approval for the issuance of securities in connection with such events.

Compliance with the Quoted Companies Alliance Corporate Governance Code

We are required to follow the AIM Rules for Companies published by London Stock Exchange plc, and have adopted the Corporate Governance Code published by the Quoted Companies Alliance.

ITEM 16H. MINE SAFETY DISCLOSURE.

Not applicable.

PART III

ITEM 17. FINANCIAL STATEMENTS

Our audited consolidated financial statements are included in this annual report beginning at Page F-1.

ITEM 18. FINANCIAL STATEMENTS

We have elected to provide financial statements pursuant to Item 17.

ITEM 19. EXHIBITS

The following exhibits are filed herewith unless otherwise indicated:

Exhibit Number	Exhibit Description	Included herein	Form	Filing Date
1.1	Articles of Association of 4D pharma plc, effective as of March 18, 2021		F-4/A	01/27/21
2.1	Form of share certificate of 4D pharma plc ordinary share		F-4/A	01/27/21
2.2	Deposit Agreement among 4D pharma plc., JPMorgan Chase Bank, N.A., as depositary thereunder, and all Holders and Beneficial Owners from time to time of American Depositary Receipts issued thereunder evidencing American Depositary Shares representing deposited Shares		F-6	02/18/21
2.3	Warrant Agreement between Longevity Acquisition Corporation and Continental Stock Transfer & Trust Company, dated August 28, 2018		F-4/A	02/16/21

2.4	Form of Warrant		F-4/A	02/16/21
2.5	Description of Securities registered under Section 12 of the Securities Act of 1933, as amended	X		
4.1	Agreement and Plan of Merger by and among Longevity Acquisition Corporation, 4D pharma plc and Dolphin Merger Sub Limited, dated October 21, 2020		F-4	11/25/20
4.2	Form of Assumption Agreement among 4D pharma plc, Longevity Acquisition Corporation and Continental Stock Transfer & Trust Company		F-4/A	02/16/21
4.3#	Strategic Collaboration Agreement by and between The University of Texas M.D. Anderson Cancer Center and 4D pharma plc, dated November 10, 2017		F-4/A	01/08/21
4.4	Amendment to Strategic Collaboration Agreement by and Between The University of Texas, M.D. Anderson Cancer Center and 4D pharma plc, dated February 24, 2021		F-1/A	10/07/21
4.5#	Research Collaboration and Option to License Agreement by and between Merck Sharp & Dohme Corp. and 4D pharma plc, dated October 7, 2019		F-4/A	01/08/21
4.6	Lease Agreement by and among Bishopsgate Long Term Property Fund Nominees No. 1 Limited and Bishopsgate Long Term Property Fund Nominees No. 2 Limited and 4D pharma plc, dated May 3, 2017		F-4/A	01/27/21
4.7	Lease Agreement between Istituto Biomar and 4D Pharma Leon SLU, dated April 7, 2016		F-4/A	01/27/21
4.8+	Service Agreement between Duncan Peyton and 4D pharma plc, dated February 10, 2014		F-4/A	01/27/21
4.9+	Service Agreement between Alexander Stevenson and 4D pharma plc, dated February 10, 2014		F-4/A	01/27/21
4.11+	Service Agreement between Katrin Rupalla and 4D pharma plc, dated August 18, 2020		F-4/A	02/16/21
4.12+	Service Agreement between Sandy Macrae and 4D pharma plc, dated August 19, 2019		F-4/A	02/16/21
4.13+	Service Agreement between Edgardo Baracchini and 4D pharma plc, dated December 6, 2018		F-4/A	02/16/21
4.14	Service Agreement between John Doyle and 4D pharma plc, dated January 5, 2022	X		
4.15+	4D pharma plc 2015 Long Term Incentive Plan and related forms		F-4/A	01/27/21
4.16+	Form of lock-up agreement by and among 4D pharma plc and certain of 4D pharma's shareholders		F-4/A	01/08/21
4.17+	4D pharma plc 2021 Long Term Incentive Plan and related forms	X		
8.1	Subsidiaries of 4D pharma plc	X		
12.1	Certification Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	X		
12.2	Certification Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	X		
13.1*	Certification Pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	X		
13.2*	Certification Pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	X		
101.INS	Inline XBRL Instance Document.	X		
101.SCH	Inline XBRL Taxonomy Extension Schema.	X		
101.CAL	Inline XBRL Taxonomy Extension Schema Calculation Linkbase.	X		
101.DEF	Inline XBRL Taxonomy Extension Schema Definition Linkbase.	X		
101.LAB	Inline XBRL Taxonomy Extension Schema Label Linkbase.	X		
101.PRE	Inline XBRL Taxonomy Extension Schema Presentation Linkbase.	X		
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)	X		

+ Indicated management contract or compensatory plan
Portions of this exhibit (indicated by asterisks) have been excluded because such information is both (i) not material and (ii) would be competitively harmful if publicly disclosed.
* Furnished herewith.

4D PHARMA PLC

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and the Board of Directors of 4D pharma plc

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of 4D pharma plc and its subsidiaries (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2021, and the related notes to the consolidated financial statements (collectively, the financial statements). In our opinion, the 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 three years in the period ended December 31, 2021, in conformity with accounting principles generally accepted in the United States of America.

Emphasis of Matter - Going Concern

The accompanying 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. This raises substantial doubt about the Company's ability to continue as a going concern. Management's plans in regard to these matters also are described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's 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. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the 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 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 financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ RSM US LLP

We have served as the Company's auditor since 2020.

Boston, MA
March 31, 2022

4D PHARMA PLC
CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share amounts)

	December 31,	
	2021	**2020**
ASSETS		
Current assets:		
Cash and cash equivalents	$ 20,973	$ 11,990
Research and development tax credits receivable	9,237	4,799
Prepayments and other current assets	4,291	4,055
Total current assets	34,501	20,844
Property and equipment, net	3,973	5,082
Right-of-use assets (operating leases)	906	1,129
Intangible assets, net	6,127	6,303
Goodwill	13,018	13,489
Deferred recapitalization costs	-	2,010
Research and development tax credits receivable	269	242
Total assets	$ 58,794	$ 49,099
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 1,675	$ 4,540
Accrued expenses and other current liabilities	3,933	2,557
Operating lease liabilities, current	108	94
Deferred revenues, current	902	1,318
Total current liabilities	6,618	8,509
Long term debt, net	11,842	-
Long term operating lease liabilities, net	854	1,092
Deferred revenues, net	-	306
Deferred tax	14	18
Derivative liabilities	6,756	-
Other liabilities	294	203
Total liabilities	26,378	10,128
Commitments and Contingencies (Note 11)		
Stockholders' equity:		
Common Stock, $0.003 par value, 308,236,883 authorized; 180,300,967 and 131,467,935 shares outstanding at December 31, 2021 and 2020, respectively	646	479
Additional paid in capital	236,264	210,876
Accumulated other comprehensive loss	(24,321)	(24,149)
Accumulated deficit	(180,173)	(148,235)
Total stockholders' equity	$ 32,416	$ 38,971
Total liabilities and stockholders' equity	$ 58,794	$ 49,099

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

4D PHARMA PLC
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In thousands, except share and per share amounts)

	December 31,		
	2021	**2020**	**2019**
Revenues	$ 718	$ 690	$ 269
Operating expenses:			
Research and development	21,632	23,384	29,193
General and administrative expenses	15,888	13,015	10,380
Foreign currency losses (gains)	459	(699)	957
Total operating expenses	37,979	35,700	40,530
Loss from operations	(37,261)	(35,010)	(40,261)
Other income (expense), net:			
Interest income	1	6	78
Interest expense	(581)	-	-
Other income	4,847	4,496	6,883
Loss on issuance of securities in recapitalization transaction	(17,744)	-	-
Change in fair value of derivative liabilities	18,778	-	-
Change in fair value of contingent consideration payable	-	-	2,967
Total other income (expense), net	5,301	4,502	9,928
Net loss before income tax benefit	(31,960)	(30,508)	(30,333)
Income tax benefit	22	13	-
Net loss	(31,938)	(30,495)	(30,333)
Other comprehensive income:			
Foreign currency translation adjustment	(172)	1,566	1,113
Comprehensive loss	$ (32,110)	$ (28,929)	$ (29,220)
Net loss per common share, basic and diluted	$ (0.19)	$ (0.27)	$ (0.46)
Weighted-average number of common shares used in computing basic and diluted net loss per common share	169,523,024	114,149,743	65,493,842

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

4D PHARMA PLC
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(In thousands, except share and per share amounts)

	Common stock		Additional Paid-In	Accumulated Other Comprehensive	Accumulated	Total Stockholders'
	Shares	Amount	Capital	Loss	Deficit	Equity
Balance, December 31, 2018	65,493,842	$ 266	$ 174,036	$ (26,828)	$ (87,407)	$ 60,067
Other comprehensive income	-	-	-	1,113		1,113
Net loss	-	-	-	-	(30,333)	(30,333)
Share-based compensation	-	-	340	-	-	340
Balance, December 31, 2019	65,493,842	266	174,376	(25,715)	(117,740)	31,187
Issuance of common stock, net	65,898,400	213	32,719	-	-	32,932
Issuance of warrants	-	-	3,352	-	-	3,352
Warrant exercises	75,693	-	98	-	-	98
Other comprehensive income	-	-	-	1,566	-	1,566
Net loss	-	-	-	-	(30,495)	(30,495)
Share-based compensation	-	-	331	-	-	331
Balance, December 31, 2020	131,467,935	479	210,876	(24,149)	(148,235)	38,971
Common stock issued in recapitalization transaction	31,048,192	106	(106)	-	-	-
Issuance of common stock, net	17,685,012	61	24,739	-	-	24,800
Warrants exercised	31,859	-	44	-	-	44
Options exercised	67,969	-	-	-	-	-
Other comprehensive loss	-	-	-	(172)	-	(172)
Net loss	-	-	-	-	(31,938)	(31,938)
Share-based compensation	-	-	711	-	-	711
Balance, December 31, 2021	180,300,967	$ 646	$ 236,264	$ (24,321)	$ (180,173)	$ 32,416

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

4D PHARMA PLC
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands, except share and per share amounts)

	December 31,		
	2021	**2020**	**2019**
Cash Flows from Operating Activities:			
Net loss	$ (31,938)	$ (30,495)	$ (30,333)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	1,353	1,572	1,644
Stock based compensation	711	331	340
Loss on issuance of securities in recapitalization transaction	17,744	-	-
Change in fair value of derivative liabilities	(18,778)	-	-
Amortization of debt discount	119	-	-
Change in fair value of contingent consideration	-	-	(2,967)
Other non-cash expenses	85	13	74
Changes in assets and liabilities:			
Prepayments and other current assets	(281)	(1,168)	168
Research and development tax credits receivable	(4,586)	2,422	(939)
Accounts payable	(2,866)	2,677	(903)
Deferred revenues	(719)	(689)	2,197
Operating lease obligations	(189)	(185)	(148)
Other liabilities and accrued expenses	1,429	(1,748)	2,184
Net cash used in operating activities	(37,916)	(27,270)	(28,683)
Cash Flows from Investing Activities:			
Purchase of software	-	(19)	(73)
Purchase of property and equipment	(279)	(211)	(681)
Proceeds on disposal of assets	-	-	55
Maturities of short-term investments	-	-	12,982
Net cash (used in) provided by investing activities	(279)	(230)	12,283
Cash Flows from Financing Activities:			
Net proceeds from recapitalization transaction	9,615	-	-
Net proceeds from issuance of common stock	24,800	32,932	-
Net proceeds from issuance of warrants	-	3,352	-
Net proceeds from warrant exercises	44	98	-
Proceeds from issuance of debt	12,500	-	-
Payment of debt issuance costs	(535)	-	-
Deferred merger costs	-	(1,901)	-
Lease liability payments	(6)	(14)	(14)
Net cash provided by (used in) financing activities	46,418	34,467	(14)
Effect of exchange rate changes on cash and cash equivalents	760	(8)	1,000
Change in cash and cash equivalents	8,983	6,959	(15,414)
Cash and cash equivalents at beginning of year	11,990	5,031	20,445
Cash and cash equivalents at end of year	$ 20,973	$ 11,990	$ 5,031
Supplemental disclosures of non-cash investing and financing activities			
Cash paid for interest	$ 638	$ 224	$ 230
Lease liabilities from obtaining right-of-use assets	$ -	$ -	$ 1,446
Recognition of warrants issued with loan as debt discount	$ 181	$ -	$ -

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

NOTE 1 – NATURE OF THE BUSINESS

4D pharma plc (the "Company") and its subsidiary undertakings were established with the mission of leveraging the deep and varied interactions between the human body and the gut microbiome – the trillions of bacteria that colonize the human gastrointestinal tract – to develop an entirely novel class of drug: Live Biotherapeutics. The Company is focused on understanding how individual strains of bacteria function and how their interactions with the human host can be exploited to treat particular diseases, from cancer to asthma to conditions of the central nervous system.

The Company is incorporated in England and Wales and its operations are largely undertaken in Europe. The Company's common stock are listed on the Alternative Investment Market of the London Stock Exchange ("AIM") as "DDDD". As of March 22, 2021, the Company's common stock and warrants are also listed on Nasdaq ("LBPS" and "LBPSW") through American Depositary Shares ("ADSs") with each ADS representing 8 shares of common stock.

On March 22, 2021 the Company completed a recapitalization with Longevity Acquisition Corporation (NASDAQ: LOAC) a publicly-traded special purpose acquisition company ("SPAC"). Shareholders of LOAC received ADSs of the Company, and LOAC became a wholly-owned subsidiary of the Company. See Note 3 for further information.

Liquidity and capital resources

Since inception, the Company has incurred net losses and negative cash flows from operations. During the year ended December 31, 2021, the Company incurred a net loss of $31.9 million and used $37.9 million of cash in operations. As of December 31, 2021, the Company had an accumulated deficit of $180.2 million. Management expects to incur additional operating losses in the future as the Company continues to further develop, seek regulatory approval for and, if approved, commence commercialization of its product candidates.

As of December 31, 2021, the Company's cash and cash equivalents were $21.0 million. The Company expects that its existing cash and cash equivalents, will be sufficient to satisfy its working capital needs, capital asset purchases, outstanding commitments and other liquidity requirements associated with our existing operations into the fourth quarter of 2022, which raises substantial doubt regarding the Company's ability to continue as a going concern for a period of one year after the date that the financial statements are issued. Certain elements of the Company's operating plan to alleviate the conditions that raise substantial doubt are outside of the Company's control and cannot be included in management's evaluation under the requirements of Accounting Standards Codification (ASC) 205-40, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern. Accordingly, the Company has concluded that substantial doubt exists about the Company's ability to continue as a going concern for a period of at least twelve months from the date of the issuance of these consolidated financial statements.

The Company has historically financed its operations primarily through the sale of common stock. The Company intends to continue to raise additional capital through sales of common stock, but there can be no assurance that these funds will be available or that they are readily available at terms acceptable to the Company or in an amount sufficient to enable the Company to continue its development and commercialization of its products or sustain operations in the future.

NOTE 2 – SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

(a) Basis of presentation

The consolidated financial statements have been prepared in accordance with U.S. GAAP and include all adjustments necessary for the fair presentation of the Company's financial position for the periods presented. The consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries. All material intercompany accounts and transactions have been eliminated during the consolidation process.

(b) Functional and Reporting Currency

The functional currency of the Company and its subsidiaries (other than the foreign subsidiaries mentioned below) is the Great Britain Pound Sterling ("GBP"). The operations of the two foreign subsidiaries are conducted in EUROs. Balances denominated in, or linked to, foreign currencies are stated on the basis of the exchange rates prevailing at the balance sheet date. For foreign currency transactions included in the consolidated statement of operations and comprehensive loss, the exchange rates applicable to the relevant transaction dates are used. Transaction gains or losses arising from changes in the exchange rates used in remeasurement of such balances are carried to financing income or expenses. Assets and liabilities of the two subsidiaries are translated from their functional currency to GBP at the balance sheet date exchange rates. Income and expense items are translated at the average rates of exchange prevailing during the year. Translation adjustments are reflected in the consolidated balance sheets as a component of accumulated other comprehensive income or loss.

The reporting currency for the Company and its subsidiaries is the United States dollar ("USD"), and these consolidated financial statements are presented in USD. Dollar amounts included herein are in thousands, except per share data. Stockholders' equity is translated into USD from GBP at historical exchange rates. Assets and liabilities are translated at the exchange rates as of the balance sheet date. Income and expenses are translated at the average exchange rates prevailing during the reporting period. Adjustments resulting from translating the financial statements into USD are recorded as a separate component of accumulated other comprehensive loss in stockholders' equity.

(c) Use of estimates

The preparation of financial statements in conformity with U. S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reporting periods. Actual results could differ from those estimates and be based on events different from those assumptions. As part of these consolidated financial statements, the Company's significant estimates include (1) goodwill impairment; (2) the estimated useful lives of intangible assets and property and equipment; (3) revenue recognition, in regards to the deferred revenues; (4) the inputs used in determining the fair value of equity-based awards; (5) the inputs used in determining the fair value of derivative liabilities; and (6) valuation allowance relating to the Company's deferred tax assets.

(d) JOBS Act Accounting Election

The Company is an "emerging growth company" or "EGC", as defined in the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act"). Under the JOBS Act, an EGC can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. The Company has elected to use the extended transition period for complying with any new or revised financial accounting standards.

(e) Cash and cash equivalents and short-term investments

The Company considers all highly liquid investments that have maturities of three months or less when acquired to be cash equivalents. Cash equivalents are valued at cost, which approximates their fair value. Short-term investments comprise deposits with maturities of more than three months, but no greater than twelve months. The Company deposits its cash primarily in checking, money market accounts, as well as certificates of deposit. The Company does not generally enter into investments for trading or speculative purposes, rather to preserve its capital for the purpose of funding operations. The Company deposits its cash investments in financial institutions that it believes have high credit quality and has not experienced any losses on such accounts nor does it believe it is exposed to any unusual credit risk beyond the normal credit risk associated with commercial banking relationships. At December 31, 2021 and 2020, the Company's cash and cash equivalents were held at a number of accredited financial institutions.

(f) Concentrations of credit risks

Concentrations of credit risk have been provided for customers and suppliers who individually represent greater than 10% of the applicable measure during the periods stated.

The Company derived 100% of its revenue for the year ended December 31, 2021 from a collaboration partner. See Note 13, Revenues for additional information.

The Company had one supplier that accounted for 15% of purchases for the period ended December 31, 2021. The accounts payable balance at December 31, 2021 contained two balances which constituted 27% of the total balance outstanding at that date. The Company had two suppliers that accounted for 32% of purchases for the period ended December 31, 2020. The accounts payable balance at December 31, 2020 contained one balance which constituted 45% of the total balance outstanding at that date.

(g) Deferred Recapitalization Costs

Specific incremental legal, accounting and other fees and costs directly attributable to a proposed or actual offering of securities may properly be deferred and charged against the gross proceeds of such an offering. As of December 31, 2020, there were $2,010 of merger costs, primarily consisting of legal, accounting and printing fees, that were capitalized in assets on the consolidated balance sheet. Upon completion of the merger, these costs were charged against the gross proceeds recorded in stockholders' equity. See Note 3 for further information on the recapitalization.

(h) Fair value of financial instruments

The Company measures and discloses fair value in accordance with ASC 820, *"Fair Value,"* which defines fair value, establishes a framework and gives guidance regarding the methods used for measuring fair value, and expands disclosures about fair value measurements. Fair value is an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. As a basis for considering such assumptions there exists a three-tier fair-value hierarchy, which prioritizes the inputs used in measuring fair value as follows:

Level 1 - unadjusted quoted prices are available in active markets for identical assets or liabilities that the Company has the ability to access as of the measurement date.

Level 2 - pricing inputs are other than quoted prices in active markets that are directly observable for the asset or liability or indirectly observable through corroboration with observable market data.

Level 3 - pricing inputs are unobservable for the non-financial asset or liability and only used when there is little, if any, market activity for the non-financial asset or liability at the measurement date. The inputs into the determination of fair value require significant management judgment or estimation. Fair value is determined using comparable market transactions and other valuation methodologies, adjusted as appropriate for liquidity, credit, market and/or other risk factors.

This hierarchy requires the Company to use observable market data, when available, and to minimize the use of unobservable inputs when determining fair value.

The Company's financial instruments primarily consist of cash and cash equivalents, trade and other payables with initial maturity of up to 12 months. The estimated fair values of these financial instruments approximate their carrying values as presented, due to their short maturities. The fair value of the Company's debt approximated its recorded value as the rate of interest is readily available to the Company.

(In thousands, except share and per share amounts)

The Company's recurring fair value measurements at December 31, 2021 are as follows:

	Fair Value as of December 31,2021	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Liabilities:				
Derivative liability (Note 10)	$ 6,756	$ 2,305	$ 1,132	$ 3,319

The Company had no recurring fair value measurements at December 31, 2020.

(i) Segment information

The Company manages its operations as a single operating segment for the purposes of assessing performance and making operating decisions. The Company's singular focus is development of a disruptive class of drug – Live Biotherapeutic products (LBPs) – leveraging the profound impact of the gut microbiome on human health and disease. Long-lived assets by geography are as follows as of December 31, 2021: UK $8,796, Spain $9,328, Ireland $5,899 and United States $1. Long-lived assets by geography are as follows as of December 31, 2020: UK $9,383, Spain $10,615 and Ireland $6,004.

(j) Property and equipment

Property and equipment are recorded at cost, net of accumulated depreciation and any accumulated impairment losses. Depreciation is computed using the straight-line method over the estimated useful lives of the assets. The useful lives of property and equipment, including right-of-use assets, are as follows:

- Plant and machinery – straight line over three to ten years
- Fixtures, fitting and office equipment – straight line over four to five years
- Land and buildings – straight line over the shorter of the lease or a five to ten-year period

Upon retirement or sale, the cost of disposed assets and their related accumulated depreciation are removed from the balance sheet. Any resulting net gains or losses on dispositions of property and equipment are included as a component of operating expenses within the Company's consolidated statements of operations and comprehensive loss. Repair and maintenance costs that do not significantly add value to the property and equipment, or prolong its life, are charged to operating expense as incurred.

(k) Leases

The Company enters into operating lease arrangements for real estate assets related to office space and finance lease arrangements for vehicles and other equipment. In following ASC 842, the Company determines if an arrangement contains a lease at its inception by assessing whether there is an identified asset and whether the arrangement conveys the right to control the use of the identified asset in exchange for consideration. Lease liabilities are included in current and long-term portions for each of financing and operating leases in our consolidated balance sheets. Right-of-use assets represent our right to use an underlying asset for the lease term and lease liabilities represent our obligation to make payments arising from the lease. Lease right-of-use assets and lease liabilities are recognized at the lease commencement date based on the present value of lease payments over the lease term. Lease payments consist of the fixed payments under the arrangement. The operating lease liabilities is adjusted for any unpaid lease incentives, such as tenant improvement allowances and certain other immaterial non-lease components which have been included a practical expedient. Variable costs, such as maintenance and utilities based on actual usage, are not included in the measurement of right-to-use assets and lease liabilities but are expensed when the event determining the amount of variable consideration to be paid occurs. As the implicit rate of our leases is not determinable, we use an incremental borrowing rate ("IBR") based on the information available at the lease commencement date, including consideration to the Company's incremental borrowing rate, in determining the present value of lease payments.

The Company recognizes options to extend or terminate a lease when it is reasonably certain that the Company will exercise any such options. The operating lease expense is recognized on a straight-line basis over the lease term. We also elected the post-transition practical expedient to not separate lease components from non-lease components for all existing leases, as well as a policy to not apply the recognition requirements of ASC 842 for short-term leases with an initial term of 12 months of less.

(l) Asset Retirement Obligations

An asset retirement obligation ("ARO") represents a legal obligation associated with the retirement of a tangible long-lived asset that is incurred upon the acquisition, construction, development or normal operation of that long-lived asset. Our AROs are associated with leasehold improvements that, at the end of a lease, we are contractually obligated to remove in order to comply with certain lease agreements. The ARO balance, included in other liabilities, at December 31, 2021 and 2020 was $233 and $203, respectively, and will be subsequently adjusted for changes in fair value. The associated estimated asset retirement costs are capitalized as part of the carrying amount of the long-lived asset and depreciated over its useful life. Due to the time over which these obligations could be settled and the judgment used to determine the liability, the ultimate obligation may differ from the estimate. Upon settlement, any difference between actual cost and the estimate is recognized as a gain or loss in that period.

Accretion expense on the liability is recognized over the estimated productive life of the related assets and is included on the consolidated statements of operations under general and administrative expenses. For the years ended December 31, 2021, 2020 and 2019 accretion expense was $33, $27 and $22, respectively.

(m) Intangible assets

Goodwill

Goodwill represents the excess of the consideration transferred over the fair value of net assets of businesses acquired. Goodwill is evaluated for impairment on at least an annual basis, or more frequently if impairment indicators exist. When evaluating goodwill for impairment, the Company may first perform an assessment qualitatively whether it is more likely than not that a reporting unit's carrying amount exceeds its fair value. Under Accounting Standards Update ("ASU") 2017-04, "Intangibles - Goodwill and Other (Topic 350): *Simplifying the Test for Goodwill Impairment*," Step 2 from the goodwill impairment test has been eliminated and goodwill impairment is measured as the excess of the carrying amount of the reporting unit over its fair value.

Patents

Acquired patents are initially recorded at cost (or if initially recognised in a business combination at fair value), assigned an estimated useful life, and amortized primarily on a straight-line basis over their estimated useful lives of up to 20 years from the date of filing the patent. The Company periodically evaluates whether current facts or circumstances indicate that the carrying values of its acquired intangibles may not be recoverable. If such circumstances are determined to exist, an estimate of the undiscounted future cash flows of these assets, or appropriate asset groupings, is compared to the carrying value to determine whether an impairment exists. If the asset is determined to be impaired, the loss is measured based on the difference between the carrying value of the intangible asset and its fair value, which is determined based on the net present value of estimated future cash flows.

Acquired Research and Development (Intellectual Property)

Intellectual property that the Company acquired in conjunction with the acquisition of a business represents the fair value assigned to the research and development platforms and basis that discoveries will be made from. The amounts are capitalized and are accounted for as indefinite-lived intangible assets, subject to impairment testing until completion or abandonment of the projects. Intellectual property is evaluated for impairment on at least an annual basis, or more frequently if impairment indicators exist, by first assessing qualitative factors to determine whether it is more likely than not that the fair value of is less than carrying amount. If the Company concludes it is more likely than not that the fair value of a reporting unit is less than its carrying amount, a quantitative fair value test is performed. If the fair value is less than the carrying amount, an impairment loss is recognized in operating results.

Software

Software is recognised initially at cost. After initial recognition, these assets are carried at cost less any accumulated amortization and any accumulated impairment losses. Cost comprises the aggregate amount paid and the fair value of any other consideration given to acquire the asset and includes costs directly attributable to making the asset capable of operating as intended.

Amortization is computed by allocating the amortization amount of an asset on a systematic basis over its useful life and is applied separately to each identifiable component. Amortization is applied to software over three to five years on a straight-line basis.

(n) Impairment of Long-Lived Assets and Intangibles

Long-lived assets, such as property and equipment, right-of-use assets and definite-lived intangibles subject to amortization, are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset group to the undiscounted cash flows attributable to the asset group. If the carrying amount of an asset group exceeds its undiscounted cash flows, an impairment charge is recognized in the amount by which the carrying amount of the asset group exceeds its fair value.

(o) Research and development and expenditures

Research and development expenses include salaries and benefits, materials and supplies, preclinical and clinical trial expenses, stock-based compensation expense, depreciation of equipment, contract services and other outside expenses.

The Company has entered into various research and development-related contracts with research institutions, contract research organizations, contract manufacturers and other companies. These agreements are generally cancellable, and related payments are recorded as research and development expenses as incurred. Costs of certain development activities, such as manufacturing, pre-clinical and clinical trial expenses, are recognized based on an evaluation of the progress to completion of specific tasks. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the consolidated financial statements as prepaid or accrued research and development costs. Non-refundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed. Costs incurred in obtaining technology licenses are charged to research and development expense as acquired in-process research and development if the technology licensed has not reached technological feasibility and has no alternative future use.

(p) Revenue recognition

The Company adopted Accounting Standards Codification, Topic 606, *Revenue from Contracts with Customers* (“ASC 606”), during 2019. The Company generates revenue solely through collaboration arrangements with strategic partners for the development and commercialization of product candidates. The core principle of ASC 606 is that an entity should recognize revenue to depict the transfer of promised goods and/or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods and/or services. To determine the appropriate amount of revenue to be recognized for arrangements that the Company determines are within the scope of ASC 606, the Company performs the following steps: (i) Identify the contract(s) with the customer, (ii) Identify the performance obligations in the contract, (iii) Determine the transaction price, (iv) Allocate the transaction price to the performance obligations in the contract and (v) Recognize revenue when (or as) each performance obligation is satisfied.

The Company recognizes collaboration revenue under certain of the Company's license or collaboration agreements that are within the scope of ASC 606. The Company's contracts with customers typically include promises related to licenses to intellectual property and research and development services. If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenue from non-refundable, up-front fees allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgement 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 for purposes of recognizing revenue from non-refundable, up-front fees. Accordingly, the transaction price is generally comprised of a fixed fee due at contract inception and variable consideration in the form of milestone payments due upon the achievement of specified events and tiered royalties earned when customers recognize net sales of licensed products. The Company measures the transaction price based on the amount of consideration to which it expects to be entitled in exchange for transferring the promised goods and/or services to the customer. The Company utilizes the "most likely amount" method to estimate the amount of variable consideration, to predict the amount of consideration to which it will be entitled for its one open contract. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved. At the inception of each arrangement that includes development and regulatory milestone payments, the Company evaluates whether the associated event is considered probable of achievement and estimates the amount to be included in the transaction price using the most likely amount method. Currently, the Company has one contract with an option to acquire exclusive licenses for identified targets for development product candidates which it evaluated and determined that it was not a material right related to the MSD Agreement, as defined in Note 13.

(q) Income tax

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in the Company's tax returns. Deferred tax assets and liabilities are determined based on the difference between the consolidated financial statement and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

The Company accounts for uncertainty in income taxes recognized in the consolidated financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more-likely-than-not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the consolidated financial statements. The amount of the benefit that may be recognized is the largest amount that has a greater than 50% likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

(r) Share-based payments

Equity settled share-based payment transactions are measured with reference to the fair value of equity awards at the date of grant and recognized on a straight-line basis over the vesting period, based on the Company's estimate of shares that will eventually vest. Fair value is measured using a suitable option pricing model, which takes into account any market conditions.

(In thousands, except share and per share amounts)

At each reporting date before vesting, the cumulative expense is calculated, representing both the extent to which the vesting period has expired and management's best estimate of the achievement or otherwise of non-market conditions. This calculation determines the number of equity instruments that will ultimately vest with the movement in cumulative expense since the previous reporting date recognized in the Company's consolidated statements of operations and other comprehensive loss, with a corresponding entry in equity.

Where equity settled share-based payments have lapsed due to a failure to meet the vesting conditions, to the extent that they relate to performance criteria, the value of the adjustment is recognized in the consolidated statements of operations and comprehensive loss. Where share-based payments fail to vest as a result of market-based vesting criteria, the fair value of the award is included in the consolidated statements of operations and comprehensive loss as an expense until the fair value is recognized in full.

(s) Earnings (loss) per share

Basic earnings (loss) per share is computed by dividing income (loss) available to common stockholders by the weighted-average number of common shares outstanding during the period. Diluted loss per common share is computed similar to basic loss per share, except that the denominator is increased to include the number of additional potential common shares that would have been outstanding if the potential common shares had been issued and if the additional common shares were dilutive. Potential common shares are excluded from the computation for a period in which a net loss is reported or if their effect is anti-dilutive. Basic and diluted loss per common share is the same for all periods presented because all outstanding stock options and warrants are anti-dilutive.

At December 31, 2021, 2020 and 2019, the Company excluded the outstanding securities summarized below (shown as common stock equivalents), which entitle the holders thereof to acquire shares of common stock, from its calculation of earnings per share, as their effect would have been anti-dilutive.

	December 31,		
	2021	2020	2019
Common stock warrants	45,903,056	21,924,307	-
Common stock units	2,892,096	-	-
Common stock options	7,760,534	485,056	925,589
Total	56,555,686	22,409,363	925,589

(t) Recent issued accounting pronouncements not yet adopted

In May 2021, the FASB issued ASU No. 2021-04, Earnings Per Share (Topic 260), *Debt-Modifications and Extinguishments (Subtopic 470-50), Compensation-Stock Compensation (Topic 718), and Derivatives and Hedging-Contracts in Entity's Own Equity (Subtopic 815-40): Issuer's Accounting for Certain Modifications or Exchanges of Freestanding Equity-Classified Written Call Options* ("ASU 2021-04"). ASU 2021-04 provides clarification and reduces diversity in accounting for modifications or exchanges of freestanding equity-classified written call options (such as warrants) that remain equity classified after modification or exchange. This guidance is effective for annual periods beginning after December 15, 2021, including interim periods within that fiscal year. Companies should apply the new standard prospectively to modifications or exchanges occurring after the effective date of the new standard. Early adoption is permitted. The adoption of ASU 2021-04 is not anticipated to materially impact the Company's consolidated financial statements.

In June 2016, the FASB issued ASU No. 2016-13, Financial Instruments — Credit Losses (Topic 326) ("ASU 2016-13") and subsequent amendments to the initial guidance including ASU No. 2018-19, ASU No. 2019-04, and ASU No. 2019-05 (collectively, "Topic 326"). Topic 326 requires entities to measure all expected credit losses for financial assets held at the reporting date based on historical experience, current conditions, and reasonable and supportable forecasts. This replaces the existing incurred loss model and is applicable to the measurement of credit losses on financial assets measured at amortized cost. This standard is effective for public business entities, excluding entities eligible to be smaller reporting companies for fiscal years beginning after December 15, 2019, including interim periods within those fiscal years. For all other entities, this standard is effective for annual and interim periods beginning after December 15, 2022 and early adoption is permitted for annual and interim periods beginning after December 15, 2018. As a smaller reporting company, the Company expects to adopt this standard in fiscal year 2023. The Company is currently assessing the impact that the adoption of this ASU will have on the consolidated financial statements.

There are no other recently issued accounting pronouncements that are expected to have a material effect on the Company's financial position, results of operations or cash flows.

(u) Subsequent Events

Management has evaluated subsequent events that have occurred through the date these financial statements were issued. There were no events that require adjustment to or disclosure in the Company's financial statements, except as disclosed. See Note 16 for further information on subsequent events.

NOTE 3 – RECAPITALIZATION

On March 22, 2021, Longevity Acquisition Corp ("LOAC") merged with and into 4D Pharma (BVI) Limited ("Merger Sub"), a new wholly owned subsidiary of the Company, with Merger Sub continuing as the surviving company. Each of LOAC's common shares issued and outstanding prior to the effective time of the merger (excluding shares held by the Company and LOAC and dissenting shares, if any) were automatically converted into the right to receive certain per share merger consideration (as defined below), and each warrant to purchase LOAC's ordinary shares and right to receive LOAC's ordinary shares that were outstanding immediately prior to the effective time of the merger was assumed by the Company and automatically converted into a warrant to purchase common stock of the Company and a right to receive common stock of the Company, payable in Company ADSs, respectively. The per share merger consideration consisted of 7.5315 common shares of the Company, payable in Company ADSs (each ADS representing 8 ordinary shares), for each issued and outstanding ordinary shares of LOAC. LOAC had cash and cash equivalents of $11.5 million at the time of the merger after paying all of its debtors.

Management concluded the Merger is a recapitalization through an asset acquisition and not a business combination as LOAC does not meet the definition of a business pursuant to ASC 805. According to the guidance in ASC 805, the Company obtained control as a result of the transaction. Specifically, Company obtained control as: (i) it owns 100% of the issued and outstanding shares of LOAC; (ii) LOAC merged with and into a wholly-owned subsidiary of the Company, the separate existence of LOAC ceased, and the wholly-owned subsidiary of the Company is the surviving company; and (iii) the Company's board of directors and officers prior to the effective time are the initial board of directors and officers of the Company following the effective time. The Company was the accounting acquirer and issued equity in exchange for the net assets of LOAC. No goodwill or intangible assets will be recorded in this transaction.

The Company received gross net assets of $11,543 before issuance costs of $16,683, including the fair value of the Backstop Warrants issued. See below for further discussion on the Backstop Warrants. The recapitalization included several securities as follows:

- 31,048,192 shares to LOAC shareholders and associated investors.
- 4,000,000 Public warrants, with a 5-year term, exercisable into 15,063,000 common shares of the Company at $1.53 per share
- 320,000 private warrants, with a 5-year term, exercisable into 1,205,040 common shares of the Company at $1.53 per share
- 240,000 representative (LOAC advisor) units, which are exercisable until August 28, 2023, exercisable at $11.50 per unit or $1.39 per common share of the Company. Each unit can be exercised for both 8.28465 common shares, exercising into 1,988,316 common shares of the Company and a warrant to purchase 3.76575 common shares at an exercise price of $1.53 per common share into 903,780 common shares of the Company. Each warrant granted on exercise of the representative unit would convert to a public warrant and would carry the same rights and remaining term as the issued Public warrants.

The accounting for concurrent securities offerings is highly complex and required significant analysis and judgment in the application of the appropriate accounting guidance. The Company evaluated the public and private warrants as well as the representative units and determined if each security should be equity-classified or liability-classified instruments. All of these warrants and the representative units contain provisions that are not an input to the fair value of an options, thus they are not indexed to the Company's own stock. The Company determined that these warrants and the representative units should be classified as non-current derivative liabilities recognized at their inception date fair value. The resulting aggregate issuance date fair value on these warrants and representative units' issuance date was determined to be $12,593. See Note 10 for further information on the derivative liabilities.

(In thousands, except share and per share amounts)

Concurrent with the merger, the Company issued 7,530,000 warrants to certain investors as part of the Backstop agreement ("Backstop Warrants"). These warrants are exercisable into 7,530,000 common shares of the Company at $0.0034 per share. These warrants are only exercisable, on a ratable basis, for a 60-day period after the number of warrants exercised in the preceding month has been confirmed. The Backstop Warrants were not part of the consideration transferred in the recapitalization, rather they were a direct and incremental cost incurred by the Company, as such, the value of the backstop warrants is included in the transaction costs.

The Company evaluated the Backstop Warrants to determine if they should be equity-classified or liability-classified instruments and determined that the Backstop Warrants contain a contingency which could result in the modification of the exercise price, thus they are not eligible for an exception from derivative accounting. The Company determined that the Backstop Warrants should be classified as non-current warrant liabilities recognized at their inception date fair value. The resulting aggregate issuance date fair value on the Backstop Warrants issuance date was determined to be $12,854.

The proceeds of the recapitalization were first allocated to the warrants and representative units based on their full fair value. The remaining proceeds from recapitalization were less than the total transaction costs, including the fair value of the Backstop Warrants, so a loss on the recapitalization transaction was recorded to other income (expense) in the Company's consolidated statement of operations and comprehensive loss for the year ended December 31, 2021 of $17,744. No allocation of residual recapitalization proceeds remained to be allocated to the common shares issued in the recapitalization.

NOTE 4 – PREPAYMENTS AND OTHER CURRENT ASSETS

Prepayments and other current assets consisted of the following:

	December 31,	
	2021	**2020**
Prepayments	$ 2,932	$ 2,394
VAT receivables	991	1,263
Other assets – goods to be consumed in R&D activities	368	398
	$ 4,291	$ 4,055

NOTE 5 – PROPERTY AND EQUIPMENT

Property and equipment, net, consisted of the following:

	December 31,	
	2021	**2020**
Cost		
Property and machinery	$ 8,107	$ 8,728
Fixtures, fittings and office equipment	287	294
Land and buildings	1,623	1,674
Total cost	10,017	10,696
Accumulated depreciation	6,044	5,614
Total property and equipment, net	$ 3,973	$ 5,082

Depreciation and related amortization expense was $1,233, $1,309 and $1,183 for the years ended December 31, 2021, 2020 and 2019, respectively.

(In thousands, except share and per share amounts)

NOTE 6 – GOODWILL AND INTANGIBLE ASSETS

Goodwill:

Balance at December 31, 2019	$	12,651
Translation differences		838
Balance at December 31, 2020		13,489
Translation differences		(471)
Balance at December 31, 2021	$	13,018

Intangible assets, net, consisted of the following:

	December 31, 2021			
	Software	Patents	Intellectual Property	Total
Gross amount beginning of period	$ 400	$ 1,477	$ 6,158	$ 8,035
Additions	-	-	-	-
Translation differences	(3)	(14)	(58)	(75)
Gross amount end of period	397	1,463	6,100	7,960
Disposals				
Accumulated amortization	(370)	(1,463)	-	(1,833)
Net Book value	$ 27	$ -	$ 6,100	$ 6,127

	December 31, 2020			
	Software	Patents	Intellectual Property	Total
Gross amount beginning of period	$ 365	$ 1,418	$ 5,910	$ 7,693
Additions	19	-	-	19
Translation differences	16	59	248	323
Gross amount end of period	400	1,477	6,158	8,035
Accumulated amortization	(339)	(1,393)	-	(1,732)
Net Book value	$ 61	$ 84	$ 6,158	$ 6,303

Estimated amortization expense for each of the next five years is:

Year		
2022	$	22
2023		2
2024		2
2025		1
Total	$	27

Amortization expense was $120, $262 and $276 for the years ended December 31, 2021, 2020 and 2019, respectively.

At the acquisition dates, goodwill amounted to $13.3 million, intellectual property amounted to $6.1 million and patent rights amounted to $1.5 million for the acquisitions of 4D Pharma Research Limited (2015), 4D Pharma Leon S.L.U. (2016), 4D Pharma Cork Limited (formerly Tucana Health Limited) (2016) and The Microbiota Company Limited (2014). These entities together provide the necessary facilities and resources to enable the Company to successfully research, manufacture, gain approval for and commercialise Live Biotherapeutic products.

(In thousands, except share and per share amounts)

NOTE 7 – LEASES

Operating Lease obligations

The UK lease was for our head office in Leeds, England. The premises comprise office space and parking and are for a ten-year term which commenced in May 2017. A tenant lease break clause is available in May 2022 which has not been included in the lease calculations as there is no indication that this would be executed. Lease escalation costs have been included on a fixed rate basis as a practical expedient. The lease includes a provision to return the premises to their original condition on exit, as such an asset retirement obligation has been included in other liabilities of $192 and $165 at December 31, 2021 and 2020, respectively.

The Spanish lease relates to our manufacturing premises in Leon, Spain. The agreement is for a ten-year term which commenced in April 2016 and includes a tenant lease break clause that can be executed after providing six months' written notice at any point five years from the commencement date, again this break clause has not been included in the lease value as there is no evidence that this will be executed. Lease escalation cost have also been included on a fixed rate basis as a practical expedient. The lease includes the requirement to make certain repairs and as such an asset retirement obligation has been included in other liabilities at $41 and $38 at December 31, 2021 and 2020, respectively.

The existing leases are considered net leases as their non-lease components, such as common area maintenance, are paid separately from rent and based on actual costs incurred. Therefore, such variable non-lease components were not included in the right-of-use asset and liability and are reflected as expenses in the periods incurred.

Operating lease cost was $316 and $311 for the years ended December 31, 2021 and 2020, respectively. Cash paid for amounts included in the measurement of operating lease liabilities was $322 and $301 for the years ended December 31, 2021 and 2020, respectively. Short term lease cost was $186 and $174 for the years ended December 31, 2021 and 2020, respectively. Cash paid for short term leases was $143 and $155 for the years ended December 31, 2021 and 2020, respectively.

	December 31,	
	2021	**2020**
Assets		
Right of use assets	$ 906	$ 1,129
Liabilities		
Current portion of operating lease liabilities	108	94
Long term operating lease liabilities, net	854	1,092
	$ 962	$ 1,186
Weighted-average remaining lease term (years)	5	6

Maturities of operating leases liabilities are as follows:

	December 31,
	2021
2022	$ 310
2023	326
2024	329
2025	330
2026	235
2027	24
Total lease payments	1,554
Less: Imputed interest	(592)
	$ 962

(In thousands, except share and per share amounts)

NOTE 8 – ACCRUED EXPENSES AND OTHER CURRENT LIABLITIES

Accrued expenses and other current liabilities consisted of the following:

	December 31,	
	2021	2020
Clinical trials expenses	$ 2,243	$ 231
Patents and other research expenses	58	302
Payroll expenses	84	149
Building and office expenses	438	337
Professional consultants expenses	527	839
Tax expenses	411	305
Deferred grant income	30	82
Short-term finance lease	-	5
Other expenses	142	307
	$ 3,933	$ 2,557

NOTE 9 – LOAN

On July 29, 2021, the Company entered into a Loan and Security Agreement (the “Loan Agreement”), by and between the Company, as borrower, the subsidiaries of the Company party thereto as co-borrowers, the lenders party thereto (the “Lenders”) and Oxford Finance Luxembourg S.À R.L, as collateral agent for the Lenders (the “Collateral Agent”). The Loan Agreement provides for a term loan facility maturing on July 1, 2026 in an aggregate principal amount of up to $30.0 million. $12.5 million of such term loan was available and borrowed on the closing date. $7.5 million of such term loan is available upon the achievement of certain milestones. The remaining $10 million of such term loan is uncommitted and available at the discretion of the Lenders. The proceeds of the term loans may be used for general corporate purposes.

The term loans accrue interest at a per annum rate equal to the sum of (i) the greater of (A) the 30 day U.S. Dollar LIBOR reported in The Wall Street Journal on the last business day of the month that immediately precedes the month in which the interest will accrue and (B) 0.10% and (ii) 8.15%. The interest rate was set at 8.25% as of December 31, 2021. The term loans are interest only through September 1, 2023 or, subject to the achievement of certain milestones, September 1, 2024.

The Company will be required to make a final payment fee of 6.00% or, if the interest only period is extended following the achievement of certain milestones, 6.50%, of the amount of the term loan drawn. The final payment fee is payable on the earlier of (i) the prepayment of the term loan, (ii) the acceleration of the term loan, or (iii) the maturity date. At the Company’s option, the Company may elect to prepay the loans subject to a prepayment fee equal to the following percentage of the principal amount being prepaid: 3% if a term loan is prepaid during the first 12 months following the date of borrowing, 2% if a term loan is prepaid after 12 months but prior to 24 months following the date of borrowing, and 1% if a term loan is prepaid any time after 24 months following the borrowing date but prior to the maturity date. The Company is recording the final payment fee over the loan term using the effective interest rate method. As of December 31, 2021, the Company has recorded a liability of $61 included in other liabilities.

The Company’s obligations under the Loan Agreement are secured by substantially all of the assets of the Company and certain of its subsidiaries formed in Scotland, Ireland and the State of Delaware, United States.

The Loan Agreement contains customary affirmative and negative covenants, including covenants limiting the ability of the Company and its subsidiaries to, among other things, incur debt, grant liens, make acquisitions, undertake changes in control, make investments, make certain dividends or distributions, repurchase stock, dispose of assets, and enter into transactions with affiliates, in each case, subject to limitations and exceptions set forth in the Loan Agreement. Subject to the satisfaction of certain equity raise conditions by March 31, 2022, the Company is also required to maintain compliance with a minimum liquidity covenant of maintaining an unrestricted cash of $7.5 million in a collateral account subject to a control agreement in favor of the Lenders. As of March 31, 2022, the Company hasn’t met the equity raise conditions, and as such, the Company must maintain $7.5 million of cash as restricted for the lenders.

The Loan Agreement also contains customary events of default that include, among other things, certain payment defaults, covenant defaults, a material adverse change default, insolvency and bankruptcy defaults, cross defaults to other agreements, inaccuracy of representations and warranties defaults, a delisting default and government approvals defaults. If an event of default exists, the Lender may require immediate payment of all obligations under the Loan Agreement and may exercise certain other rights and remedies provided for under the Loan Agreement, the other loan documents and applicable law. Under certain circumstances, a default interest rate will apply on all obligations during the existence of an event of default under the Loan Agreement at a per annum rate equal to 5.00% above the applicable interest rate.

In addition, in connection with the Loan Agreement, the Company issued the Lenders warrants to purchase 212,568 of the Company's ordinary shares at an exercise price of $1.18 per share (the "Initial Warrants"). The Initial Warrants will be exercisable for 5 years from the date of issuance. Additionally, on the closing date, pursuant to the terms of a letter agreement among the Company, the Collateral Agent and the Lenders, the Company agreed to issue to the Lenders, on each date the Company draws additional term loans and in accordance with each Lender's pro rata share of such additional term loans, one or more warrants (the "Additional Warrants") to purchase an aggregate number of the Company's ordinary shares that is equal to 2.00% of the aggregate amount of such additional term loans funded. The Additional Warrants will have a per share price equal to the lower of (i) the closing price for an ordinary share of the Company on the last trading day prior to the funding date of such term loan or (ii) the trailing 10-day average closing price of an ordinary share of the Company for the ten trading days immediately prior to the funding date of the additional term loan. The Additional Warrants will otherwise have terms that are substantially similar to the Initial Warrants, including being exercisable for a term of 5 years.

As the ongoing fair value measurement is required for the warrants, the proceeds were allocated to the warrants in an amount equal to their fair value. The remaining proceeds were then allocated to the loan. The warrants are treated as a discount to the loan and the discount will be amortized under the effective interest method over the repayment term. The Company computed the value of the warrants of $181, using the Black-Scholes method. See Note 10 for the key assumptions used to value the warrants. Additionally, the debt issuance costs are treated as a discount to the loan. The debt discounts are amortized to interest expense using the effective interest rate method over the debt term. For the year ended December 31, 2021, amortization of $119 was included in interest expense. As of December 31, 2021 the net loan was $11,842, including net debt discounts of $658.

NOTE 10 – DERIVATIVES

The Company evaluated the public and private warrants as well as the Backstop Warrants and the representative units and lender warrants as either equity-classified or liability-classified instruments based on an assessment of the warrants and representative units' specific terms and applicable authoritative guidance in Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") 480, Distinguishing Liabilities from Equity ("ASC 480") and ASC 815, Derivatives and Hedging ("ASC 815"). The assessment considers whether the warrants and representative units are freestanding financial instruments pursuant to ASC 480, meet the definition of a liability pursuant to ASC 480, and whether the warrants and representative units meet all of the requirements for equity classification under ASC 815, including whether the warrants and representative units are indexed to the Company's own common stock, among other conditions for equity classification. Pursuant to such evaluation, the Company further evaluated the public and private warrants, the backstop warrants and the representative units under *ASC 815-40, Derivatives and Hedging — Contracts in Entity's Own Equity*, and concluded that the warrants and representative units and lender warrants do not meet the criteria to be classified in stockholders' equity.

The Backstop Warrants issued as a result of the merger transaction include provisions such that the exercisability of the warrants is contingent on the exercise of the public warrants assumed in the merger transaction. Since this contingency could result in the modification of the exercise price, thus the warrants are not eligible for an exception from derivative accounting. Accordingly, the Company has recorded the Backstop Warrants as a liability at fair value, with subsequent changes in their fair values recognized in the consolidated statements of operations and comprehensive loss at each reporting date. The Company measured the fair value of these Backstop Warrants as of December 31, 2021, and recorded other income of $9,489 resulting from the decrease of the liability associated with the fair value of the Backstop Warrants for the year ended December 31, 2021. The Company computed the value of the Backstop Warrants using the Monte Carlo method.

(In thousands, except share and per share amounts)

A summary of quantitative information with respect to the valuation methodology and significant unobservable inputs used for the Company's Backstop Warrant liabilities that are categorized within Level 3 of the fair value hierarchy as of December 31, 2021 and March 22, 2021 is as follows:

	December 31, 2021	March 22, 2021
Number of shares underlying the warrants	7,530,000	7,530,000
Stock price	$ 0.71	$ 1.93
Volatility	70.0%	85.0%
Risk-free interest rate	1.14%	0.87%
Expected dividend yield	0%	0%
Expected warrant life	4.22 years	5 years

The private warrants assumed in the merger transaction include provisions that provide for potential changes to the settlement amounts dependent upon the characteristics of the holder of the warrant. Since the holder is not an input to the fair value of an option under ASC 815, and thus the warrants are not indexed to the Company's own stock and not eligible for an exception from derivative accounting. Accordingly, the Company has recorded the private warrants as a liability at fair value, with subsequent changes in their fair values recognized in the consolidated statements of operations and comprehensive loss at each reporting date. The Company measured the fair value of these assumed private warrants as of December 31, 2021, and recorded other income of $1,225 resulting from the decrease of the liability associated with the fair value of the warrants for the year ended December 31, 2021. The Company computed the value of the assumed private warrants using the Black-Scholes method.

A summary of quantitative information with respect to the valuation methodology and significant unobservable inputs used for the Company's assumed private warrant liability that are categorized within Level 2 of the fair value hierarchy as of December 31, 2021 and March 22, 2021 is as follows:

	December 31, 2021	March 22, 2021
Number of shares underlying the warrants	1,205,040	1,205,040
Stock price	$ 0.71	$ 1.93
Volatility	94.82%	90.2%
Risk-free interest rate	1.15%	0.86%
Expected dividend yield	0%	0%
Expected warrant life	4.22 years	5 years

The public warrants and the representative units are not indexed to the Company's stock since the Company's functional currency is GBP. According to ASC 815, equity-linked financial instruments issued with a strike price denominated in a currency different than the Company's functional currency incurs an exposure to changes in currency exchange rates and thus cannot be considered to be indexed to the Company's own stock. The determination of whether an equity-linked financial instrument is indexed to the Company's own stock is not affected by the currency in which the underlying shares are traded. All of the warrants and units assumed in the recapitalization transaction, as discussed in Note 3, have a strike price denominated in USD and the Company's functional currency is GBP. The private warrants were already determined to be liabilities and are discussed above. The Company measured the fair value of the public warrants and the representative units as of December 31, 2021, and recorded other income of $7,976 resulting from the decrease of the liability associated with the fair value of the warrants and units for the year ended December 31, 2021. The Company used the value per share for the public warrants based on the Nasdaq value for the date of the financial statements. The value of the public warrants was $0.58 and $1.96 as of December 31, 2021 and March 22, 2021, respectively. The Company measured the fair value of the representative units in two portions, the underlying common shares and underlying warrants. Since the warrants embedded in the representative units have the same characteristics of the public warrants, the Company computed the value of these warrants using the same value as the public warrants. The Company computed the value of the common shares underlying the representative warrants using the Black-Scholes method.

(In thousands, except share and per share amounts)

A summary of quantitative information with respect to the valuation methodology and significant unobservable inputs used for the Company's assumed representative units liability (common shares portion) that are categorized within Level 2 of the fair value hierarchy as of December 31, 2021 and March 22, 2021 is as follows:

	December 31, 2021	March 22, 2021
Number of shares underlying the warrants	1,988,316	1,988,316
Stock price	$ 0.71	$ 1.40
Volatility	96.58%	113.40%
Risk-free interest rate	0.62%	0.23%
Expected dividend yield	0%	0%
Expected warrant life	1.66 years	2.44 years

The Company determined that the warrants issued in connection with the Loan Agreement were not indexed to the Company's stock and has accounted for these warrants as liabilities since the Company's functional currency is GBP. According to ASC 815, equity-linked financial instruments issued with a strike price denominated in a currency different than the Company's functional currency incurs an exposure to changes in currency exchange rates and thus cannot be considered to be indexed to the Company's own stock. The determination of whether an equity-linked financial instrument is indexed to the Company's own stock is not affected the currency in which the underlying shares are traded. The Company measured the fair value of these loan warrants as of December 31, 2021, and recorded other income of $88 resulting from the decrease of the liability associated with the fair value of the warrants for the year ended December 31, 2021.

A summary of quantitative information with respect to the valuation methodology and significant unobservable inputs used for the Company's loan warrants liability that are categorized within Level 2 of the fair value hierarchy as of December 31, 2021 and July 29, 2021 is as follows:

	December 31, 2021	July 29, 2021
Number of shares underlying warrants	212,568	212,568
Exercise price	$ 1.18	$ 1.18
Stock price on date of issuance	$ 0.71	$ 1.23
Volatility	94.82%	90.28%
Risk-free interest rate	1.15%	0.74%
Expected dividend yield	0%	0%
Expected warrant life	4.22 years	5 years

Recurring Level 3 Activity and Reconciliation

The table below provides a reconciliation of the beginning and ending balances for the liabilities measured at fair value using significant unobservable inputs (Level 3). The table reflects gains and losses for the year ended December 31, 2021, for all financial liabilities categorized as Level 3 as of December 31, 2021.

Fair Value Measurements Using Significant Unobservable Inputs (Level 3):

Derivatives	December 31, 2020	Initial Measurements	Decrease in Fair Value	Translation differences	December 31, 2021
Backstop warrants	$ -	$ 12,854	$ (9,489)	$ (46)	$ 3,319
Total	$ -	$ 12,854	$ (9,489)	$ (46)	$ 3,319

NOTE 11 – COMMITMENTS AND CONTINGENCIES

The Company enters into contracts in the normal course of business with Contract Research Organizations, Contract Manufacturing Organizations, universities, and other third parties for preclinical research studies, clinical trials and testing and manufacturing services. These contracts generally do not contain minimum purchase commitments and are cancellable by us upon prior written notice although, purchase orders for clinical materials are generally non-cancellable. Payments due upon cancellation consist only of payments for services provided or expenses incurred, including noncancellable obligations of our service providers, up to the date of cancellation or upon completion of a manufacturing run. These payments where these costs are material they have been included based on assumptions regarding those that are reasonably likely to be incurred.

COVID-19

In 2020, the global COVID-19 pandemic hit the United States and UK affecting almost all aspects of the global economy, the pharmaceutical industry and the Company included. The Company's operations and financial results have already been adversely impacted by the COVID-19 pandemic in the United Kingdom, United States and the rest of the world. Enrolment of patients in the clinical trials and maintaining patients in the ongoing clinical trials were delayed or limited to lesser or greater extent as the Company's clinical trial sites limited their onsite staff, temporarily closed or adjusted the way they worked during the COVID-19 pandemic. As a result of measures imposed by the governments in affected regions, many commercial activities, businesses and schools have been suspended as part of quarantines and other measures intended to contain this pandemic. These factors resulting from COVID-19 remain ongoing and other unforeseen pandemics could have similar or worse consequences, delaying the anticipated readouts from our clinical trials and our regulatory submissions. Additionally, certain third parties with whom we engage, including our collaborators, contract organisations, third-party manufacturers, suppliers, clinical trial sites, regulators and other third parties with whom we conduct business were often and can be similarly affected, adjusting their operations and assessing their capacity in light of the COVID-19 and other pandemics. While the extent of the impact of the current COVID-19 pandemic on the Company's future business and financial results continues to carry uncertainty, the effect of a continued and prolonged public health crisis from further significant mutations to COVID-19 or other pandemics could have a material negative impact on the Company's business, financial condition and operating results.

NOTE 12 – STOCKHOLDERS' EQUITY

Common stock

On February 18, 2020 the Company raised £22 million ($28.6 million) (£20.9 million ($27.2 million) net of transaction costs) through the issuance of 44 million common stock at a share price of 50 pence ($0.65) per share. A warrant was also issued on the basis of one share for every two common shares issued and have an exercise price of 100 pence ($1.30) per share and is exercisable for five years from the date of issuance.

On July 8, 2020, the Company raised £7.7 million ($9.7 million) (£7.1 million ($9.0 million) net of transaction costs) through the issuance of 21,898,400 shares of common stock at a share price of 35 pence ($0.44) per share.

On March 22, 2021 the Company completed its recapitalization with LOAC and received $11.5 million ($7.7 million net of transaction costs) through the issuance of 31 million shares of common stock at £1.10 ($1.51) per share. Additionally, the Company also issued 4.3 million warrants to purchase 16.3 million shares of common stock at £1.10 ($1.51) per common share and assumed 240,000 units to purchase the Company's common stock and warrants.

On March 22, 2021, concurrently with the merger of LOAC, the Company raised $25.0 million ($23.0 million net of transaction costs) through the issuance of 16.4 million common stock at a share price of £1.10 ($1.51) per share.

On April 15, 2021, following filing of our Annual Report on Form 20-F, the Directors who were unable to participate in the March 2021 financing, purchased 1.3 million shares of common stock, at the same terms as the March 2021 financing, for a total of approximately £1.4 million ($2.0 million).

(In thousands, except share and per share amounts)

Units

On March 22, 2021, as part of the recapitalization with LOAC, the Company issued 240,000 units. Each unit is for 8.28465 common shares and a warrant to purchase 3.76575 common share at a price of $1.39 per common share. The units are exercisable at $11.50 per unit and expire on August 28, 2023. The relative fair value of the units assumed of $3,215 was allocated from the total net proceeds of the merger on a relative basis to the common stock, warrants and units.

Warrants

On February 18, 2020, the Company issued 22 million warrants as part of the February 2020 issuance of common stock. The warrants have an exercise price of 100 pence ($1.24) per share and are immediately exercisable for five years from the date of issuance. The warrants were evaluated under ASC Topic 480, *"Distinguishing Liabilities from Equity" and ASC Topic 815, "Derivatives and Hedging"*, and the Company determined that equity classification was appropriate. The relative fair value of the warrants issued of $3,352 was allocated from the total net proceeds of the common stock issuance on a relative basis to the common stock and warrants. The intrinsic value of exercisable but unexercised in-the-money common stock warrants at December 31, 2020 was $8,688.

On March 22, 2021, the Company issued 4.0 million public warrants to purchase 15.1 million common shares and 0.3 million private warrants to purchase 1.2 million common shares as part of the LOAC recapitalization. The warrants have an exercise price of £1.10 ($1.53) per common share and are immediately exercisable for five years from the date of issuance. The warrants were evaluated under ASC Topic 480, *"Distinguishing Liabilities from Equity" and ASC Topic 815, "Derivatives and Hedging"*, and the Company determined that liability classification was appropriate.

On July 29, 2021, the Company issued 212,568 warrants to purchase 212,568 common shares as part of the Loan Agreement with the lenders. The warrants have an exercise price of $1.18 per common share and are immediately exercisable for five years from the date of issuance. The warrants are treated as a discount on the loan issued of $181. The warrants were evaluated under ASC Topic 480, *"Distinguishing Liabilities from Equity" and ASC Topic 815, "Derivatives and Hedging"*, and the Company determined that liability classification was appropriate. See notes 9 and 10 for further information.

The following table summarizes the common stock warrant activity for the year ended December 31, 2021:

Balance at January 1, 2021	21,924,307
Issuances	12,062,568
Exercises	(31,859)
Balance at December 31, 2021	33,955,016

Options

The Company has a long-term incentive plan, the 4D Pharma plc 2015 Long Term Incentive Plan (the "Plan") which was established in 2015 and expires in 10 years. The Plan limits the number of shares issued to no more than 10% of the issued common stock. The number of shares available for issuance as of December 31, 2020 was 12,661,738. Share options are awarded to management and key staff as a mechanism for attracting and retaining key members of staff. These options vest over period of three years from the date of grant and are exercisable until the tenth anniversary of the award. Exercise of the award is subject to the employee remaining a full-time member of staff at the point of exercise and the vesting conditions being met.

Vesting conditions are based on a mixture of the Company's total shareholder return market performance, relative to an appropriate comparator group, and certain individual (non-market) performance criteria. The market performance options, which vest three years after the grant date only if the Company's common stock achieves certain levels of total shareholder return when compared to the total shareholder return of a peer group of pharmaceutical companies quoted on the market in which the Company is listed. The individual performance options, vest three years after the grant date only if the performance measure has been completed.

(In thousands, except share and per share amounts)

The reconciliation of movement in share options in the years ended December 31, 2021 and 2020 is as follows:

	Number of Options	Weighted Average Exercise Price	Non-Vested Options	Weighted Average Grant date Fair Value
Outstanding at December 31, 2019	925,588	$ 0.0033	915,902	1.68
Granted	262,093	0.0033	262,093	0.96
Vested and exercised	-	0.0033	(224,949)	1.49
Expired/cancelled	(702,625)	0.0033	(702,625)	1.47
Outstanding at December 31, 2020	485,056	$ 0.0033	250,421	1.20
Granted	7,520,152	0.7000	7,520,152	0.50
Vested and exercised	(67,969)	0.0033	(566,899)	0.58
Expired/cancelled	(176,705)	0.0033	(176,706)	1.08
Outstanding at December 31, 2021	7,760,534	$ 0.6800	7,026,968	0.86
Options exercisable	733,566	$ 0.5100		
Options vested	733,566	$ 0.5100		
Options expected to vest	3,724,957	$ 0.6900		

The weighted average remaining contractual life of options outstanding, options vested and options expected to vest at December 31, 2021 was 9.88 years, 9.25 years and 9.94 years, respectively.

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 Company's common stock for those stock options that had exercise prices lower than the fair value of the Company's common stock. The Company used the value of the Company's common stock as valued on the AIM stock market as the fair value per common stock. The share price as of December 31, 2021, was £0.536 ($0.725) and the aggregate intrinsic value for options outstanding, exercisable and expected to vest was $357, $186 and $117, respectively. The share price for December 31, 2020, was £1.29 ($1.7626) and the aggregate intrinsic value for options outstanding, exercisable and expected to vest was $853, $413 and $375, respectively.

During the year ended December 31, 2020, the following events resulted in the amendment to terms of outstanding stock option awards. On July 22, 2020, in connection with an employee departure, the Company's renumeration committee vested 21,352 performance-based stock options that otherwise would not have vested. On December 13, 2020 an employee left employment of the Company but became a consultant to the Company. For the employee, the Company's renumeration committee determined to vest 166,667 performance-based stock options and to allow 74,074 options with market conditions to continue to vest over an 18-month period.

The Company calculated the change in stock-based compensation cost associated with the previously described stock option modifications pursuant to the applicable guidance in ASC 718. The change in compensation cost was determined by calculating the difference between (a) the estimated fair value of each option award immediately prior to the modifications and (b) the estimated fair value of each option award immediately after the modifications. The fair value of each option award immediately prior to and immediately after modification was estimated using the Black-Scholes option-pricing model to determine an incremental fair value, consistent with and in accordance with the Company's existing accounting policy for stock compensation. The total additional compensation cost associated with the previously described modifications was determined to be $56, which was expensed in the year ended December 31, 2020, and $34, which will be expensed over the remaining service period for the consultant. Additional compensation expense of $24 was expensed in the year ended December 31, 2021.

On December 17, 2021, the Company issued options to purchase 7,520,152 shares of common stock to its management and key staff at an exercise price of £0.518 ($0.70). The options vest over four years based on based on time vesting and expire ten years from the date of grant. The aggregate fair value of the options granted was $3,871.

(In thousands, except share and per share amounts)

Fair value is generally measured using a Black Scholes model, taking into account the terms and conditions upon which the share options were issued. The grant-date fair value of options with market conditions was discounted for the estimated probability utilizing various factors including stock price, volatility, the risk-free rate, and the associated market condition trigger. The following weighted-average assumptions were used to calculate the fair value of stock options granted during the periods indicated:

	December 17, 2021	December 13, 2020	July 22, 2020
Risk-free interest rate	1.215%	0.09%	0.08%
Expected volatility	86.64%	35.74%	40.11%
Expected dividend yield	0.00%	0.00%	0.00%
Expected term (in years)	5.84 years	1.56 years	0.77 years

The expected life of the options is based on historical data and is not necessarily indicative of exercise patterns that may occur. Volatility is based on Company historical volatility on the AIM. The Company has never paid dividends and does not currently anticipate paying any in the foreseeable future.

Stock-based compensation expense for the years ended December 31, 2021, 2020 and 2019, was $711, $331 and $340, respectively. As of December 31, 2021, total unrecognized stock-based compensation expense relating to unvested stock options was $4,550. This amount is expected to be recognized over a weighted-average period of 3.92 years.

NOTE 13 – REVENUE

In October 2019, the Company entered into a research collaboration and option agreement with MSD (Merck Sharp & Dohme Corp.) (“the MSD Agreement”). The MSD Agreement is for the use of the Company’s MicroRx discovery platform to discover, design and develop mucosal vaccines candidates derived from selected 4D Live Biotherapeutics (“LBP”), when used in conjunction with selected antigens from MSD in up to three indications. The MSD Agreement covers the grant of a non-exclusive, non-transferable, sublicensable license under Company patent rights and know-how to perform MSD’s activities under the research program and work plan. The MSD Agreement also specifies the Company’s obligation to conduct research and development activities during the three-year research program term. A joint research committee will direct the research program and its activities are indistinguishable from the research services being provided.

The non-exclusive license is considered of limited value without the Company’s development activities during the research term. As such, the license is not capable of being distinct until after successful identification of candidates, grant of an exclusive license, clinical development and regulatory approval and alone do not have standalone functionality to MSD. On analyses of market deal terms, Management determined that analyzed collectively, the option payments for exclusive licenses are at market for a development and commercialization license on a pre-clinical mucosal vaccine candidate and do not represent options that provide a material right to MSD and therefore do not give rise to a performance obligation in the contract.

Under the MSD Agreement, the Company received a non-refundable, upfront payment, of $2.5 million, a $5 million equity investment, and is eligible to receive up to $347.5 million per indication in option exercise fees and in development, regulatory and sales milestone payments, ranging from low seven figures to high eight figures, plus royalties on sales of any licensed product deriving from the collaboration. Such royalty rates range from low- to high-single digit royalties. The option payments for exclusive license and achievement and timing of the milestones depend on the success of identifying candidates, development, approval and sales progress, if any, of vaccines in the future.

The Company has initially estimated a total transaction price of $2.5 million, consisting of the fixed upfront payment determined to be the single bundled performance obligation consisting of the non-exclusive license, research and development services and governance activities. Upon execution of the MSD Agreement and as of December 31, 2021, variable consideration consisting of exclusive option license payments and milestone payments has been constrained and excluded from the transaction price given the significant uncertainty of achievement of the development and regulatory milestones.

The Company has allocated the transaction price entirely to the single bundled performance obligation and recorded the $2.5 million initially as deferred revenue and will recognize revenue over the period the research and development services are provided using an input method as a measure of progress towards completion of the performance obligation according to actual research and development costs and labor effort incurred compared to the estimated total research and development costs and labor effort, to estimate progress toward satisfaction of the performance obligation, and will remeasure its progress towards completion of the performance obligation at the end of each reporting period. For the years ended December 31, 2021, 2020 and 2019, the Company has recognized $718, $690 and $269, respectively, in collaboration revenues. Associated development costs and labor effort of $1,513, $1,345 and $215, are included within research and development costs in the consolidated statements of operations and comprehensive loss for the years ended December 31, 2021, 2020 and 2019, respectively.

Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as a current portion of deferred revenue in the accompanying consolidated balance sheets. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion. As of December 31, 2021, the Company has $902 as current deferred revenues.

NOTE 14 – INCOME TAXES

The Company and its subsidiaries file separate income tax returns.

United States of America

In 2020, the Company incorporated a subsidiary in the United States. The applicate income tax rate for this company is 30%. Prior to then, neither the Company nor any of its subsidiaries were incorporated in the United States and no operations are currently undertaken in the United States, therefore the Company is not is subject to a US federal corporate income tax rate.

United Kingdom

The Company is incorporated in the United Kingdom (UK). It also has one active subsidiary engaged in research and development activity and two dormant subsidiaries incorporated in the UK. The applicable UK statutory income tax rate for these companies is 25%.

Other Jurisdictions

The Company also has an Irish subsidiary engaged in research and development activity, a Spanish subsidiary engaged in the production of live biotherapeutics and a subsidiary in the US operating as a service company. The applicable Irish and Spanish income tax rates for these companies in 12.5% and 25% respectively.

The average standard rate for activities undertaken in all jurisdictions was 19.0% for the years ended December 31, 2021, 2020 and 2019.

(In thousands, except share and per share amounts)

For the years ended December 31, 2021, 2020 and 2019 loss before income tax benefit is as follows:

	December 31,		
	2021	2020	2019
Loss before income taxes arising in UK	$ 32,324	$ 29,938	$ 27,751
Loss before income taxes arising in Ireland	361	918	1,539
(Profit)/loss before income taxes arising in Spain	(1,003)	(340)	1,043
Loss/(profit) before income taxes arising in United States	278	(8)	-
Total loss before income tax	$ 31,960	$ 30,508	$ 30,333

	For the Years Ended December 31,					
	2021		2020		2019	
Loss before income taxes	($ 31,960)	%	($ 30,508)	%	($ 30,333)	%
Expected tax benefit	(6,072)	(19.0%)	(5,797)	(19.0%)	(5,763)	(19.0%)
Costs included in R&D tax credit	2,463	7.7%	2,255	7.4%	4,070	13.4%
Non-taxable income	(911)	(2.9%)	(846)	(2.8%)	(1,299)	(4.3%)
Expenses not deductible	(970)	(3.0%)	-	-	-	-
Change in deferred tax rate	(6,394)	(20.0%)	-	-	-	-
Foreign tax differential	171	0.5%	(248)	(0.8%)	69	(0.2%)
Change in valuation allowance	11,985	37.5%	4,504	14.8%	3,111	10.3%
Other	(294)	(0.9%)	119	0.4%	(188)	(0.6%)
Income tax benefit	($ 22)	0.1%	($ 13)	0%	$ -	0%

The provision for income taxes includes income taxes currently payable and deferred taxes resulting from net operating loss carryforwards and temporary differences between the financial statement and tax bases of assets and liabilities. Valuation allowances are recorded to reduce deferred tax assets when it is not more likely than not that a tax benefit will be realized.

The difference between the actual income tax benefit and that computed by applying average standard tax rate to pre-tax loss from continuing operations is summarized below:

	Years Ended December 31,		
	2021	2020	2019
Current tax expense (benefit)	$ (19)	$ 2	$ -
Deferred tax benefit	(3)	(15)	-
Income tax benefit	$ (22)	$ (13)	$ -

The tax effects of the temporary differences that give rise to significant portions of deferred income tax assets and liabilities are presented below:

	December 31,	
	2021	2020
Deferred tax assets/(liabilities):		
Net operating tax loss carried forwards	$ 28,369	$ 17,025
Property and equipment, net	(141)	(179)
Right of use assets	(81)	(90)
Intangible assets	(1,525)	(1,166)
Warrants	(56)	-
Stock-based compensation expense	591	319
Operating lease liabilities	86	103
Other	27	-
Valuation allowance	(27,284)	(16,030)
Net deferred tax liability	$ (14)	$ (18)

(In thousands, except share and per share amounts)

For each of the years ended December 31, 2021 and 2020 the Company did not have unrecognized tax benefits, and therefore no interest or penalties related to unrecognized tax benefits were accrued. Management does not expect that the amount of unrecognized tax benefits will change significantly within the next twelve months.

The Company mainly files income tax returns in the UK with other returns in Spain and Ireland. The Company is not subject to U.S. federal income tax examination by tax authorities. The UK tax returns for the Company's UK subsidiaries are typically open to enquiry for up to two years after the year end though the UK tax authorities have the power to re-open closed periods in certain circumstances.

As of December 31, 2021, the Company has net operating losses (NOLs) of approximately $108,154, $551 and $5,711 in the UK, Spain and Ireland respectively. NOLs may be carried forward indefinitely. The recapitalization in March 2021 could potentially limit the Company's usage of its NOLs. The Company hasn't had a tax study completed in order to determine how much, if any, that limitation would be. As a result, the deferred tax assets and corresponding valuation allowance could change substantially.

Research and development tax credits

For companies with research and development expenses, the UK government provides a notifiable state aid in the form of an enhanced research and development deduction to Corporation tax, The Company has elected to take the enhanced deduction as a cash payment rather than carry the costs as a deduction against future taxable income. The Irish government has a similar program for qualifying research and development expenses. Under the Irish program, the Company is entitled to receive a rebate up to a maximum of the employment taxes paid, which is reimbursed over a period of three years from the balance sheet date. Research and development tax credit receivables consisted of the following:

	December 31,	
	2021	2020
UK research and development tax credits	$ 8,684	$ 4,315
Irish research and development tax credits	279	453
Spain research and development tax credits	609	-
Translation differences	(66)	273
Total	9,506	5,041
Less: current portion	(9,237)	(4,799)
Research and development tax credits receivable, net	$ 269	$ 242

For the years ended December 31, 2021, 2020 and 2019, the Company has recorded other income of $4,798, $4,791 and $6,840, respectively for the research and development tax credits.

NOTE 15 – RELATED PARTY TRANSACTIONS

One of the directors of our subsidiary, Antonio Fernandez is also a director of Biomar Microbial Technologies ("Biomar"), which charged rent and building service costs to the Company of $131, $153 and $51 for the years ended December 31, 2021, 2020 and 2019, respectively. The Company charged Biomar $38, $41 and $35 for services as of December 31, 2021, 2020 and 2019, respectively. As of December 31, 2021 and 2020, $15 and $4, respectively, was due from Biomar for these services.

One of the Company's directors, Axel Glassmacher, is also a director of the Cancer Drug Development Forum ("CDDF"), which charged membership fees to the Company of $8 for the year ended December 31, 2021. There were no corresponding fees for the year ended December 31, 2020.

MSD purchased 7,661,000 shares of the Company's common stock in February 2020 and currently holds 4.6% of the Company's total outstanding common stock. The Company entered into the MSD Agreement with MSD in October 2019. See Note 10 for further information regarding this agreement. Additionally, the Company also has an ongoing trail evaluating the combination of KEYTRUDA (pembrolizumab) in combination with MRx-0518 in patients with solid tumours who progresses on prior PD-1 inhibitor therapy. Under the terms of the agreement MSD will provide KEYTRUDA free of charge to the trial.

NOTE 16 – SUBSEQUENT EVENTS

Management has evaluated subsequent events that have occurred through the date these financial statements were issued. There were no events that require adjustment to or disclosure in the Company's financial statements, except as disclosed.

SIGNATURE

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 registration statement on its behalf.

4D pharma plc

By: */s/ Duncan Peyton*
Name: Duncan Peyton
Title: Chief Executive Officer
Date: March 31, 2022

Exhibit 2.5

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

Set forth below is a summary of certain information concerning the share capital of 4D Pharma plc ("4D Pharma," the "Company," "we" or "us"), as well as a description of certain provisions of our articles of association and relevant provisions of the United Kingdom Companies Act 2006 (as amended from time to time and including any statutory modification or re-enactment thereof, the "U.K. Companies Act"). The summary includes certain references to, and descriptions of, material provisions of our articles of association and English law. The summary below contains only material information concerning our share capital and corporate status and does not purport to be complete and is qualified in its entirety by reference to our articles of association, a copy of which is filed as Exhibit 1.1 to the Annual Report on Form 20-F of the Company for the fiscal year ended December 31, 2021, and applicable English law. We encourage holders to read the articles and the applicable provisions of English law for additional information. Further, please note that if you are a holder of ordinary shares represented by American Depositary Shares, or ADSs, then you are not treated as one of our shareholders and do not have any shareholder rights.

General

We were incorporated as a private limited company with the legal name 4D Pharma plc under the laws of England and Wales on February 2014 with the company number 08840579. Our principal executive offices are located at 5th Floor, 9 Bond Court, Leeds, LS1 2JZ, United Kingdom. The principal legislation under which we operate and our ordinary shares are issued is the U.K. Companies Act. Our ordinary shares have been listed on are listed on the Alternative Investment Market of the London Stock Exchange ("**AIM**") since February 2014 under the symbol "DDDD," our ADSs have been listed on the Nasdaq Global Market in the United States since March 2021 under the symbol "LBPS" and our new warrants have been listed on the Nasdaq Global Market in the United States since March 2021 under the symbol "LBPSW."

Share Capital

As of December 31, 2021, there are 180,300,967 ordinary shares issued. The nominal value of our ordinary shares, including ordinary shares in the form of ADSs, is £0.0025 per ordinary share. Each issued ordinary share is fully paid.

General Description of 4D Pharma Ordinary Shares

The ordinary shares underlying our ADSs comprise a single class of ordinary shares with a nominal value of 0.25 pence each.

The following information is a summary of our ordinary shares:

- Our ordinary shares carry the right to receive dividends and distributions paid by us, if any.
- The holders of our ordinary shares have the right to receive notice of, and to attend and vote at, all our general meetings.
- Subject to the U.K. Companies Act, any equity securities issued by us for cash must first be offered to our shareholders in proportion to their existing holdings of our ordinary shares.
- The U.K. Companies Act allow for the disapplication of pre-emption rights, which may be waived by a special resolution of not less than three-fourths of our shareholders, either generally or specifically, for a maximum period not exceeding five years.
- Our ordinary shares are not redeemable; however, we may purchase or contract to purchase any of our ordinary shares on or off-market, subject to the U.K. Companies Act and our articles of association. We may only purchase our ordinary shares out of distributable reserves or the proceeds of a new issue of shares made for the purpose of funding the repurchase.

If we are wound up (whether the liquidation is voluntary, under supervision of the Court or by the Court), the liquidator is under a duty to collect in and realize our assets and to distribute them to our creditors and, if there is a surplus, to our shareholders according to their entitlements. This applies whether the assets consist of property of one kind or of different kinds.

Share rights

Subject to the U.K. Companies Act, the articles and to any rights for the time being attached to any existing share, ordinary shares may be issued with such rights or restrictions as we may from time to time by ordinary resolution determine, or, if we have not so determined, as our board of directors may determine.

Subject to the U.K. Companies Act, any share may be issued which is to be redeemed or is to be liable to be redeemed at the option of 4D Pharma or the holder, on such terms, conditions and in such manner as our board of directors may determine.

Voting rights

Subject to any rights or restrictions attached to any shares from time to time, the 4D Pharma shareholders, their duly appointed proxies shall have voting as provided in the U.K. Companies Act, except that on a vote on a resolution on a show of hands at a meeting, a proxy has one vote for and one vote against the resolution if the proxy has been duly appointed by more than one member entitled to vote on the resolution and either:

- the proxy has been instructed by one or more of those members to vote in one way and has been instructed by one or more other of those members to vote in the other way; or

- the proxy has been instructed by one or more of those members to vote in one way and is given discretion as to how to vote by one or more other of those members and wishes to use that discretion to vote in the other way.

At any general meeting a resolution put to the vote of the meeting shall be decided on a show of hands unless a poll is (before or on the declaration of the result of the show of hands) demanded. Subject to the provisions of the Companies Act, a poll may be demanded by:

- the chairman of the meeting;
- not less than five members present in person having the right to vote on the resolution;
- a member or members present in person representing in aggregate not less than one tenth of the total voting rights of all the members having the right to vote at the meeting; or
- a member or members present in person holding shares in the Company conferring a right to vote at the meeting, being shares on which an aggregate sum has been paid up equal to not less than one tenth of the total sum paid up on all the shares conferring that right.

Restrictions on Voting

No shareholder shall, unless the directors otherwise determine, be entitled to vote, either in person or by proxy, at any general meeting or at any separate class meeting in respect of any share held by such shareholder unless all calls or other sums payable by such shareholder in respect of that share have been paid.

Our board of directors may from time to time make calls upon the shareholders in respect of any money unpaid on their shares and each shareholder shall (subject to us serving on such shareholder at least 14 days' notice specifying the time or times and place of payment) pay at the time or times so specified the amount called on such holder's shares.

Variation of Rights

The rights attached to any class of shares may be varied or abrogated, in accordance with the provisions of the U.K. Companies Act and with either the written consent of the holders of not less than three-fourths in nominal value of the issued shares of that class (calculated excluding any shares held as treasury shares), or with the sanction of a special resolution (being a 75% majority of 4D Pharma shareholders, present at a general meeting in person or by proxy) passed at a separate meeting of the holders of those shares. At every such separate general meeting (except an adjourned meeting) the quorum must be two or more persons holding or representing by proxy not less than one-third in nominal value of the issued shares of the class (calculated excluding any shares held as treasury shares).

The rights conferred upon the holders of any shares are not, unless otherwise expressly provided in the rights attaching to those shares, deemed to be varied by the creation or issue of further shares ranking equally with them.

Share transfers

The ordinary shares are in registered form. Any ordinary shares may be held in uncertificated form.

A member may transfer certificated shares to another person by a written instrument of transfer in any usual form (or any other form approved by our board of directors) executed by or on behalf of the member and, in the case of a share which is not fully paid, by or on behalf of that person. Our board of directors may refuse to register the transfer of a certificated share which is in respect of a partly paid share provided that any refusal does not prevent open and proper dealings of any class of shares which are admitted to trading on AIM. Our board of directors may also refuse to register the transfer of a certificated share unless the transfer is in respect of only one class of share, is duly stamped (or certified as not chargeable to stamp duty) and is deposited to our registered office or any place that our board of directors may determine and is accompanied by the relevant share certificate or such other evidence our board of directors may reasonably require.

The transferor of an ordinary share is deemed to remain the holder until the transferee's name is entered in the share register.

Subject to the provisions of our articles of association, title to uncertificated shares may be transferred in accordance with the Uncertificated Securities Regulations 2001. Our board of directors is required to register a transfer of any uncertificated share in accordance with those regulations. Our board of directors may refuse to register any such transfer which is in favor of more than four persons jointly or in any other circumstance permitted by those regulations. Provisions of the articles of association do not apply to any uncertificated shares to the extent that such provisions are inconsistent with the holding of shares in uncertificated form or with the transfer of shares by means of a relevant system.

Our board of directors can decline to register any transfer of any share which is not a fully paid share or any transfer of any share on which we have a lien.

Dividends

Subject to it having sufficient distributable reserves, we may by ordinary resolution (being a resolution passed by a 50% majority of our shareholders in person or by proxy) from time to time declare dividends not exceeding the amount recommended by our board of directors. Our board of directors may pay interim dividends, and also any fixed rate dividend, whenever our financial position, in the opinion of our board of directors, justifies its payment.

All dividends on shares are to be paid according to the amounts paid up on their nominal value, or otherwise in accordance with the terms concerning entitlement to dividends on which shares were issued.

All unclaimed dividends may be made use of by our board of directors for our benefit until claimed. Any dividend unclaimed for a period of 12 years from the date when it was declared or became due for payment shall revert to 4D Pharma.

Our board of directors by way of scrip dividend instead of cash in respect of any dividend.

Shareholder meetings

Our board of directors is required to convene annual general meetings in accordance with the U.K. Companies Act. The U.K. Companies Act provides that a general meeting (other than an adjourned meeting) must be called by notice of at least 21 days' in the case of an annual general meeting (unless shareholders approve a notice period of 14 days' by special resolution (being a resolution passed by a 75% majority of 4D Pharma shareholders present at a general meeting in person or by proxy) and at least 14 days' in any other case). Our board of directors may convene a general meeting which is not an annual general meeting whenever it thinks fit.

We are required to give notice of a general meeting to each member (other than a person who, under our articles of association or pursuant to any restrictions imposed on any shares, is not entitled to receive such a notice or to whom we, in accordance with applicable law, have not sent and are not required to send our latest annual report and accounts), to our directors and to our auditors. For these purposes "members" are the persons registered in our register of members as being holders of shares at any particular time on any particular record date fixed by our board of directors that (in accordance with the Uncertificated Securities Regulations 2001) is not more than 21 days before the sending out of the notice convening the meeting. The notice of a general meeting may specify a time by which a person must be entered on our register of members in order to have the right to attend or vote at the meeting.

A member who is entitled to attend and vote at a general meeting is entitled to appoint another person, or two or more persons in respect of different shares held by him, as his proxy to exercise all or any of his rights to attend and to speak and to vote at the meeting.

Every member who is present at a general meeting in person or by proxy is entitled to one vote on a resolution put to the meeting on a show of hands and to one vote for every share of which he is the holder on a resolution put to the meeting on a poll.

Alteration of share capital

We may alter its share capital in any way permitted by the U.K. Companies Act and applicable law and confer any preference or other advantage on one or more of the shares resulting from any division or sub- division of its share capital. We may, by special resolution (being a resolution passed by a 75% majority of 4D Pharma shareholders present at a general meeting in person or by proxy), reduce its share capital, share premium account, capital redemption reserve or any other undistributable reserves.

Change of Control

There is no specific provision in the articles of association that would have the effect of delaying, deferring or preventing a change of control.

Distributions on Winding Up

On a winding up, the liquidator may, with the sanction of a special resolution of shareholders and any other sanctions required by law, divide amongst the shareholders (excluding the company itself to the extent it is a shareholder by virtue only of its holding of shares as treasury shares) in specie or in kind the whole or any part of our assets (whether they shall consist of property of the same kind or not) and may set such values and may determine how such division shall be carried out as between the shareholders or different classes of shareholder. The liquidator may, with the sanction of a special resolution of the shareholders and any other sanctions required by law, vest the whole or any part of such assets in trustees upon such trusts for the benefit of the shareholders as the liquidator shall think fit, but no shareholder shall be compelled to accept any shares or other assets upon which there is any liability.

CREST

To be traded on AIM, securities must be able to be transferred and settled through the CREST system. CREST is a computerized paperless share transfer and settlement system which allows securities to be transferred by electronic means, without the need for a written instrument of transfer. The articles of association are consistent with CREST membership and, amongst other things, allow for the holding, evidencing and transferring of shares through CREST in uncertificated form.

Directors

Number of Directors

Unless and until otherwise determined by an ordinary resolution of shareholders, we may not have less than two directors and no more than ten directors on our board of directors.

Appointment of Directors

Subject to the provisions of the articles of association we may, by ordinary resolution of the shareholders, elect any person who is willing to act to be a director, either to fill a casual vacancy or as an addition to the existing board. No person that is not a director retiring from the existing board is eligible for appointment as a director unless recommended by the board of directors, or unless not less than seven and not more than 42 days before the date appointed for the meeting a notice is given to the company by a member expressing an intention to propose such person for appointment as a director, and such notice has also been signed by that person expressing a willingness to be elected.

Without prejudice to the power to appoint any person to be a director by shareholder resolution, the board has power to appoint any person to be a director, either to fill a casual vacancy or as an addition to the existing board but so that the total number of directors does not exceed any maximum number fixed by or in accordance with the Articles.

Any director appointed by the board will hold office only until the following annual general meeting. Such a director is eligible for re-appointment at that meeting.

Rotation of Directors

At every annual general meeting, there shall retire from office at least one third of the directors. A retiring director shall be eligible for re-appointment. A director retiring at a meeting shall, if he or she is not re- appointed at such meeting, retain office until the meeting appoints someone in his or her place, or if it does not do so, until the conclusion of such meeting.

Directors' Interests

The directors may authorize, to the fullest extent permitted by law, any matter proposed to them which would otherwise result in a director infringing his or her duty to avoid a situation in which he or she has, or can have, a direct or indirect interest that conflicts, or possibly may conflict, with our interests. A director shall not, save as otherwise agreed by him or her, be accountable to us for any benefit which he or she derives from any matter authorized by the directors and any contract, transaction or arrangement relating thereto shall not be liable to be avoided on the grounds of any such benefit.

Subject to the requirements under sections 175, 177 and 182 of the Companies Act, a director who is any way, whether directly or indirectly, interested in a proposed or existing transaction or arrangement with us shall declare the nature of his interest at a meeting of the directors.

A director shall not vote in respect of any contract, arrangement or transaction whatsoever in which he or she has an interest which is to his or her knowledge a material interest otherwise than by virtue of interests in shares or debentures or other securities of or otherwise in or through our company. A director shall not be counted in the quorum at a meeting in relation to any resolution on which he or she is debarred from voting.

A director shall be entitled to vote (and be counted in the quorum) in respect of any resolution concerning any of the following matters:

- the giving of any guarantee, security or indemnity in respect of (i) money lent or obligations incurred by him or any other person at the request of, or for the benefit of, the Company or any of its subsidiary undertakings, or (ii) a debt or obligation of the of the Company or any of its subsidiary undertakings for which he himself has assumed responsibility under a guarantee or indemnity or by the giving of security;
- any contract concerning the subscription of or purchase of shares, debentures or other securities of the Company by him under an offer to members;
- any contract concerning any issue or offer of shares or debentures or other securities of or by the Company or any of its subsidiary undertakings for subscription or purchase, in respect of which he is or may be entitled to participate in his capacity as a holder of any such securities or as an underwriter or sub-underwriter;
- any contract concerning another company in which he is interested, directly or indirectly, and whether as an officer or member or otherwise, provided that he does not hold an interest representing one per cent or more of any class of the equity share capital of such company (or of any third company through which his interest is derived and calculated exclusive of any shares of that class in that company held as treasury shares) or of the voting rights available to members of the relevant company (any such interest being deemed for the purposes of this article to be a material interest in all circumstances);
- any contract for the benefit of employees of the Company or of any of its subsidiary undertakings which does not accord to him any privilege or benefit not generally accorded to the employees to whom the contract or arrangement relates;
- any contract concerning the purchase or maintenance of insurance either for or for the benefit of any director or for persons who include directors; and
- any proposal for the Company (i) to provide him with an indemnity permitted by the Statutes, (ii) to provide him with funds in circumstances permitted by the Statutes to meet his defense expenditure in respect of any civil or criminal proceedings or regulatory investigation or other regulatory action or in connection with any application for any category of relief permitted by the Statutes, or (iii) to do anything to enable him to avoid incurring any such expenditure.

If a question arises at a meeting of the board or of a committee of the board as to the right of a director to vote or be counted in the quorum, and such question is not resolved by his or her voluntarily agreeing to abstain from voting or not to be counted in the quorum, the question shall be determined by the chairman and his or her ruling in relation to any director other than himself or herself shall be final and conclusive except in a case where the nature or extent of the interest of the director concerned has not been fairly disclosed.

Directors' Fees and Remuneration

Each of the non-executive directors shall be paid a fee in such sums as may from time to time be determined by the directors provided that the aggregate of all such fees so paid to a director shall not exceed £0.2 million per annum, or such higher amount as may from time to time be determined by ordinary resolution of shareholders.

Each director may be paid all proper and reasonable expenses incurred in attending and returning from meetings of the directors or committees of the directors or general meetings of the company or separate meetings of the holders of any class of shares or debentures of the company or otherwise in connection with the business of our Company.

Any director who is appointed to any executive office or who serves on any committee or who devotes special attention to the business of our company, or who otherwise performs services which in the opinion of the 4D Pharma Board are outside the scope of the ordinary duties of a director, may be paid such extra remuneration by way of salary, percentage of profits or otherwise as the 4D Pharma Board may determine.

Borrowing Powers

Our board of directors may exercise all the powers to borrow money and to mortgage or charge all or any part of our undertaking, property, assets (present or future) and uncalled capital and to issue debentures, debenture stock and other securities, whether outright or as collateral security for any debt, liability or obligation of us or of any third party, subject to and in accordance with the U.K. Companies Act.

Our board of directors must restrict our borrowings and exercise all voting and other rights or powers of control exercisable by us in relation to its subsidiaries so as to secure that the aggregate amount remaining outstanding of all monies borrowed by us and its subsidiaries shall not at any time, without the previous sanction of an ordinary resolution of the shareholders, exceed a sum equal to three times the aggregate of:

- the amount paid up on our issued share capital and on any share capital that has been unconditionally allotted but not issued; and
- the amounts standing to the credit of our reserves (including any share premium account, capital redemption reserve and revaluation reserve) after adding any credit balance or deducting any debit balance on the profit and loss account;

all as shown in the latest audited consolidated balance sheet, subject to certain adjustments.

Indemnity

Every one of our directors or other officers shall be indemnified out of our funds against all costs, charges, expenses, losses and liabilities sustained or incurred by him or her for negligence, default, breach of duty or breach of trust or otherwise in relation to our affairs or the affairs of an associated company, or in connection with our activities, or the activities of an associated company.

Other English Law Considerations

Notification of Voting Rights

A shareholder in a public company incorporated in the United Kingdom whose shares are admitted to trading on AIM is required pursuant to Rule 5 of the Disclosure Guidance and Transparency Rules of the U.K. Financial Conduct Authority to notify us of the percentage of his, her or its voting rights if the percentage of voting rights which he, she or it holds as a shareholder or through his, her or its direct or indirect holding of financial instruments (or a combination of such holdings) reaches, exceeds or falls below 3%, 4%, 5%, and each 1% threshold thereafter up to 100% as a result of an acquisition or disposal of shares or financial instruments.

Mandatory Purchases and Acquisitions

Pursuant to Sections 979 to 991 of the U.K. Companies Act, where a takeover offer has been made for us and the offeror has acquired or unconditionally contracted to acquire not less than 90% in value of the shares to which the offer relates and not less than 90% of the voting rights carried by those shares, the offeror may give notice to the holder of any shares to which the offer relates which the offeror has not acquired or unconditionally contracted to acquire that he, she or it wishes to acquire, and is entitled to so acquire, those shares on the same terms as the general offer. The offeror would do so by sending a notice to the outstanding minority shareholders telling them that it will compulsorily acquire their shares.

Such notice must be sent within three months of the last day on which the offer can be accepted in the prescribed manner. The squeeze-out of the minority shareholders can be completed at the end of six weeks from the date the notice has been given, subject to the minority shareholders failing to successfully lodge an application to the court to prevent such squeeze-out any time prior to the end of those six weeks following which the offeror can execute a transfer of the outstanding shares in its favor and pay the consideration to us, which would hold the consideration on trust for the outstanding minority shareholders. The consideration offered to the outstanding minority shareholders whose shares are compulsorily acquired under the U.K. Companies Act must, in general, be the same as the consideration that was available under the takeover offer.

Sell Out

The U.K. Companies Act also gives our minority shareholders a right to be bought out in certain circumstances by an offeror who has made a takeover offer for all of our shares. The holder of shares to which the offer relates, and who has not otherwise accepted the offer, may require the offeror to acquire his, her or its shares if, prior to the expiry of the acceptance period for such offer, (i) the offeror has acquired or unconditionally agreed to acquire not less than 90% in value of the voting shares, and (ii) not less than 90% of the voting rights carried by those shares. The offeror may impose a time limit on the rights of minority shareholders to be bought out that is not less than three months after the end of the acceptance period. If a shareholder exercises his, her or its rights to be bought out, the offeror is required to acquire those shares on the terms of this offer or on such other terms as may be agreed.

Disclosure of Interest in Shares

Pursuant to Part 22 of the U.K. Companies Act, we are empowered by notice in writing to any person whom we know or have reasonable cause to believe to be interested in our shares, or at any time during the three years immediately preceding the date on which the notice is issued has been so interested, within a reasonable time to disclose to us particulars of that person's interest and (so far as is within such person's knowledge) particulars of any other interest that subsists or subsisted in those shares.

Under the articles of association, if a person defaults in supplying us with the required particulars in relation to the shares in question, or default shares, within the prescribed period of 14 days from the date of the service of notice, the directors may by notice direct that:

- in respect of the default shares, the relevant shareholder shall not be entitled to vote (either in person or by proxy) at any general meeting or to exercise any other right conferred by a shareholding in relation to general meetings; and
- where the default shares represent at least 0.25% of their class, (i) any dividend or other money payable in respect of the default shares shall be retained by us without liability to pay interest and/or (ii) no transfers by the relevant shareholder of any default shares may be registered (unless the shareholder is not in default and the shareholder provides a certificate, in a form satisfactory to the directors, to the effect that after due and careful enquiry the shareholder is satisfied that none of the shares to be transferred are default shares).

Purchase of Own Shares

Under the laws of England and Wales, a limited company may only purchase its own shares out of the distributable profits of the company or the proceeds of a fresh issue of shares made for the purpose of financing the purchase, provided that they are not restricted from doing so by their articles of association.

A limited company may not purchase its own shares if, as a result of the purchase, there would no longer be any issued shares of the company other than redeemable shares or shares held as treasury shares. Shares must be fully paid in order to be repurchased.

Subject to the above, we may purchase our own shares in the manner prescribed below. We may make an "on-market" purchase of our own fully paid shares pursuant to an ordinary resolution of shareholders. The resolution authorizing an on-market purchase must:

- specify the maximum number of shares authorized to be acquired;
- determine the maximum and minimum prices that may be paid for the shares; and
- specify a date, not being later than five years after the passing of the resolution, on which the authority to purchase is to expire.

We may purchase our own fully paid shares in an "off-market" purchase otherwise than on a recognized investment exchange pursuant to a purchase contract authorized by resolution of shareholders before the purchase takes place. Any authority will not be effective if any shareholder from whom we propose to purchase shares votes on the resolution and the resolution would not have been passed if he, she or it had not done so. The resolution authorizing the purchase must specify a date, not being later than five years after the passing of the resolution, on which the authority to purchase is to expire.

For these purposes, on-market purchases can only be made on AIM. Any purchase of our ADSs through Nasdaq would be an off-market purchase.

Distributions and Dividends

Under the U.K. Companies Act, before a company can lawfully make a distribution or dividend, it must ensure that it has sufficient distributable reserves (on a non-consolidated basis). The basic rule is that a company's profits available for the purpose of making a distribution are its accumulated, realized profits, so far as not previously utilized by distribution or capitalization, less its accumulated, realized losses, so far as not previously written off in a reduction or reorganization of capital duly made. The requirement to have sufficient distributable reserves before a distribution or dividend can be paid applies to us and to each of our subsidiaries that has been incorporated under the laws of England and Wales.

It is not sufficient that we, as a public company, have made a distributable profit for the purpose of making a distribution. An additional capital maintenance requirement is imposed on us to ensure that the net worth of the company is at least equal to the amount of its capital. A public company can only make a distribution:

- if, at the time that the distribution is made, the amount of its net assets (that is, the total excess of assets over liabilities) is not less than the total of its called up share capital and undistributable reserves; and
- if, and to the extent that, the distribution itself, at the time that it is made, does not reduce the amount of the net assets to less than that total.

City Code on Takeovers and Mergers

As a public company incorporated in England and Wales with our registered office in England and Wales which has shares admitted to AIM, we are subject to the U.K. Takeover Code, which is issued and administered by the U.K. Panel on Takeovers and Mergers, or the Takeover Panel. The U.K. Takeover Code provides a framework within which takeovers of companies subject to it are conducted. In particular, the U.K. Takeover Code contains certain rules in respect of mandatory offers. Under Rule 9 of the U.K. Takeover Code, if a person:

- acquires an interest in our shares which, when taken together with shares in which he or she or persons acting in concert with him or her are interested, carries 30% or more of the voting rights of our shares; or
- who, together with persons acting in concert with him or her, is interested in shares that in the aggregate carry not less than 30% and not more than 50% of the voting rights of our shares, and such persons, or any person acting in concert with him or her, acquires additional interests in shares that increase the percentage of shares carrying voting rights in which that person is interested, the acquirer and depending on the circumstances, its concert parties, would be required (except with the consent of the Takeover Panel) to make a cash offer for our outstanding shares at a price not less than the highest price paid for any interests in the shares by the acquirer or its concert parties during the previous twelve months.

Corporate Governance Code

The AIM Rules for Companies published by the London Stock Exchange require us to include on our website details of a recognized corporate governance code that our board of directors has decided to apply, how we comply with that code and, where we depart from our chosen corporate governance code, an explanation of the reasons for doing so.

Since 2015, our board of directors has sought to apply The QCA Corporate Governance Code (2018 edition). Our board of directors views this as an appropriate corporate governance framework for our company and consideration has been given to each of the ten principles set out in the code.

NEW WARRANTS ASSUMED BY US

The following description of the new warrants issued by us pursuant to the merger (the "**Merger**") we consummated with Longevity Acquisition Corporation ("**Longevity**"), a publicly-traded special purpose acquisition company, contains only material information concerning such warrants and does not purport to be complete and is qualified in its entirety by reference to the Warrant Agreement and Assumption Agreement filed as exhibits to the Annual Report on Form 20-F of the Company for the fiscal year ended December 31, 2020.

The warrants are exercisable, as described herein, for our ordinary shares on the basis that each warrant will give the holder the right to purchase 3.76575 ordinary shares for a warrant exercise price of $1.53 per whole share, subject to adjustment as described herein. The ordinary shares may be delivered in the form of ADSs based on the eight to one exchange ratio.

The warrants will expire five years from March 22, 2021, at 5:00 p.m., New York City time or upon earlier exercise or redemption.

Warrants originally issued by Longevity pursuant to its initial public offering registration statement on Form S-1 (Registration No. 333-226699), referred to as the "public warrants," are not exercisable for cash unless there is an effective and current registration statement covering the issuance of the underlying ordinary shares issuable upon exercise of the warrants and a current prospectus relating to such underlying shares. Notwithstanding the foregoing, if a registration statement covering the issuance of the underlying ordinary shares issuable upon exercise of the public warrants is not effective within 90 days from the closing of the Merger, warrant holders may, until such time as there is an effective registration statement and during any period when an effective registration statement has not been maintained, exercise warrants on a cashless basis pursuant to an available exemption from registration under the Securities Act. If an exemption from registration is not available, holders will not be able to exercise their warrants on a cashless basis.

Warrants originally issued by Longevity on a private placement basis, referred to as the "private warrants," are identical to the public warrants except that such private warrants are exercisable for cash (even if a registration statement covering the issuance of the ordinary shares issuable upon exercise of such warrants is not effective) or on a cashless basis, at the holder's option, and are not redeemable by Longevity prior to the Merger or us after the Merger, in each case so long as they are still held by the initial purchasers or their affiliates. In addition, for as long as the private warrants are held by the underwriter for Longevity's initial public offering or its designees or affiliates they may not be exercised after August 29, 2023.

The warrants can be called for redemption (excluding the private warrants but including any outstanding warrants issued upon exercise of the unit purchase option issued to the underwriter for Longevity's initial public offering and/or its designees), in whole and not in part, at a price of $0.01 per warrant:

- at any time while the warrants are exercisable,
- upon not less than 30 days' prior written notice of redemption to each warrant holder,
- if, and only if, after the Merger the reported last sale price of the underlying ordinary shares equals or exceeds the greater of $2.39 per ordinary share (as adjusted for stock splits, stock dividends, reorganizations and recapitalizations) or $19.12 per ADS (based on the ADS Exchange Ratio), for any 20 trading days within a 30 trading day period ending on the third trading business day prior to the notice of redemption to warrant holders, and
- if, and only if, there is a current registration statement in effect with respect to the issuance of the shares underlying such warrants at the time of redemption and for the entire 30-day trading period referred to above and continuing each day thereafter until the date of redemption.

The right to exercise will be forfeited unless the warrants are exercised prior to the date specified in the notice of redemption. On and after the redemption date, a record holder of a warrant will have no further rights except to receive the redemption price for such holder's warrant upon surrender of such warrant.

If and when the warrants become redeemable, the redemption right cannot be exercised if the issuance of the underlying ordinary shares upon exercise of the warrants is not exempt from registration or qualification under applicable state blue sky laws or we are unable to effect such registration or qualification.

If we call the warrants for redemption as described above, our management will have the option to require all holders that wish to exercise warrants to do so on a "cashless basis." In such event, each holder would pay the exercise price by surrendering the warrants for that number of underlying shares equal to the quotient obtained by dividing (x) the product of the number of ordinary shares underlying the warrants, multiplied by the difference between the exercise price of the warrants and the "fair market value" (defined below) by (y) the fair market value. The "fair market value" shall mean the average reported last sale price of the underlying shares for the 10 trading days ending on the third trading day prior to the date on which the notice of redemption is sent to the holders of warrants. Whether the option to require all holders to exercise their warrants on a "cashless basis" is exercised will depend on a variety of factors including the price of the underlying shares at the time the warrants are called for redemption, cash needs at such time and concerns regarding dilutive issuances.

Continental Stock Transfer & Trust Company is the warrant agent for the warrants.

The exercise price and number of underlying ordinary shares issuable on exercise of the warrants may be adjusted in certain circumstances including in the event of a share dividend, extraordinary dividend or our recapitalization, reorganization, merger or consolidation. However, the warrants will not be adjusted for issuances of shares at a price below their respective exercise prices.

The warrants may be exercised upon surrender of the warrant certificate on or prior to the expiration date at the offices of the warrant agent, with the exercise form on the reverse side of the warrant certificate completed and executed as indicated, accompanied by full payment of the exercise price (or on a cashless basis, if applicable), by certified or official bank check payable to us, for the number of warrants being exercised. The warrant holders do not have the rights or privileges of holders of shares and any voting rights until they exercise their warrants and have received underlying shares.

Except as described above, no warrants issued as public warrants are exercisable and no shares will be issued on exercise unless, at the time a holder seeks to exercise such warrant, a prospectus relating to the shares issuable upon exercise of the warrants is current and the shares had been registered or qualified or deemed to be exempt under the securities laws of the state of residence of the holder of the warrants.

Under the terms of the warrant agreement, Longevity agreed, and we have assumed the obligation, to use best efforts to meet the conditions above and to maintain a current prospectus relating to the underlying shares issuable upon exercise of the warrants until the expiration of the warrants. However, we cannot assure holders that we will be able to do so and, if we do not maintain a current prospectus relating to the underlying shares issuable upon exercise of the warrants, except as described above, holders will be unable to exercise their warrants and we will not be required to settle any such warrant exercise. If the prospectus relating to the underlying shares issuable upon the exercise of the warrants is not current or if the underlying shares are not qualified or exempt from qualification in the jurisdictions in which the holders of the warrants reside, we will not be required to net cash settle or cash settle the warrant exercise, the warrants may have no value, the market for the warrants may be limited and the warrants may expire worthless.

Warrant holders may elect to be subject to a restriction on the exercise of their warrants such that an electing warrant holder would not be able to exercise their warrants to the extent that, after giving effect to such exercise, such holder would beneficially own in excess of 9.8% of the share capital outstanding.

Description of Our American Depositary Shares

American Depositary Receipts

We have appointed JPMorgan Chase Bank, N.A. ("**JPMorgan**"), as depositary. The depositary's office is located at 383 Madison Avenue, Floor 11, New York, NY 10179.

A copy of the form of the deposit agreement is on file with the SEC under cover of a registration statement on Form F-6. A copy of the deposit agreement is available from the SEC's website (www.sec.gov). Please refer to registration number 333-253268 when retrieving such copy.

Each ADS represents an ownership interest in eight ordinary shares deposited with the custodian, as agent of the depositary, under the deposit agreement among ourselves, the depositary, and all ADR holders, and all beneficial owners of an interest in the ADSs evidenced by ADRs from time to time. Each ADS represents any securities, cash or other property deposited with the depositary but which they have not distributed directly to the holders. Unless certificated ADRs are specifically requested by the holder all ADSs are issued on the books of our depositary in book-entry form and periodic statements will be mailed to the holder which reflect the holder's ownership interest in such ADSs. In our description, references to American depositary receipts or ADRs shall include the statements holders will receive which reflect their ownership of ADSs.

The holders may hold ADSs either directly or indirectly through their broker or other financial institution. If a holder holds ADSs directly, by having an ADS registered in their name on the books of the depositary, they are an ADR holder. This description assumes they are an ADR holder and hold their ADSs directly. If holders have a beneficial ownership interest in ADSs but hold the ADSs through their broker or financial institution nominee, they are a beneficial owner of ADSs and must rely on the procedures of such broker or financial institution to assert the rights of an ADR holder described in this section. Holders should consult with their broker or financial institution to find out what those procedures are. If a holder is a beneficial owner, they will only be able to exercise any right or receive any benefit under the deposit agreement solely through the ADR holder which holds the ADR(s) evidencing the ADSs owned by the holder, and the arrangements between the holder and such ADR holder may affect their ability to exercise any rights they may have. For all purposes under the deposit agreement, an ADR holder is deemed to have all requisite authority to act on behalf of any and all beneficial owners of the ADSs evidenced by the ADR(s) registered in such ADR holder's name. The depositary's only notification obligations under the deposit agreement shall be to the ADR holders, and notice to an ADR holder shall be deemed, for all purposes of the deposit agreement, to constitute notice to any and all beneficial owners of the ADSs evidenced by such ADR holder's ADRs.

ADR holders or beneficial owners will not be treated as shareholders of ours and they will not have any shareholder rights. English law governs shareholder rights. Because the depositary or its nominee will be the shareholder of record for the shares represented by all outstanding ADSs, shareholder rights rest with such record holder. Holders' rights are those of an ADR holder or of a beneficial owner. Such rights derive from the terms of the deposit agreement to be entered into among the depositary and all registered holders and beneficial owners from time to time of ADSs issued under the deposit agreement and, in the case of a beneficial owner, from the arrangements between the beneficial owner and the holder of the corresponding ADRs. Obligations of 4D Pharma, the depositary and its agents are also set out in the deposit agreement. Because the depositary or its nominee will actually be the registered owner of the shares, holders must rely on it to exercise the rights of a shareholder on their behalf. The deposit agreement, the ADRs and the ADSs are governed by New York law. Under the deposit agreement, an ADR holder or a beneficial owner of ADSs agrees that any legal suit, action or proceeding brought by holders against or involving us or the depositary, arising out of or based upon the deposit agreement, the ADSs, the ADRs or the transactions contemplated thereby, may only be instituted in a federal court in New York, New York, or, except for claims arising under the Securities Act of 1933 or Securities Exchange Act of 1934, any state court in New York, New York, and holders irrevocably waive any objection which they may have to the laying of venue of any such proceeding and irrevocably submit to the exclusive jurisdiction of such courts in any such suit, action or proceeding, provided, however, pursuant to applicable law and the Company's Articles of Association, any claim brought by holders arising under the Securities Act of 1933 may be instituted only in any federal court in the United States, and any claim brought by holders or on behalf of the Company with regard to the internal affairs of the Company, including the ability to bring such a claim, shall be governed by and construed in accordance with the laws of England and Wales, and may only be instituted against the Company, its directors, officers or employees as provided in the Company's Articles of Association in the courts of England and Wales.

The following is a summary of what we believe to be the material terms of the deposit agreement. Notwithstanding this, because it is a summary, it may not contain all the information that holders may otherwise deem important. For more complete information, holders should read the entire deposit agreement and the form of ADR which contains the terms of their ADSs. Holders can read a copy of the deposit agreement which is filed as an exhibit to, or incorporated by reference in, the most recent Form F-6 registration statement (or amendment thereto) filed with the SEC. Holders may also obtain a copy of the form of deposit agreement at the SEC's Public Reference Room which is located at 100 F Street, NE, Washington, DC 20549. Holders may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-732-0330. Holders may also find the registration statement and the attached deposit agreement on the SEC's website at http://www.sec.gov.

Share Dividends and Other Distributions

How will Holders receive dividends and other distributions on the shares underlying my ADSs?

We may make various types of distributions with respect to our securities. The depositary has agreed that, to the extent practicable, it will pay to holders the cash dividends or other distributions it or the custodian receives on shares or other deposited securities, after converting any cash received into U.S. dollars (if it determines such conversion may be made on a reasonable basis) and, in all cases, making any necessary deductions provided for in the deposit agreement. The depositary may utilize a division, branch or affiliate of JPMorgan to direct, manage and/or execute any public and/or private sale of securities under the deposit agreement. Such division, branch and/or affiliate may charge the depositary a fee in connection with such sales, which fee is considered an expense of the depositary. Holders will receive these distributions in proportion to the number of underlying securities that their ADSs represent.

Except as stated below, the depositary will deliver such distributions to ADR holders in proportion to their interests in the following manner:

- *Cash.* The depositary will distribute any U.S. dollars available to it resulting from a cash dividend or other cash distribution or the net proceeds of sales of any other distribution or portion thereof (to the extent applicable), on an averaged or other practicable basis, subject to (i) appropriate adjustments for taxes withheld, (ii) such distribution being impermissible or impracticable with respect to certain ADR holders, and (iii) deduction of the depositary's and/or its agents' expenses in (1) converting any foreign currency to U.S. dollars to the extent that it determines that such conversion may be made on a reasonable basis, (2) transferring foreign currency or U.S. dollars to the United States by such means as the depositary may determine to the extent that it determines that such transfer may be made on a reasonable basis, (3) obtaining any approval or license of any governmental authority required for such conversion or transfer, which is obtainable at a reasonable cost and within a reasonable time and (4) making any sale by public or private means in any commercially reasonable manner. *If exchange rates fluctuate during a time when the depositary cannot convert a foreign currency, holders may lose some or all of the value of the distribution*.
- *Shares.* In the case of a distribution in shares, the depositary will issue additional ADRs to evidence the number of ADSs representing such shares. Only whole ADSs will be issued. Any shares which would result in fractional ADSs will be sold and the net proceeds will be distributed in the same manner as cash to the ADR holders entitled thereto.
- *Rights to receive additional shares.* In the case of a distribution of rights to subscribe for additional shares or other rights, if we timely provide evidence satisfactory to the depositary that it may lawfully distribute such rights, the depositary will distribute warrants or other instruments in the discretion of the depositary representing such rights. However, if we do not timely furnish such evidence, the depositary may: (i) sell such rights if practicable and distribute the net proceeds in the same manner as cash to the ADR holders entitled thereto; or (ii) if it is not practicable to sell such rights by reason of the non-transferability of the rights, limited markets therefor, their short duration or otherwise, do nothing and allow such rights to lapse, in which case ADR holders will receive nothing and the rights may lapse. We have no obligation to file a registration statement under the Securities Act in order to make any rights available to ADR holders.
- *Other Distributions.* In the case of a distribution of securities or property other than those described above, the depositary may either (i) distribute such securities or property in any manner it deems equitable and practicable or (ii) to the extent the depositary deems distribution of such securities or property not to be equitable and practicable, sell such securities or property and distribute any net proceeds in the same way it distributes cash.

- *Elective Distributions.* In the case of a dividend payable at the election of our shareholders in cash or in additional shares, we will notify the depositary at least 30 days prior to the proposed distribution stating whether or not we wish such elective distribution to be made available to ADR holders. The depositary shall make such elective distribution available to ADR holders only if (i) we shall have timely requested that the elective distribution is available to ADR holders, (ii) the depositary shall have determined that such distribution is reasonably practicable and (iii) the depositary shall have received satisfactory documentation within the terms of the deposit agreement including any legal opinions of counsel that the depositary in its reasonable discretion may request. If the above conditions are not satisfied, the depositary shall, to the extent permitted by law, distribute to the ADR holders, on the basis of the same determination as is made in the local market in respect of the shares for which no election is made, either (x) cash or (y) additional ADSs representing such additional shares. If the above conditions are satisfied, the depositary shall establish procedures to enable ADR holders to elect the receipt of the proposed dividend in cash or in additional ADSs. There can be no assurance that ADR holders or beneficial owners of ADSs generally, or any ADR holder or beneficial owner of ADSs in particular, will be given the opportunity to receive elective distributions on the same terms and conditions as the holders of shares.
  If the depositary determines in its discretion that any distribution described above is not practicable with

respect to any specific ADR holder, the depositary may (after consultation with the Company, if practicable, in the case where the depositary believes such distribution is not practicable with respect to all ADR holders) choose any method of distribution that it deems practicable for such ADR holder, including the distribution of foreign currency, securities or property, or it may retain such items, without paying interest on or investing them, on behalf of the ADR holder as deposited securities, in which case the ADSs will also represent the retained items.

Any U.S. dollars will be distributed by checks drawn on a bank in the United States for whole dollars and cents. Fractional cents will be withheld without liability and dealt with by the depositary in accordance with its then current practices.

The depositary is not responsible if it fails to determine that any distribution or action is lawful or reasonably practicable.

There can be no assurance that the depositary will be able to convert any currency at a specified exchange rate or sell any property, rights, shares or other securities at a specified price, nor that any of such transactions can be completed within a specified time period. All purchases and sales of securities will be handled by the depositary in accordance with its then current policies, which are currently set forth on https://www.adr.com/disclosure/disclosures, the location and contents of which the depositary shall be solely responsible for.

Deposit, Withdrawal and Cancellation

How does the depositary issue ADSs?

The depositary will issue ADSs if holders or a holder’s broker deposit shares or evidence of rights to receive shares with the custodian and pay the fees and expenses owing to the depositary in connection with such issuance.

Shares deposited in the future with the custodian must be accompanied by certain delivery documentation and shall, at the time of such deposit, be registered in the name of JPMorgan, as depositary for the benefit of ADR holders or in such other name as the depositary shall direct.

The custodian will hold all deposited shares for the account and to the order of the depositary, in each case for the benefit of ADR holders, to the extent not prohibited by law. ADR holders and beneficial owners thus have no direct ownership interest in the shares and only have such rights as are contained in the deposit agreement. The custodian will also hold any additional securities, property and cash received on or in substitution for the deposited shares. The deposited shares and any such additional items are referred to as “deposited securities”.

Deposited securities are not intended to, and shall not, constitute proprietary assets of the depositary, the custodian or their nominees. Beneficial ownership in deposited securities is intended to be, and shall at all times during the term of the deposit agreement continue to be, vested in the beneficial owners of the ADSs representing such deposited securities. Notwithstanding anything else contained herein, in the deposit agreement, in the form of ADR and/or in any outstanding ADSs, the depositary, the custodian and their respective nominees are intended to be, and shall at all times during the term of the deposit agreement be, the record holder(s) only of the deposited securities represented by the ADSs for the benefit of the ADR holders. The depositary, on its own behalf and on behalf of the custodian and their respective nominees, disclaims any beneficial ownership interest in the deposited securities held on behalf of the ADR holders.

Upon each deposit of shares, receipt of related delivery documentation and compliance with the other provisions of the deposit agreement, including the payment of the fees and charges of the depositary and any taxes or other fees or charges owing, the depositary will issue an ADR or ADRs in the name or upon the order of the person entitled thereto evidencing the number of ADSs to which such person is entitled. All of the ADSs issued will, unless specifically requested to the contrary, be part of the depositary's direct registration system, and an ADR holder will receive periodic statements from the depositary which will show the number of ADSs registered in such ADR holder's name. An ADR holder can request that the ADSs not be held through the depositary's direct registration system and that a certificated ADR be issued.

How do ADR holders cancel an ADS and obtain deposited securities?

When holders turn in their ADR certificate at the depositary's office, or when they provide proper instructions and documentation in the case of direct registration ADSs, the depositary will, upon payment of certain applicable fees, charges and taxes, deliver the underlying shares to holders or upon their written order. Delivery of deposited securities in certificated form will be made at the custodian's office. At the holder's risk, expense and request, the depositary may deliver deposited securities at such other place as holders may request.

The depositary may only restrict the withdrawal of deposited securities in connection with:

- temporary delays caused by closing our transfer books or those of the depositary or the deposit of shares in connection with voting at a shareholders' meeting, or the payment of dividends;
- the payment of fees, taxes and similar charges; or
- compliance with any U.S. or foreign laws or governmental regulations relating to the ADRs or to the withdrawal of deposited securities.

This right of withdrawal may not be limited by any other provision of the deposit agreement.

Record Dates

The depositary may, after consultation with us if practicable, fix record dates (which, to the extent applicable, shall be as near as practicable to any corresponding record dates set by us) for the determination of the ADR holders who will be entitled (or obligated, as the case may be):

- to receive any distribution on or in respect of deposited securities,
- to give instructions for the exercise of voting rights at a meeting of holders of shares,
- to pay any fees, charges or expenses assessed by, or owing to the depositary, or
- to receive any notice or to act or be obligated in respect of other matters,

all subject to the provisions of the deposit agreement.

Voting Rights

How do holders vote?

If a holder is an ADR holder and the depositary asks the holder to provide it with voting instructions, the holder may instruct the depositary how to exercise the voting rights for the shares which underlie their ADSs. As soon as practicable after receiving notice from us of any meeting at which the holders of shares are entitled to vote, or of our solicitation of consents or proxies from holders of shares, the depositary shall fix the ADS record date in accordance with the provisions of the deposit agreement, provided that if the depositary receives a written request from us in a timely manner and at least 30 days prior to the date of such vote or meeting, the depositary shall, at our expense, distribute to the ADR holders a notice stating (i) final information particular to such vote and meeting and any solicitation materials, (ii) that each ADR holder on the record date set by the depositary will, subject to any applicable provisions of the laws of England and Wales, be entitled to instruct the depositary to exercise the voting rights, if any, pertaining to the shares underlying such ADR holder's ADSs and (iii) the manner in which such instructions may be given, including instructions to give a discretionary proxy to a person designated by us. Each ADR holder is solely responsible for the forwarding of such notices to the beneficial owners of ADSs registered in such ADR holder's name. Following actual receipt by the ADR department responsible for proxies and voting of ADR holders' instructions (including, without limitation, instructions of any entity or entities acting on behalf of the nominee for DTC), the depositary shall, in the manner and on or before the time established by the depositary for such purpose, endeavor to vote or cause to be voted the shares represented by the ADSs evidenced by such ADR holders' ADRs in accordance with such instructions insofar as practicable and permitted under the provisions of or governing our shares.

ADR holders and beneficial owners of ADSs are strongly encouraged to forward their voting instructions to the depositary as soon as possible. For instructions to be valid, the ADR department of the depositary that is responsible for proxies and voting must receive them in the manner and on or before the time specified, notwithstanding that such instructions may have been physically received by the depositary prior to such time. The depositary will not itself exercise any voting discretion. Notwithstanding anything contained in the deposit agreement or any ADR, the depositary may, to the extent not prohibited by any law, rule or regulation, or by the rules and/or requirements of the stock exchange or market on which the ADSs are listed or traded, in lieu of distribution of the materials provided to the depositary in connection with any meeting of, or solicitation of consents or proxies from, holders of deposited securities, distribute to the ADR holders a notice that provides such ADR holders with, or otherwise publicizes to such ADR holders, instructions on how to retrieve such materials or receive such materials upon request (*i.e.*, by reference to a website containing the materials for retrieval or a contact for requesting copies of the materials).

There is no guarantee that ADR holders and beneficial owners of ADSs generally, or any ADR holder or beneficial owner of ADSs in particular, will receive voting materials in time to instruct the depositary to vote and it is possible that holders, or persons who hold their ADSs through brokers, dealers or other third parties, will not have the opportunity to exercise a right to vote.

Reports and Other Communications

Will ADR holders be able to view our reports?

The depositary will make available for inspection by ADR holders at the offices of the depositary and the custodian the deposit agreement, the provisions of or governing deposited securities, and any written communications from us which are both received by the custodian or its nominee as a holder of deposited securities and made generally available to the holders of deposited securities.

Additionally, if we make any written communications generally available to holders of our shares, and we furnish copies thereof (or English translations or summaries) to the depositary, it will distribute the same to ADR holders.

Fees and Expenses

What fees and expenses will holders be responsible for paying?

The depositary may charge each person to whom ADSs are issued, including, without limitation, issuances against deposits of shares, issuances in respect of share distributions, rights and other distributions, issuances pursuant to a stock dividend or stock split declared by us or issuances pursuant to a merger, exchange of securities or any other transaction or event affecting the ADSs or deposited securities, and each person surrendering ADSs for withdrawal of deposited securities or whose ADSs are cancelled or reduced for any other reason, $5.00 for each 100 ADSs (or any portion thereof) issued, delivered, reduced, cancelled or surrendered, or upon which a share distribution or elective distribution is made or offered, as the case may be. The depositary may sell (by public or private sale) sufficient securities and property received in respect of a share distribution, rights and/or other distribution prior to such deposit to pay such charge.

The following additional charges shall also be incurred by the ADR holders and beneficial owners of ADSs, by any party depositing or withdrawing shares or by any party surrendering ADSs and/or to whom ADSs are issued (including, without limitation, issuance pursuant to a stock dividend or stock split declared by us or an exchange of stock regarding the ADSs or the deposited securities or a distribution of ADSs), whichever is applicable:

- a fee of U.S.$1.50 per ADR or ADRs for transfers of certificated or direct registration ADRs;
- a fee of up to U.S.$0.05 per ADS held upon which any cash distribution made pursuant to the deposit agreement or in the case of an elective cash/stock dividend, upon which a cash distribution or an issuance of additional ADSs is made as a result of such elective dividend;
- an aggregate fee of up to U.S.$0.05 per ADS per calendar year (or portion thereof) for services performed by the depositary in administering the ADRs (which fee may be charged on a periodic basis during each calendar year and shall be assessed against ADR holders as of the record date or record dates set by the depositary during each calendar year and shall be payable in the manner described in the next succeeding provision);
- a fee for the reimbursement of such fees, charges and expenses as are incurred by the depositary and/or any of its agents (including, without limitation, the custodian and expenses incurred on behalf of ADR holders in connection with compliance with foreign exchange control regulations or any law, rule or regulation relating to foreign investment) in connection with the servicing of the shares or other deposited securities, the sale of securities (including, without limitation, deposited securities), the delivery of deposited securities or otherwise in connection with the depositary's or its custodian's compliance with applicable law, rule or regulation (which fees and charges shall be assessed on a proportionate basis against ADR holders as of the record date or dates set by the depositary and shall be payable at the sole discretion of the depositary by billing such ADR holders or by deducting such charge from one or more cash dividends or other cash distributions);
- a fee for the distribution of securities (or the sale of securities in connection with a distribution), such fee being in an amount equal to the $0.05 per ADS issuance fee for the execution and delivery of ADSs which would have been charged as a result of the deposit of such securities (treating all such securities as if they were shares) but which securities or the net cash proceeds from the sale thereof are instead distributed by the depositary to those ADR holders entitled thereto;
- stock transfer or other taxes and other governmental charges;
- SWIFT, cable, telex and facsimile transmission and delivery charges incurred at holders' request in connection with the deposit or delivery of shares, ADRs or deposited securities;
- transfer or registration fees for the registration of transfer of deposited securities on any applicable register in connection with the deposit or withdrawal of deposited securities; and
- fees of any division, branch or affiliate of the depositary utilized by the depositary to direct, manage and/or execute any public and/or private sale of securities under the deposit agreement.

To facilitate the administration of various depositary receipt transactions, including disbursement of dividends or other cash distributions and other corporate actions, the depositary may engage the foreign exchange desk within JPMorgan Chase Bank, N.A. (the "Bank") and/or its affiliates in order to enter into spot foreign exchange transactions to convert foreign currency into U.S. dollars ("FX Transactions"). For certain currencies, FX Transactions are entered into with the Bank or an affiliate, as the case may be, acting in a principal capacity. For other currencies, FX Transactions are routed directly to and managed by an unaffiliated local custodian (or other third-party local liquidity provider), and neither the Bank nor any of its affiliates is a party to such FX Transactions.

The foreign exchange rate applied to an FX Transaction will be either (i) a published benchmark rate, or (ii) a rate determined by a third-party local liquidity provider, in each case plus or minus a spread, as applicable. The depositary will disclose which foreign exchange rate and spread, if any, apply to such currency on the "Disclosure" page (or Successor page) of www.adr.com (as updated by the depositary from time to time, "ADR.com"). Such applicable foreign exchange rate and spread may (and neither the depositary, the Bank nor any of their affiliates is under any obligation to ensure that such rate does not) differ from rates and spreads at which comparable transactions are entered into with other customers or the range of foreign exchange rates and spreads at which the Bank or any of its affiliates enters into foreign exchange transactions in the relevant currency pair on the date of the FX Transaction. Additionally, the timing of execution of an FX Transaction varies according to local market dynamics, which may include regulatory requirements, market hours and liquidity in the foreign exchange market or other factors. Furthermore, the Bank and its affiliates may manage the associated risks of their position in the market in a manner they deem appropriate without regard to the impact of such activities on us, the depositary, ADR holders or beneficial owners of ADSs. The spread applied does not reflect any gains or losses that may be earned or incurred by the Bank and its affiliates as a result of risk management or other hedging related activity. Notwithstanding the foregoing, to the extent we provide U.S. dollars to the depositary, neither the Bank nor any of its affiliates will execute an FX Transaction as set forth herein. In such case, the depositary will distribute the U.S. dollars received from us.

Further details relating to the applicable foreign exchange rate, the applicable spread and the execution of FX Transactions will be provided by the depositary on ADR.com. We and by holding an ADS or an interest therein, ADR holders and beneficial owners of ADSs will each be acknowledging and agreeing that the terms applicable to FX Transactions disclosed from time to time on ADR.com will apply to any FX Transaction executed pursuant to the deposit agreement.

We will pay all other charges and expenses of the depositary and any agent of the depositary (except the custodian) pursuant to agreements from time to time between us and the depositary.

The fees and charges holders may be required to pay may vary over time and may be changed by us and by the depositary. ADR holders will receive prior notice of the increase in any such fees and charges. The right of the depositary to charge and receive payment of fees, charges and expenses as provided above shall survive the termination of the deposit agreement.

The depositary may make available to us a set amount or a portion of the depositary fees charged in respect of the ADR program or otherwise upon such terms and conditions as we and the depositary may agree from time to time. The depositary collects its fees for issuance and cancellation of ADSs directly from investors depositing shares or surrendering ADSs for the purpose of withdrawal or from intermediaries acting for them. The depositary collects fees for making distributions to investors by deducting those fees from the amounts distributed or by selling a portion of distributable property to pay the fees. The depositary may collect its annual fee for depositary services by deduction from cash distributions, or by directly billing investors, or by charging the book-entry system accounts of participants acting for them. The depositary will generally set off the amounts owing from distributions made to ADR holders. If, however, no distribution exists and payment owing is not timely received by the depositary, the depositary may refuse to provide any further services to ADR holders that have not paid those fees and expenses owing until such fees and expenses have been paid. At the discretion of the depositary, all fees and charges owing under the deposit agreement are due in advance and/or when declared owing by the depositary.

Payment of Taxes

ADR holders or beneficial owners must pay any tax or other governmental charge payable by the custodian or the depositary on any ADS or ADR, deposited security or distribution. If any taxes or other governmental charges (including any penalties and/or interest) shall become payable by or on behalf of the custodian or the depositary with respect to any ADR, any deposited securities represented by the ADSs evidenced thereby or any distribution thereon, such tax or other governmental charge shall be paid by the applicable ADR holder to the depositary and by holding or owning, or having held or owned, an ADR or any ADSs evidenced thereby, the ADR holder and all beneficial owners of such ADSs, and all prior registered holders of such ADRs and prior beneficial owners of such ADSs, jointly and severally, agree to indemnify, defend and save harmless each of the depositary and its agents in respect of such tax or governmental charge. Each ADR holder and beneficial owner of ADSs, and each prior ADR holder and beneficial owner of ADSs, by holding or having held an ADR or an interest in ADSs, acknowledges and agrees that the depositary shall have the right to seek payment of any taxes or governmental charges owing with respect to the relevant ADRs from any one or more such current or prior ADR holder or beneficial owner of ADSs, as determined by the depositary in its sole discretion, without any obligation to seek payment of amounts owing from any other current or prior ADR holder or beneficial owner of ADSs. If an ADR holder owes any tax or other governmental charge, the depositary may (i) deduct the amount thereof from any cash distributions, or (ii) sell deposited securities (by public or private sale) and deduct the amount owing from the net proceeds of such sale. In either case the ADR holder remains liable for any shortfall. If any tax or governmental charge is unpaid, the depositary may also refuse to effect any registration, registration of transfer, split-up or combination of deposited securities or withdrawal of deposited securities until such payment is made. If any tax or governmental charge is required to be withheld on any cash distribution, the depositary may deduct the amount required to be withheld from any cash distribution or, in the case of a non-cash distribution, sell the distributed property or securities (by public or private sale) in such amounts and in such manner as the depositary deems necessary and practicable to pay such taxes and distribute any remaining net proceeds or the balance of any such property after deduction of such taxes to the ADR holders entitled thereto.

ADR holders or beneficial owners will be agreeing to indemnify us, the depositary, its custodian and any of our or their respective officers, directors, employees, agents and affiliates against, and hold each of them harmless from, any claims by any governmental authority with respect to taxes, additions to tax, penalties or interest arising out of any refund of taxes, reduced rate of withholding at source or other tax benefit obtained.

Reclassifications, Recapitalizations and Mergers

If we take certain actions that affect the deposited securities, including (i) any change in par value, split-up, consolidation, cancellation or other reclassification of deposited securities or (ii) any distributions of shares or other property not made to ADR holders or (iii) any recapitalization, reorganization, merger, consolidation, liquidation, receivership, bankruptcy or sale of all or substantially all of our assets, then the depositary may choose to, and shall if reasonably requested by us:

- amend the form of ADR;
- distribute additional or amended ADRs;
- distribute cash, securities or other property it has received in connection with such actions;
- sell any securities or property received and distribute the proceeds as cash; or
- none of the above.

If the depositary does not choose any of the above options, any of the cash, securities or other property it receives will constitute part of the deposited securities and each ADS will then represent a proportionate interest in such property.

Amendment and Termination

How may the deposit agreement be amended?

We may agree with the depositary to amend the deposit agreement and the ADSs without holders' consent for any reason. ADR holders must be given at least 30 days' notice of any amendment that imposes or increases any fees or charges on a per ADS basis (other than stock transfer or other taxes and other governmental charges, transfer or registration fees, SWIFT, cable, telex or facsimile transmission costs, delivery costs or other such expenses), or otherwise prejudices any substantial existing right of ADR holders or beneficial owners of ADSs. Such notice need not describe in detail the specific amendments effectuated thereby, but must identify to ADR holders and beneficial owners a means to access the text of such amendment. If an ADR holder continues to hold an ADR or ADRs after being so notified, such ADR holder and the beneficial owner of the corresponding ADSs are deemed to agree to such amendment and to be bound by the deposit agreement as so amended. No amendment, however, will impair holders' right to surrender their ADSs and receive the underlying securities, except in order to comply with mandatory provisions of applicable law.

Any amendments or supplements which (i) are reasonably necessary (as agreed by us and the depositary) in order for (A) the ADSs to be registered on Form F-6 under the Securities Act of 1933 or (B) the ADSs or shares to be traded solely in electronic book-entry form and (ii) do not in either such case impose or increase any fees or charges to be borne by ADR holders, shall be deemed not to prejudice any substantial rights of ADR holders or beneficial owners of ADSs. Notwithstanding the foregoing, if any governmental body or regulatory body should adopt new laws, rules or regulations which would require amendment or supplement of the deposit agreement or the form of ADR to ensure compliance therewith, we and the depositary may amend or supplement the deposit agreement and the form of ADR (and all outstanding ADRs) at any time in accordance with such changed laws, rules or regulations, which amendment or supplement to the deposit agreement in such circumstances may become effective before a notice of such amendment or supplement is given to ADR holders or within any other period of time as required for compliance.

Notice of any amendment to the deposit agreement or form of ADRs shall not need to describe in detail the specific amendments effectuated thereby, and failure to describe the specific amendments in any such notice shall not render such notice invalid, provided, however, that, in each such case, the notice given to the ADR holders identifies a means for ADR holders and beneficial owners to retrieve or receive the text of such amendment (*i.e.*, upon retrieval from the SEC's, the depositary's or our website or upon request from the depositary).

How may the deposit agreement be terminated?

The depositary may, and shall at our written direction, terminate the deposit agreement and the ADRs by mailing notice of such termination to the ADR holders at least 30 days prior to the date fixed in such notice for such termination; provided, however, if the depositary shall have (i) resigned as depositary under the deposit agreement, notice of such termination by the depositary shall not be provided to ADR holders unless a successor depositary shall not be operating under the deposit agreement within 60 days of the date of such resignation, and (ii) been removed as depositary under the deposit agreement, notice of such termination by the depositary shall not be provided to ADR holders unless a successor depositary shall not be operating under the deposit agreement on the 60th day after our notice of removal was first provided to the depositary. Notwithstanding anything to the contrary herein, the depositary may terminate the deposit agreement without notifying us, but subject to giving 30 days' notice to the ADR holders, under the following circumstances: (i) in the event of our bankruptcy or insolvency, (ii) if we effect (or will effect) a redemption of all or substantially all of the deposited securities, or a cash or share distribution representing a return of all or substantially all of the value of the deposited securities, or (iii) there occurs a merger, consolidation, sale of all or substantially all assets or other transaction as a result of which securities or other property are delivered in exchange for or in lieu of deposited securities. After the date so fixed for termination, the depositary and its agents will perform no further acts under the deposit agreement and the ADRs, except to receive and hold (or sell) distributions on deposited securities and deliver deposited securities being withdrawn. As soon as practicable after the date so fixed for termination, the depositary shall use its reasonable efforts to sell the deposited securities and shall thereafter (as long as it may lawfully do so) hold in an account (which may be a segregated or unsegregated account) the net proceeds of such sales, together with any other cash then held by it under the deposit agreement, without liability for interest, in trust for the pro rata benefit of the ADR holders who have not theretofore surrendered their ADRs. After making such sale, the depositary shall be discharged from all obligations in respect of the deposit agreement and the ADRs, except to account for such net proceeds and other cash. After the date so fixed for termination, we shall be discharged from all obligations under the deposit agreement except for our obligations to the depositary and its agents.

Limitations on Obligations and Liability to ADR holders

Limits on our obligations and the obligations of the depositary; limits on liability to ADR holders and beneficial owners of ADSs

Prior to the issue, registration, registration of transfer, split-up, combination, or cancellation of any ADRs, or the delivery of any distribution in respect thereof, and from time to time in the case of the production of proofs as described below, we or the depositary or its custodian may require:

- payment with respect thereto of (i) any stock transfer or other tax or other governmental charge, (ii) any stock transfer or registration fees in effect for the registration of transfers of shares or other deposited securities upon any applicable register and (iii) any applicable fees and expenses described in the deposit agreement;

- the production of proof satisfactory to it of (i) the identity of any signatory and genuineness of any signature and (ii) such other information, including without limitation, information as to citizenship, residence, exchange control approval, beneficial or other ownership of, or interest in, any securities, compliance with applicable law, regulations, provisions of or governing deposited securities and terms of the deposit agreement and the ADRs, as it may deem necessary or proper; and

- compliance with such regulations as the depositary may establish consistent with the deposit agreement.

The issuance of ADRs, the acceptance of deposits of shares, the registration, registration of transfer, split-up or combination of ADRs or the withdrawal of shares, may be suspended, generally or in particular instances, when the ADR register or any register for deposited securities is closed or when any such action is deemed advisable by the depositary; provided that the ability to withdraw shares may only be limited under the following circumstances: (i) temporary delays caused by closing transfer books of the depositary or our transfer books or the deposit of shares in connection with voting at a shareholders' meeting, or the payment of dividends, (ii) the payment of fees, taxes, and similar charges, and (iii) compliance with any laws or governmental regulations relating to ADRs or to the withdrawal of deposited securities.

The deposit agreement expressly limits the obligations and liability of the depositary, ourselves and each of our and the depositary's respective agents, provided, however, that no provision of the deposit agreement is intended to constitute a waiver or limitation of any rights which ADR holders or beneficial owners of ADSs may have under the Securities Act of 1933 or the Securities Exchange Act of 1934, to the extent applicable. In the deposit agreement it provides that neither we nor the depositary nor any such agent will be liable to ADR holders or beneficial owners of ADSs if:

- any present or future law, rule, regulation, fiat, order or decree of the United States, England, Wales or any other country or jurisdiction, or of any governmental or regulatory authority or securities exchange or market or automated quotation system, the provisions of or governing any deposited securities, any present or future provision of our charter, any act of God, war, terrorism, nationalization, epidemic, pandemic, expropriation, currency restrictions, work stoppage, strike, civil unrest, revolutions, rebellions, explosions, computer failure or circumstance beyond our, the depositary's or our respective agents' direct and immediate control shall prevent or delay, or shall cause any of them to be subject to any civil or criminal penalty in connection with, any act which the deposit agreement or the ADRs provide shall be done or performed by us, the depositary or our respective agents (including, without limitation, voting);
- it exercises or fails to exercise discretion under the deposit agreement or the ADRs including, without limitation, any failure to determine that any distribution or action may be lawful or reasonably practicable;
- it performs its obligations under the deposit agreement and ADRs without gross negligence or willful misconduct;
- it takes any action or refrains from taking any action in reliance upon the advice of or information from legal counsel, accountants, any person presenting shares for deposit, any ADR holder, or any other person believed by it to be competent to give such advice or information, or in the case of the depositary only, our company; or
- it relies upon any written notice, request, direction, instruction or document believed by it to be genuine and to have been signed, presented or given by the proper party or parties.

The depositary shall not be a fiduciary or have any fiduciary duty to ADR holders or beneficial owners of ADSs. Neither the depositary nor its agents have any obligation to appear in, prosecute or defend any action, suit or other proceeding in respect of any deposited securities, the ADSs or the ADRs. We and our agents shall only be obligated to appear in, prosecute or defend any action, suit or other proceeding in respect of any deposited securities, the ADSs or the ADRs, which in our opinion may involve us in expense or liability, if indemnity satisfactory to us against all expense (including fees and disbursements of counsel) and liability is furnished as often as may be required. The depositary and its agents may fully respond to any and all demands or requests for information maintained by or on its behalf in connection with the deposit agreement, any ADR holder or holders, any ADRs or otherwise related to the deposit agreement or ADRs to the extent such information is requested or required by or pursuant to any lawful authority, including without limitation laws, rules, regulations, administrative or judicial process, banking, securities or other regulators. The depositary shall not be liable for the acts or omissions made by, or the insolvency of, any securities depository, clearing agency or settlement system. Furthermore, the depositary shall not be responsible for, and shall incur no liability in connection with or arising from, the insolvency of any custodian that is not a branch or affiliate of JPMorgan. Notwithstanding anything to the contrary contained in the deposit agreement or any ADRs, the depositary shall not be responsible for, and shall incur no liability in connection with or arising from, any act or omission to act on the part of the custodian except to the extent that any ADR holder has incurred liability directly as a result of the custodian having (i) committed fraud or willful misconduct in the provision of custodial services to the depositary or (ii) failed to use reasonable care in the provision of custodial services to the depositary as determined in accordance with the standards prevailing in the jurisdiction in which the custodian is located. The depositary and the custodian(s) may use third party delivery services and providers of information regarding matters such as, but not limited to, pricing, proxy voting, corporate actions, class action litigation and other services in connection with the ADRs and the deposit agreement, and use local agents to provide services such as, but not limited to, attendance at any meetings of security holders. Although the depositary and the custodian will use reasonable care (and cause their agents to use reasonable care) in the selection and retention of such third-party providers and local agents, they will not be responsible for any errors or omissions made by them in providing the relevant information or services. The depositary shall not have any liability for the price received in connection with any sale of securities, the timing thereof or any delay in action or omission to act nor shall it be responsible for any error or delay in action, omission to act, default or negligence on the part of the party so retained in connection with any such sale or proposed sale.

The depositary has no obligation to inform ADR holders or beneficial owners of ADSs about the requirements of any laws, rules or regulations or any changes therein or thereto.

Additionally, none of us, the depositary or the custodian shall be liable for the failure by any ADR holder or beneficial owner of ADSs to obtain the benefits of credits or refunds of non-U.S. tax paid against such ADR holder's or beneficial owner's income tax liability. The depositary is under no obligation to provide ADR holders or beneficial owners of ADSs, or any of them, with any information about the tax status of our company. Neither we nor the depositary shall incur any liability for any tax or tax consequences that may be incurred by ADR holders or beneficial owners of ADSs on account of their ownership or disposition of the ADRs or ADSs.

Neither the depositary nor its agents will be responsible for any failure to carry out any instructions to vote any of the deposited securities, for the manner in which any such vote is cast, or for the effect of any such vote. The depositary may rely upon instructions from us or our counsel in respect of any approval or license required for any currency conversion, transfer or distribution. The depositary shall not incur any liability for the content of any information submitted to it by us or on our behalf for distribution to ADR holders or for any inaccuracy of any translation thereof, for any investment risk associated with acquiring an interest in the deposited securities, for the validity or worth of the deposited securities, for the credit-worthiness of any third party, for allowing any rights to lapse upon the terms of the deposit agreement or for the failure or timeliness of any notice from us. The depositary shall not be liable for any acts or omissions made by a successor depositary whether in connection with a previous act or omission of the depositary or in connection with any matter arising wholly after the removal or resignation of the depositary. Neither the depositary, the Company, nor any of their respective agents shall be liable to ADR holders or beneficial owners of ADSs for any indirect, special, punitive or consequential damages (including, without limitation, legal fees and expenses) or lost profits, in each case of any form incurred by any person or entity (including, without limitation, ADR holders and beneficial owners of ADSs), whether or not foreseeable and regardless of the type of action in which such a claim may be brought.

The depositary and its agents may own and deal in any class of securities of our company and our affiliates and in ADSs.

Disclosure of Interest in ADSs

To the extent that the provisions of or governing any deposited securities may require disclosure of or impose limits on beneficial or other ownership of deposited securities, other shares and other securities and may provide for blocking transfer, voting or other rights to enforce such disclosure or limits, ADR holders and beneficial owners of ADSs agree to comply with all such disclosure requirements and ownership limitations and to comply with any reasonable instructions we may provide in respect thereof. We reserve the right to instruct ADR holders (and through any such ADR holder, the beneficial owners of ADSs evidenced by the ADRs registered in such ADR holder's name) to deliver their ADSs for cancellation and withdrawal of the deposited securities so as to permit us to deal directly with the ADR holder and/or beneficial owner of ADSs as a holder of shares and, by holding an ADS or an interest therein, ADR holders and beneficial owners of ADSs will be agreeing to comply with such instructions.

Each ADR holder and beneficial owner agrees to provide such information as the Company may request in a disclosure notice (a "**Disclosure Notice**") given pursuant to the U.K. Companies Act or the Articles of Association of the Company. Each ADR holder and beneficial owner acknowledges that it understands that failure to comply with a Disclosure Notice may result in the imposition of sanctions against the holder of the underlying Company 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 U.K. Companies Act and the Articles of Association which currently may include, subject to the granting of an appropriate order by the court, the withdrawal of the voting rights of such ordinary shares and the imposition of restrictions on the rights to receive dividends on and to transfer such ordinary shares. In addition, each ADR holder and beneficial owner agrees to comply with the provisions of the Disclosure Guidance and Transparency Rules published by the United Kingdom Financial Conduct Authority (as amended from time to time, the "**DTRs**") with regard to the notification to the Company of interests in Company ordinary shares underlying ADSs and certain financial instruments, which currently provide, *inter alia*, that an ADR holder and beneficial owner must notify the Company of the percentage of its voting rights he holds as a shareholder or holds or is deemed to hold through his direct or indirect holding of certain financial instruments (or a combination of such holdings) if the percentage of those voting rights reaches, exceeds or falls below specified thresholds.

Books of Depositary

The depositary or its agent will maintain a register for the registration, registration of transfer, combination and split-up of ADRs, which register shall include the depositary's direct registration system. ADR holders may inspect such records at the depositary's office at all reasonable times, but solely for the purpose of communicating with other ADR holders in the interest of the business of our company or a matter relating to the deposit agreement. Such register (and/or any portion thereof) may be closed at any time or from time to time, when deemed expedient by the depositary. Additionally, at the reasonable request of the Company, the depositary may close the issuance book portion of the ADR register in order to enable the Company to comply with applicable law.

The depositary will maintain facilities for the delivery and receipt of ADRs.

Appointment

In the deposit agreement, each ADR holder and each beneficial owner of ADSs, upon acceptance of any ADSs (or any interest therein) issued in accordance with the terms and conditions of the deposit agreement will be deemed for all purposes to:

- be a party to and bound by the terms of the deposit agreement and the applicable ADR or ADRs, and
- appoint the depositary its attorney-in-fact, with full power to delegate, to act on its behalf and to take any and all actions contemplated in the deposit agreement and the applicable ADR or ADRs, to adopt any and all procedures necessary to comply with applicable laws and to take such action as the depositary in its sole discretion may deem necessary or appropriate to carry out the purposes of the deposit agreement and the applicable ADR and ADRs, the taking of such actions to be the conclusive determinant of the necessity and appropriateness thereof.

Each ADR holder and beneficial owner of ADSs is further deemed to acknowledge and agree that (i) nothing in the deposit agreement or any ADR shall give rise to a partnership or joint venture among the parties thereto nor establish a fiduciary or similar relationship among such parties, (ii) the depositary, its divisions, branches and affiliates, and their respective agents, may from time to time be in the possession of non-public information about our company, the ADR holders, the beneficial owners of ADSs and/or their respective affiliates, (iii) the depositary and its divisions, branches and affiliates may at any time have multiple banking relationships with us, ADR holders, beneficial owners of ADSs and/or the affiliates of any of them, (iv) the depositary and its divisions, branches and affiliates may, from time to time, be engaged in transactions in which parties adverse to us or the ADR holders or beneficial owners of ADSs may have interests, (v) nothing contained in the deposit agreement or any ADR(s) shall (A) preclude the depositary or any of its divisions, branches or affiliates from engaging in such transactions or establishing or maintaining such relationships, or (B) obligate the depositary or any of its divisions, branches or affiliates to disclose such transactions or relationships or to account for any profit made or payment received in such transactions or relationships, and (vi) the depositary shall not be deemed to have knowledge of any information held by any branch, division or affiliate of the depositary.

Governing Law and Consent to Jurisdiction

The deposit agreement and the ADRs are governed by and construed in accordance with the laws of the State of New York. In the deposit agreement, we have submitted to the jurisdiction of the courts of the State of New York and appointed an agent for service of process on our behalf. Without limiting the foregoing, any claim brought by any ADR holder or beneficial owner or on behalf of the Company with regard to the internal affairs of the Company, including the ability to bring such a claim, shall be governed by and construed in accordance with the laws of England and Wales, and any such claims may only be instituted against the Company, its directors, officers or employees as provided in the Company's Articles of Association in the courts of England and Wales.

By holding an ADS or an interest therein, ADR holders and beneficial owners of ADSs each irrevocably agree that any legal suit, action or proceeding brought by any holder or beneficial owner against or involving us or the depositary, arising out of or based upon the deposit agreement, the ADSs or the transactions contemplated thereby, may only be instituted in a federal court in New York, New York, or, except for claims arising under the Securities Act of 1933 or Securities Exchange Act of 1934, any state court in New York, New York, and each irrevocably waives any objection which it may have to the laying of venue of any such proceeding, and irrevocably submits to the exclusive jurisdiction of such courts in any such suit, action or proceeding, provided, however, pursuant to applicable law and the Company's Articles of Association, any claim brought by holders or beneficial owners arising under the Securities Act of 1933 may be instituted only in any federal court in the United States, and any claim brought by any ADR holder or beneficial owner or on behalf of the Company with regard to the internal affairs of the Company, including the ability to brings such a claim, shall be governed by and construed in accordance with the laws of England and Wales, and any such claims may only be instituted against the Company, its directors, officers or employees as provided in the Company's Articles of Association in the courts of England and Wales.

Jury Trial Waiver

The deposit agreement provides that, to the fullest extent permitted by applicable law, each party thereto (including, for avoidance of doubt, each ADR holder and beneficial owner and/or holder of interests in ADSs) irrevocably waives, to the fullest extent permitted by applicable law, the right to a jury trial in any suit, action or proceeding against us or the depositary directly or indirectly arising out of or relating to our shares or other deposited securities, the ADSs, the ADRs, the deposit agreement, or any transaction contemplated therein, or the breach thereof (whether based on contract, tort, common law or other theory), including any suit, action or proceeding under the U.S. federal securities laws. If we or the depositary were to oppose a jury trial demand based on such waiver, the court would determine whether the waiver was enforceable in the facts and circumstances of that case in accordance with applicable state and federal law, including whether a party knowingly, intelligently and voluntarily waived the right to a jury trial. The waiver to right to a jury trial of the deposit agreement is not intended to be deemed a waiver by any ADR holder or beneficial owner of ADSs of our or the depositary's compliance with the Securities Act of 1933 or the Securities Exchange Act of 1934, to the extent applicable.

4D PHARMA DELAWARE INC.

JOHN DOYLE EMPLOYMENT AGREEMENT

THIS EXECUTIVE EMPLOYMENT AGREEMENT (this "Agreement") is entered into as of January 3rd, 2022 (the "Effective Date") by and between 4D Pharma Delaware Inc. (the "Company"), and John Doyle ("Executive") (collectively referred to as the "Parties" or individually referred to as a "Party").

RECITALS

WHEREAS, the Company desires to employ Executive as its Chief Financial Officer and to enter into an agreement embodying the terms of such employment;

WHEREAS, Executive desires to accept such employment and enter into such an agreement.

AGREEMENT

NOW, THEREFORE, in consideration of the premises and mutual covenants herein and for other good and valuable consideration, the Parties agree as follows:

1. Duties and Scope of Employment.

(a) Positions and Duties. As of the Effective Date, Executive will serve as Chief Financial Officer of the Company, and will report to the Parent's Chief Executive Officer. Executive will render such business and professional services in the performance of Executive's duties, consistent with Executive's position within the Company, as shall reasonably be assigned to him by the Company or the Company's parent corporation, 4D Pharma PLC ("Parent"). This will include, but not be limited, the following duties: (i) directing and overseeing the financial activities of the Company, including by directing the preparation of current financial reports and summaries and creating forecasts predicting future growth, and (ii) conducting evaluations, development, implementation, and management strategies when the Company plans and executes acquisitions, licensing agreements, and partnerships. The period of Executive's at-will employment under the terms of this Agreement is referred to herein as the "Employment Term."

(b) Obligations. During the Employment Term, Executive will perform Executive's duties faithfully and to the best of Executive's ability and will devote Executive's full business efforts and time to the Company. For the duration of the Employment Term, Executive agrees not to actively engage in any other employment, occupation or consulting activity for any direct or indirect remuneration without the prior approval of Parent's Board of Directors (the "Board").

2. At-Will Employment. Subject to Section 6 below, the Parties agree that Executive's employment with the Company will be "at-will" employment and may be terminated at any time with or without cause, for any reason or no reason. Executive understands and agrees that neither Executive's job performance nor promotions, commendations, bonuses or the like from the Company give rise to or in any way serve as the basis for modification, amendment, or extension, by implication or otherwise, of Executive's employment with the Company.

3. Compensation.

(a) Base Salary. During the Employment Term, the Company will pay Executive an annual base salary of $385,000, as modified from time to time at the discretion of the Company (the "Base Salary"). The Base Salary will be paid in regular monthly installments on the 26th day of each month in accordance with the Company's normal payroll practices (subject to required withholding). Any increase or decrease in Base Salary (together with the then existing Base Salary) shall serve as the "Base Salary" for future employment under this

Agreement. The first and last payment will be adjusted, if necessary, to reflect a commencement or termination date other than the first or last working day of a pay period.

(b) Annual Bonus. During the Employment Term, Executive will be eligible to receive an annual performance bonus with a target amount equal to thirty-five percent (35%) of the Executive's Base Salary (the "Bonus Target"). The actual bonus amount and percentage are discretionary and will be subject to the assessment of the Executive's individual performance, the Company's performance each calendar year and consideration of prevailing market practices by the remuneration committee of the Board (the "Annual Bonus"). If the committee determines that Executive should receive an Annual Bonus for any given calendar year, the Company shall pay Executive the bonus by the end of the month following each calendar year end so long as Executive is employed with the Company as of such payment date. For the avoidance of doubt, the amount of the Annual Bonus (if any) shall be determined by the remuneration committee, in good faith its sole discretion.

(c) Stock Grant. Promptly following the Effective Date, subject to the approval of the Board, Executive will be granted an option to purchase 1,382,416 shares of the Parent's Common Stock at an exercise price per share equal to the stock's fair market value on the date of the grant (or an equivalent number of American Depositary Receipts). To be eligible, Executive must still be employed by the Company when the Board grants the option. It is intended that the Option shall, to the extent it so qualifies, be an incentive stock option as defined in Section 422 of the Internal Revenue Code of 1986, as amended (the "Code") and any regulations promulgated thereunder. 25% of the Shares subject to the option shall vest 12 months after the date Executive's vesting begins, no shares shall vest before such date, and no rights to any vesting shall be earned or accrued prior to such date. The remaining shares shall vest monthly over the next 36 months in equal monthly amounts, so that the Option will be fully vested and exercisable four (4) years from the date of grant, subject to Executive's continuing vesting eligibility. This option grant shall be subject to the terms and conditions of the Company's Stock Option Plan and Stock Option Agreement, including vesting requirements. No right to any stock is earned or accrued until such time that vesting occurs, nor does this grant confer any right to continue vesting or employment.

(i) Executive will be eligible to receive awards of stock options, restricted stock or other equity awards pursuant to any plans or arrangements the Company may have in effect from time to time. The Board or a committee of the Board shall determine in good faith and in its discretion whether Executive shall be granted any such equity awards and the terms of any such award in accordance with the terms of any applicable plan or arrangement that may be in effect from time to time.

4. Employee Benefits. During the Employment Term, Executive will be eligible to participate in the employee benefit plans currently and hereafter maintained by the Company of general applicability to other senior executives of the Company, including, without limitation, the Company's group medical insurance plan and a Company-sponsored 401(k) plan once the applicable plans and policies are put in place. Until a health insurance plan is in place at the Company, the Company will reimburse the Executive for the monthly cost of the Executives medical and dental insurance premiums up to a maximum of $3,000 per month. The Company reserves the right to cancel or change the benefit plans and programs it offers to its employees at any time.

5. Background Checks, Etc. The Company reserves the right to conduct background investigations and/or reference checks on Executive. Executive's job offer is contingent upon a clearance of such a background investigation and/or reference check, if any. Executive's job offer is also contingent on obtaining applicable security clearances, passing a drug screening, and the timely execution of the Confidential Information Agreement (as defined below).

6. Termination. The Company agrees to provide Executive with 3 months' advance notice if the Company terminates Executive's employment without Cause. Executive agrees to provide the Company with 3 months' advance notice of Executive's decision to voluntarily resign from Executive's employment. The Company may, at its discretion, accelerate Executive's resignation such that Executive's employment terminates prior to the end of the resignation notice period ("Accelerated Notice"). If the Company exercises its Accelerated Notice right, the Company agrees to pay Executive his base salary for the period of time from the date on which Executive provided notice of his resignation until 3 months therefrom (the "Notice Period"). The Company will also accelerate the vesting of any equity awards that would otherwise have vested during the Notice Period and will reimburse Executive for the costs of Executive's health insurance premiums under COBRA during the Notice Period.

(a) Cause. For purposes of this Agreement, "Cause" shall mean: (i) Executive's continued failure to substantially perform the material duties and obligations of his position with the Company, which failure, if curable within the discretion of the Company, is not cured to the reasonable satisfaction of the Company within thirty (30) days after receipt of written notice from the Company of such failure; (ii) Executive's willful failure or refusal to comply with the policies, standards and regulations established by the Company or Parent from time to time which failure, if curable in the discretion of the Company, is not cured to the reasonable satisfaction of the Company within thirty (30) days after receipt of written notice of such failure from the Company; (iii) any act of personal dishonesty, fraud, embezzlement, misrepresentation, or other unlawful act committed by Executive that benefits Executive at the expense of the Company; (iv) Executive's violation of a federal or state law or regulation applicable to the Company's business; (v) Executive's conviction of, or a plea of nolo contendere or guilty to, a felony under the laws of the United States or any state; or (vi) Executive's material breach of the terms of this Agreement or the Confidential Information Agreement (defined below).

7. Company Matters.

(a) Proprietary Information and Inventions. Executive acknowledges and agrees that Executive has signed, is bound by, and will continue to abide by the terms of the At-Will Employment, Confidential Information, Invention Assignment, and Arbitration Agreement, which Executive will execute simultaneously with this Agreement (the "Confidential Information Agreement"), including the provisions governing the non-disclosure of confidential information and restrictive covenants contained therein.

(b) Resignation on Termination. On termination of Executive's employment, regardless of the reason for such termination, Executive shall immediately (and with contemporaneous effect) resign any directorships, offices or other positions that Executive may hold in the Company or any affiliate, unless otherwise agreed in writing by the Parties.

(c) Notification of New Employer. In the event that Executive leaves the employ of the Company, Executive grants consent to notification by the Company to Executive's new employer about Executive's rights and obligations under this Agreement and the Confidential Information Agreement.

8. Arbitration. IN CONSIDERATION OF EXECUTIVE'S EMPLOYMENT WITH THE COMPANY, ITS PROMISE TO ARBITRATE ALL EMPLOYMENT-RELATED DISPUTES AND EXECUTIVE'S RECEIPT OF THE COMPENSATION, PAY RAISES AND OTHER BENEFITS PAID TO EXECUTIVE BY THE COMPANY, AT PRESENT AND IN THE FUTURE, EXECUTIVE AGREES THAT ANY AND ALL CONTROVERSIES, CLAIMS, OR DISPUTES WITH ANYONE (INCLUDING THE COMPANY AND ANY EMPLOYEE, OFFICER, DIRECTOR, SHAREHOLDER OR BENEFIT PLAN OF THE COMPANY, IN THEIR CAPACITY AS SUCH OR OTHERWISE), WHETHER BROUGHT ON AN INDIVIDUAL, GROUP, COLLECTIVE, OR CLASS BASIS, ARISING OUT OF, RELATING TO, OR RESULTING FROM EXECUTIVE'S EMPLOYMENT WITH THE COMPANY OR THE TERMINATION

OF EXECUTIVE'S EMPLOYMENT WITH THE COMPANY, INCLUDING ANY BREACH OF THIS AGREEMENT, SHALL BE SUBJECT TO BINDING ARBITRATION, AS SET FORTH IN THE CONFIDENTIAL INFORMATION AGREEMENT.

9. Assignment. This Agreement will be binding upon and inure to the benefit of (a) the heirs, executors and legal representatives of Executive upon Executive's death and (b) any successor of the Company. Any such successor of the Company will be deemed substituted for the Company under the terms of this Agreement for all purposes. For this purpose, "successor" means any person, firm, corporation or other business entity which at any time, whether by purchase, merger or otherwise, directly or indirectly acquires all or substantially all of the assets or business of the Company. None of the rights of Executive to receive any form of compensation payable pursuant to this Agreement may be assigned or transferred except by will or the laws of descent and distribution. Any other attempted assignment, transfer, conveyance or other disposition of Executive's right to compensation or other benefits will be null and void.

10. Notices. All notices, requests, demands and other communications called for under this Agreement shall be in writing and shall be delivered personally by hand or by courier, mailed by United States first-class mail, postage prepaid, or sent by email directed to the Party to be notified at the physical address or email address indicated for such Party on the signature page to this Agreement, or at such other physical address or email address as such Party may designate by ten (10) days' advance written notice to the other Parties hereto. All such notices and other communications shall be deemed given upon personal delivery, three (3) days after the date of mailing, or at the time that the email is sent (so long as such email is not returned as undeliverable).

11. Severability. In the event that any provision hereof becomes or is declared by a court of competent jurisdiction to be illegal, unenforceable or void, this Agreement will continue in full force and effect without said provision.

12. Integration. This Agreement, together with the Confidential Information Agreement represents the entire agreement and understanding between the parties as to the subject matter herein and supersedes all prior or contemporaneous agreements whether written or oral, including the unsigned offer letter that Executive received on or about October 15, 2021. No waiver, alteration, or modification of any of the provisions of this Agreement will be binding unless in writing and signed by duly authorized representatives of the parties hereto.

13. Tax Withholding. All payments made pursuant to this Agreement will be subject to withholding of applicable taxes.

14. Waiver. No Party shall be deemed to have waived any right, power or privilege under this Agreement or any provisions hereof unless such waiver shall have been duly executed in writing and acknowledged by the Party to be charged with such waiver. The failure of any Party at any time to insist on performance of any of the provisions of this Agreement shall in no way be construed to be a waiver of such provisions, nor in any way to affect the validity of this Agreement or any part hereof. No waiver of any breach of this Agreement shall be held to be a waiver of any other subsequent breach

15. Governing Law. This Agreement will be governed by the laws of the Commonwealth of Massachusetts (with the exception of its conflict of laws provisions).

16. Conflict Waiver. Each of the Parties to this Agreement understands that Wilson Sonsini Goodrich & Rosati, Professional Corporation ("WSGR"), is serving as counsel to the Company in connection with the transactions contemplated hereby, and that discussion of such transactions with Executive could be construed to create a conflict of interest. By executing this Agreement, the Parties hereto acknowledge the potential conflict of interest and waive the right to claim any conflict of interest at a later date. Furthermore, by executing this Agreement, the Parties acknowledge that if a conflict of interest exists and any litigation arises

between Executive and the Company, WSGR would represent the Company. Executive represents and warrants that Executive has had the opportunity to seek independent counsel in Executive's review of this and all related agreements and that Executive is not relying on WSGR for any legal, tax or other advice relating to such agreements.

17. Acknowledgment. Executive acknowledges that Executive has had the opportunity to discuss this matter with and obtain advice from Executive's legal counsel, has had sufficient time to, and has carefully read and fully understands all the provisions of this Agreement, and is knowingly and voluntarily entering into this Agreement.

18. Counterparts. This Agreement may be executed in multiple counterparts, each of which shall be deemed to be an original, and all such counterparts shall constitute but one instrument.

19. Effect of Headings. The section and subsection headings contained herein are for convenience only and shall not affect the construction hereof.

20. Construction of Agreement. This Agreement has been negotiated by the respective Parties, and the language shall not be construed for or against either Party.

[*Remainder of page is intentionally blank; Signature page follows*]

IN WITNESS WHEREOF, each of the Parties has executed this Agreement as of the day and year first above written.

"COMPANY"

4D PHARMA DELAWARE INC.

By: */s/ Glenn Dourado*
Glenn Dourado, President

"EXECUTIVE"

JOHN DOYLE

/s/John Doyle
John Doyle

Exhibit 4.17

RULES OF THE 4D PHARMA PLC LONG-TERM INCENTIVE PLAN

Adopted by the board of directors on
26 October 2021

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1. DEFINITIONS AND INTERPRETATION

1.1 Definitions

Unless otherwise stated, the words and expressions below have the following meanings:-

"Admission" means the day on which Shares were first admitted to trading on AIM; **"ADS"** means an American depository share in the Company;

"Award" means a Conditional Award, a Nil-cost Option or a Market Value Option; **"Board"** means the board of directors of the Company;

"Committee" means the remuneration committee of the Board or any person or persons duly authorised and appointed by them;

"Companies Act" means the UK Companies Act 2006; **"Company"** means 4D Pharma plc;

"Conditional Award" means a right to receive Shares at nil cost, subject to the rules of the Plan;

"Control" has the meaning given by section 995 of the UK Income Tax Act 2007;

"Dealing Day" means any day on which the stock exchange on which the Shares are listed is open for business;

"Dealing Restrictions" means restrictions imposed by the Company's share dealing code, the Listing Rules published by the United Kingdom Financial Conduct Authority, the EU Market Abuse Regulation 596/2014 or any other relevant laws or regulations that impose restrictions on share dealing;

"Dividend Equivalent" means the right for a Participant to receive any additional Shares or cash in accordance with rule 3.4;

"Eligible Employee" means an employee (including an executive director) of the Company or any of its Subsidiaries;

"Early Vesting Trigger" means the reason under the rules of the Plan for which an Award Vests before its Normal Vesting Date;

"Exercise Period" means the period beginning on the Release Date and ending on the tenth anniversary of the Grant Date (or such earlier date as the Committee may determine on or before the Grant Date);

"Good Leaver" means a Participant who Leaves in accordance with rule 5.2(a);

"Grant Date" means the date on which an Award is granted;

"Grant Period" means the period of 42 days beginning on:

(a) the first Dealing Day after the day on which the Company makes an announcement of its results for any period; or

(b) any day on which the Committee resolves that exceptional circumstances exist which justify the grant of Awards,

unless Dealing Restrictions prevent the Company from granting Awards during any such period, in which case Grant Period means the period of 42 days beginning on the day after such Dealing Restrictions lift;

"Group Company" means the Company, any Subsidiary of the Company, any Holding Company of the Company, any Subsidiary of a Holding Company of the Company or any other company that is associated with the Company and so designated by the Committee, and **"Group"** will be construed accordingly;

"Holding Company" has the meaning given by section 1159 of the Companies Act;

"Internal Reorganisation" means a change of Control of the Company, where immediately after such change of Control, all or substantially all of the share capital of the acquiring company is owned directly or indirectly by the persons who were shareholders in the Company immediately before the change of Control;

"Leaving" has the meaning given in rule 5.6, and **"Leaves"** and **"Left"** will be construed accordingly;

"Market Value" means the middle market quotation of a Share (as derived from AIM) on the Dealing Day immediately preceding the relevant date, unless the Committee determines that such expression means:

(a) the average of the middle market quotations of a Share (as derived from AIM) for a number of Dealing Days (not exceeding five) immediately preceding the relevant date; or

(b) such other value (calculated on a reasonable basis) as the Committee may determine;

"Market Value Exercise Price" means an amount equal to the Market Value on 1 June in the calendar year in which a Market Value Option is granted unless the Committee determines that the Market Value on the Grant Date will apply instead;

"Market Value Option" means a right to acquire Shares at a price per Share which is equal to the Market Value Exercise Price following exercise, subject to the rules of the Plan;

"Nil-cost Option" means a right to acquire Shares at nil cost (or, if the Committee determines before the Grant Date, for a Nominal Exercise Price) following exercise, subject to the rules of the Plan;

"Nominal Exercise Price" means an amount equal to the nominal cost of a Share payable per Share on the exercise of a Nil-cost Option;

"Normal Vesting Date" means such date or dates as the Committee may determine on or before the Grant Date;

"Participant" means any person who holds an Award;

"Performance Condition" means a condition to the Vesting of an Award which relates to performance;

"Performance Period" means the period over which a Performance Condition will be measured, which will be determined by the Committee on or before the Grant Date);

"Plan" means the 4D Pharma plc Long-Term Incentive Plan, as amended from time to time;

"Recovery Period" means, in relation to an Award, the period beginning on the start of the Vesting Period and, subject to rule 8.6, ending on the later of the Release Date and such date as the Committee may determine on or before the Grant Date;

"Release" means:

(a) in relation to a Conditional Award, that the Participant becomes entitled to receive the Shares under the Award to the extent it has Vested; and

(b) in relation to a Nil-cost Option or a Market Value Option, that the Award becomes capable of exercise to the extent it has Vested,

in either case, subject to the rules of the Plan, and **"Released"** and **"Unreleased"** will be construed accordingly;

"Release Date" means the date on which an Award is Released; **"Share"** means an ordinary share in the Company;

"Shareholding Policy" means the Company's shareholding policy in force from time to time, as notified to any Participant to which it applies;

"Subsidiary" has the meaning given by section 1159 of the Companies Act;

"Tax Liability" means any tax or social security contributions liability in connection with an Award for which the Participant is liable (or which may be recovered from the Participant) and for which any Group Company or former Group Company is obliged to account to any relevant authority;

"Termination Date" means the tenth anniversary of the date when the Board adopted the Plan or at any earlier time that the Committee may determine;

"Trust" means any trust established by the Company or any Group Company for the benefit of employees of the Group;

"Trustee" means the trustee or trustees for the time being of the Trust;

"Vest" means:

(a) in relation to a Conditional Award, that the number of Shares that the Participant will become entitled to receive on its Release is determined; and

(b) in relation to a Nil-cost Option or a Market Value Option, that the number of Shares over which the Award will become capable of exercise on its Release is determined,

in either case, subject to the rules of the Plan, and **"Vesting"**, **"Vested"** and **"Unvested"** will be construed accordingly;

"Vesting Date" means the date on which an Award Vests; and

"Vesting Period" means:

(a) in relation to an Award that is subject to a Performance Condition, the Performance Period; and

(b) in relation to an Award that is not subject to a Performance Condition, the period beginning on the Grant Date (or such earlier date as the Committee may determine) and ending on the Normal Vesting Date.

1.2 Interpretation

(a) References to:

(i) any body include any successor body;

(ii) any statutory provisions or related rules are to those provisions or rules as amended or re-enacted from time to time; and

(iii) the singular include the plural, and vice versa.

(b) If an Award is granted over ADSs, references in the Plan to "Shares" shall be construed as references to "ADSs" as the context requires.

(c) Headings do not form part of the Plan.

2. GRANT OF AWARDS

2.1 Grant

(a) The Committee may grant an Award to an Eligible Employee during a Grant Period at any time before the Termination Date and in such form and manner as it determines.

(b) As soon as reasonably practicable after the Grant Date, a Participant will be notified of the terms of their Award, including:

(i) its form and the number of Shares to which it relates;

(ii) that an Award has been granted over ADSs, if that is the case;

(iii) its Normal Vesting Date;

(iv) any applicable Performance Condition and Performance Period;

(v) that Dividend Equivalents will apply, if that is the case;

(vi) in the case of a Nil-cost Option, the Exercise Period and, if relevant, the Nominal Exercise Price;

(vii) in the case of a Market Value Option, the Exercise Period and the Market Value Exercise Price;

(viii) whether Shares acquired pursuant to the Award will be subject to any Shareholding Policy; and

(ix) any other terms.

(c) If an Award is divided into a different tranches that are subject to different terms, each tranche will be treated as a separate Award for the purposes of the Plan.

(d) The Committee may lapse an Award if it has not been accepted by the Participant in such form as the Committee reasonably requires before such date as the Committee prescribes.

2.2 Plan limits

(a) This rule 2.2 shall cease to apply if the Shares cease to be admitted to trading on AIM.

(b) The Committee may not grant an Award on any day if the number of Shares that could be allocated to that Award, when aggregated with the number of Shares that have already been allocated or could be allocated under awards granted in the previous ten years but since Admission under any scheme adopted by any Group Company, would exceed 10% of the Company's issued ordinary share capital.

(c) For the purposes of rule 2.2(b):

(i) Shares are "allocated" if they have been, or the Committee intends that they will be, newly issued or transferred from treasury (directly or indirectly) to satisfy an Award or any other right to Shares, provided that Shares will cease to be allocated to the extent that:

(A) the Awards or other rights to which they relate lapse, or are satisfied or are intended to be satisfied with existing Shares and/or cash; and/or

(B) institutional investor guidelines no longer require Shares transferred from treasury to be included in the limits; and

(ii) if Shares are issued by the Company to any Trustee for the purpose of enabling the Trustee to transfer such Shares to beneficiaries of the Trust in satisfaction of Awards or other rights to Shares and such Shares have been taken into account for the purposes of Rule 2.2(b) on the grant of such Awards, such Shares shall not be taken into account again upon their issue to the Trustee.

2.3 Shareholding policy

A Conditional Share Award will not be Released to and a Nil-cost Option or a Market Value Option may not be exercised by a Participant who is subject to any Shareholding Policy unless the Committee is satisfied that there are sufficient measures in place in order to enforce the Shareholding Policy, which may include:

(a) the Participant having entered into an agreement with such person and in such form as the Committee may determine, pursuant to which such person will hold any Shares to which the Participant becomes entitled under the Plan as nominee for the Participant;

(b) the share certificates relating to the Shares to which the Participant becomes entitled under the Plan being held on behalf of the Participant by such person as the Committee may nominate; and/or

(c) the Participant taking such other action as the Committee may reasonably require.

3. VESTING, RELEASE AND EXERCISE

3.1 Timing of Vesting

Unless otherwise prescribed in the rules of the Plan, an Award will Vest, subject to rule 3.2, on the later of:

(a) its Normal Vesting Date; and

(b) if relevant, the date on which the Committee determines the extent to which any Performance Condition has been satisfied,

and, as soon as reasonably practicable after the Vesting Date, the Committee shall notify the Participant of the extent to which their Award has Vested.

3.2 Extent of Vesting

(a) The Committee will determine the extent to which any Performance Condition applicable to an Award has been satisfied as soon as reasonably practicable following the end of the Performance Period, and, subject to any reduction under rule 3.2(c), the Award will Vest in accordance with such determination.

(b) If an Award Vests under the rules of the Plan before its Normal Vesting Date, the Committee will, subject to rule 3.2(c), determine the number of Shares in respect of which such Award Vests:

(i) by determining the extent to which any applicable Performance Condition has been satisfied on the date of the Early Vesting Trigger on such basis as the Committee considers reasonable; and

(ii) by reducing the Vesting level to reflect the proportion of the Vesting Period that is unexpired on the date of the Early Vesting Trigger, unless:

(A) the Committee considers it appropriate to apply a lesser reduction or none at all; or

(B) the Award is held by a Good Leaver and a reduction has been applied under rule 5.2(b)(i).

(c) In determining the extent to which a Performance Condition has been satisfied (whether under rule 3.2(a) or rule 3.2(b)) or at any other time before an Award Vests, the Committee may reduce (including to nil) the extent to which an Award would otherwise Vest (based on the formulaic application of a Performance Condition or otherwise) to reflect such circumstances as the Committee may, in its absolute discretion, determine, including (without limitation):

(i) the underlying performance (financial or otherwise) of the Participant or the Group since the beginning of the Vesting Period; and/or

(ii) circumstances that were unexpected or unforeseen at the Grant Date.

(d) An Award shall lapse to the extent that:

(i) it does not Vest under this rule 3.2; or

(ii) any other condition to which Vesting is subject has not been satisfied on the date it is due to Vest, unless such condition is waived by the Committee.

3.3 Release

(a) Unless otherwise prescribed in the rules of the Plan, an Award will be Released on its Vesting Date.

(b) An Award shall lapse to the extent that any condition to Release has not been satisfied on the date it is due to be Released, unless such condition is waived by the Committee.

(c) The Committee shall notify a Participant of the Release of their Award.

3.4 Dividend Equivalents

If the Committee determines that Dividend Equivalents will apply to an Award, the Participant shall be entitled on settlement of the Award (in accordance with rule 4.1) to an amount in cash or additional Shares equal in value to any dividends (excluding special dividends) that would have been paid on the Shares in relation to which a Conditional Award has been Released or a Nil-cost Option or a Market Value Option has been exercised (as applicable) between its Grant Date (or such earlier date as the Committee may determine, being no earlier than the beginning of the Vesting Period) and Release Date, determined on such reasonable basis as the Committee in its discretion decides. This amount will not presume the reinvestment of dividends unless the Committee determines otherwise.

3.5 Restrictions on Release

If on the date on which an Award would otherwise be Released:

(a) a Dealing Restriction applies that would prevent such Release, the Award will instead be Released on the date on which such Dealing Restriction lifts;

(b) the action or conduct of any Participant, Group Company or relevant business unit is under investigation in connection with the operation of rule 8 (or the equivalent provisions of another employee incentive plan operated by a Group Company) and such investigation has not been concluded, the Committee may determine that the Award will instead (subject to any action taken under rule 8) be Released on such date that it determines the investigation has been concluded; or

(c) an event has occurred which causes the Committee reasonably to consider that it would be appropriate to do so, the Committee may alter the date on which an Award is Released, which may include a delay in Release and/or an Award being Released in instalments.

3.6 Exercise of Nil-cost Options and Market Value Options

(a) Unless otherwise prescribed in the rules of the Plan, a Released Nil-cost Option or a Released Market Value Option may be exercised during the Exercise Period at any time that a Dealing Restriction would not prevent exercise.

(b) Exercise of a Nil-cost Option or a Market Value Option in whole or in part (and if in part, on more than one occasion) shall be effected by the Participant executing such process as the Committee may determine, and making payment (in such form as is acceptable to the Committee, which may include an undertaking to pay) of the Nominal Exercise Price or the Market Value Exercise Price.

(c) A Nil-cost Option or a Market Value Option will lapse at the end of the Exercise Period to the extent that it has not been exercised or otherwise lapsed under the rules of the Plan.

4. SETTLEMENT

4.1 Delivery of Shares or cash

(a) The number of Shares in respect of which an Award has been Released or, in the case of a Nil-cost Option or a Market Value Option been validly exercised in accordance with rule 3.6(b), will be delivered to the Participant within 30 days of the Release Date of the Conditional Award or the exercise of the Nil-cost Option or the Market Value Option (as applicable). The Company may issue new Shares or procure the transfer of Shares to satisfy its obligations to deliver Shares (subject to applicable laws).

(b) The Committee may at any time determine that, in substitution for some or all of the Shares that would otherwise have been delivered to a Participant pursuant to rule 4.1(a), the Participant will instead be paid a cash sum equal to the Market Value of such Shares on the Release Date of the Conditional Award or the exercise of the Nil-cost Option or the Market Value Option, and any such cash sum will be paid to the Participant within 30 days of the Release Date of the Conditional Award or the exercise of the Nil-cost Option or the Market Value Option net of any Tax Liability. In the case of a Market Value Option, the aggregate Market Value Exercise Price will be deducted from the Market Value of the Shares for the purposes of calculating the cash sum, as will any aggregate Nominal Exercise Price applicable to a Nil-cost Option.

(c) Any costs (including any stamp duty or stamp duty reserve tax and any dealing costs) associated with:

(i) the delivery of Shares to satisfy an Award will be borne by the Company; and

(ii) the sale of Shares (including in connection with rule 4.3) will be borne by the Participant.

4.2 Restrictions on settlement

If on the date on which an Award would otherwise be settled pursuant to rule 4.1, a Dealing Restriction would prevent such settlement, the Award will instead be settled when such Dealing Restriction lifts.

4.3 Taxation

(a) A Participant is responsible for and shall indemnify each relevant Group Company against any Tax Liability relating to their Award. Any Group Company may withhold or recover an amount equal to its reasonable estimate of such Tax Liability using such means or arrangements as it considers appropriate to ensure recovery of the Tax Liability and its payment to a relevant tax authority within any applicable time limits. These may include the sale of some or all the Shares to which the Award relates or the cash settlement under rule 4.1(b) of such part of the Award as is as near as reasonably practicably equal to its reasonable estimate of the Tax Liability relating to their Award.

(b) A Participant shall enter into such tax elections (including under section 431 of the Income Tax (Earnings and Pensions) Act 2003) as the Committee may reasonably require in respect of any Shares to be acquired under the Plan.

5. LEAVERS

5.1 Leaving before the Normal Vesting Date

If a Participant Leaves before the Normal Vesting Date of their Award other than as a Good Leaver or because they die, their Award will lapse when they Leave.

5.2 Good Leavers before the Normal Vesting Date

(a) If a Participant Leaves before the Normal Vesting Date of their Award because of:

(i) ill-health, injury or disability of such severity as to result in the Participant's Leaving (as determined by the Committee);

(ii) any reason (other than gross misconduct) after the Participant has accrued 15 years of continuous service with the Group;

(iii) the Participant's employing company ceasing to be a Group Company or the transfer of an undertaking or part of an undertaking to a person who is not a Group Company; or

(iv) any other reason (other than gross misconduct) at the Committee's discretion, they will be treated as a Good Leaver.

(b) If a Participant is a Good Leaver, their Award will subsist subject to its terms and the rules of the Plan (including its Normal Vesting Date and any Performance Condition), provided that:

(i) the number of Shares in respect of which such Award is capable of Vesting will be reduced to reflect the portion of the Vesting Period that was unexpired when the Participant Leaves, unless the Committee considers it appropriate to apply a lesser reduction or none at all; or

(ii) the Committee may decide that such Award will Vest and be Released when they Leave or on such other date before the Normal Vesting Date as the Committee may determine, in which case rule 3.2(b) shall apply and the Participant Leaving will be the Early Vesting Trigger.

5.3 Leaving on or after the Normal Vesting Date

If a Participant Leaves on or after the Normal Vesting Date of their Award, their Award will subsist subject to its terms and the rules of the Plan, unless the Participant Leaves because of gross misconduct, in which case their Award will lapse when they Leave.

5.4 Death

If a Participant Leaves because they die, all Awards will Vest and be Released when they Leave, in which case rule 3.2(b) shall apply and the Participant's death will be the Early Vesting Trigger.

5.5 Period of exercise of a Nil-cost Option or a Market Value Option

If a Participant Leaves, a Nil-cost Option or a Market Value Option:

(a) may, unless otherwise prescribed in the rules of the Plan, (to the extent it has Vested and been Released) be exercised until the later of 30 days after its Release Date and 30 days after they Leave, or where the Participant Leaves because they die, 12 months from the date of their death, unless in any case the Committee decides to allow a longer exercise period; and

(b) will lapse to the extent it is not exercised in accordance with rule 5.5(a),

provided that the Committee may determine that some or all of an unexercised Nil-cost Option or Market Value Option may lapse immediately if it, in its absolute discretion, determines that the Participant has breached any term of their employment contract (or any settlement agreement relating to their employment contract) with a Group Company that applies after they have Left.

5.6 Meaning of Leaving

For the purposes of the Plan, a Participant will be treated as Leaving when they no longer hold an office or employment (or a right to return to work) with any Group Company.

6. CORPORATE EVENTS

6.1 Takeovers

(a) Rule 6.1(b) shall apply if any of the following occurs (each, a **"Takeover Event"**):

(i) any person (either alone or together with any person acting in concert with them):

(A) obtains Control of the Company as a result of making a general offer to acquire Shares; or

(B) already having Control of the Company, makes an offer to acquire all of the Shares other than those which are already owned by them, and such offer is or becomes wholly unconditional; or

(ii) a compromise or arrangement in accordance with section 899 of the Companies Act for the purposes of a change of Control of the Company is sanctioned by the court.

(b) Unless rule 6.2 applies:

(i) if the Committee so determines in advance of the Takeover Event, all Nil-cost Options and Market Value Options may be exercised conditionally, so as to take effect upon the Takeover Event (to the extent they are Vested and Released at that time);

(ii) all Awards will Vest and be Released (and any Nil-cost Option or Market Value Option exercised conditionally under rule 6.1(b)(i) will be exercised) upon the Takeover Event, in which case rule 3.2(b) shall apply and the Takeover Event will be the Early Vesting Trigger; and

(iii) to the extent any Nil-cost Option or Market Value Option has not been exercised within 30 days of the Takeover Event (or such longer or shorter period as the Committee may determine), it shall lapse,

and, for the purposes of this rule 6.1, rule 3.2(b) and rule 3.3, "Committee" shall mean those people who were members of the Committee immediately before the Takeover Event.

6.2 Exchange of Awards

(a) If:

(i) there is an Internal Reorganisation unless the Committee determines otherwise; or

(ii) in the case of a Takeover Event, the Committee decides before such Takeover Event that an Award will be exchanged or if an offer to exchange an Award is made to and accepted by a Participant,

an Award will be exchanged for the grant of a new award (**"New Award"**) that the Committee considers to be equivalent to the Award, except that it relates to shares in a different company (whether the acquiring company or otherwise) and the rules of the Plan and the terms of the Award (including any Performance Condition) will be interpreted accordingly.

(b) For the purposes of this rule 6.2, "Committee" shall mean those people who were members of the Committee immediately before the Takeover Event.

6.3 Winding up

If the Company gives notice of a general meeting at which a resolution is proposed for the voluntary winding up of the Company (**"Resolution"**):

(a) all Nil-cost Options and Market Value Options may be exercised conditionally, so as to take effect from immediately prior to the passing of the Resolution (to the extent they are Vested and Released at that time);

(b) all Awards will Vest and be Released (and any Nil-cost Option or Market Value Option exercised conditionally under rule 6.3(a) will be exercised) immediately prior to the passing of the Resolution, in which case rule 3.2(b) shall apply and the time immediately prior to the passing of the Resolution will be the Early Vesting Trigger; and

(c) to the extent any Nil-cost Option or Market Value Option has not been exercised on the passing of the Resolution, it shall lapse.

6.4 Variation of Share capital and other corporate events

If there is a variation of the Company's share capital or the Company is or may be affected by a merger, delisting, special dividend or other event which the Committee considers will affect the current or future value of Shares (**"Relevant Event"**), the Committee may:

(a) adjust the number of Shares to which an Award relates and, if applicable, the Market Value Exercise Price; or

(b) if it determines that because of the significance of the effect of the variation or event on the value of the Shares such adjustment would be inappropriate, determine that:

(i) some or all Nil-cost Options or Market Value Options may be exercised conditionally, so as to take effect at such time on or before the Relevant Event as the Committee determines (to the extent they are Vested and Released at that time);

(ii) some or all Awards will Vest and be Released (and any Nil-cost Option or Market Value Option exercised conditionally under rule 6.4(b)(i) will be exercised) at such time on or before the Relevant Event as the Committee determines, in which case rule 3.2(b) shall apply and the Relevant Event will be the Early Vesting Trigger; and/or

(iii) to the extent any Nil-cost Option or Market Value Option has not been exercised by such time as the Committee determines, it shall lapse,

and the Committee may make such adjustments to the limits set out in rule 2.2 as it considers appropriate.

7. INTERNATIONAL TRANSFERS

If as a result of a Participant moving jurisdiction at the Company's request:

(a) the Participant would be unable to receive or hold Shares;

(b) the Participant and/or any Group Company would suffer a materially increased tax or social security liability in relation to their Award; or

(c) the Committee otherwise determines it to be appropriate,

the Committee may accelerate the Vesting and/or Release of some or all of an Award, in which case rule 3.2(b) shall apply and the time of the Participant's move will be the Early Vesting Trigger, provided that the Committee may make the Vesting and/or Release of the Award subject to such conditions as it determines appropriate, which may include restrictions on the disposal of Shares acquired before the Normal Vesting Date of the Award and/or the forfeiture of Shares if the Participant Leaves before the Normal Vesting Date of the Award.

8. REDUCTION AND RECOVERY

8.1 The Committee may apply its powers in rule 8.2 in relation to an Award if it determines, in its absolute discretion, that any of the circumstances in (a) to (h) below have occurred and its powers in rule 8.3 only if the circumstances in (e) below have occurred:

(a) a material misstatement of any Group Company's financial results for any period that falls within or overlaps with the Recovery Period;

(b) an error in the information or assumptions on which the Award was granted, or in assessing a Performance Condition that affects the extent to which the Award Vests;

(c) a material failure of risk management in, or any serious reputational damage to, any Group Company or business unit during the Recovery Period;

(d) corporate failure of any Group Company or a relevant business unit during the Recovery Period;

(e) serious misconduct or material error on the part of the Participant during the Recovery Period;

(f) in respect of a Participant who is subject to the Shareholding Policy in relation to any Award or Shares, the Participant using any personal hedging strategy, contract of insurance, option, arbitrage agreement or other arrangement to undermine the effects of the Shareholding Policy at any time during the Recovery Period;

(g) a breach by the Participant at any time during the Recovery Period of any term of their employment contract (or any settlement agreement relating to their employment contract) with a Group Company that applies after they have Left; or

(h) any other circumstances that are similar in their nature or effect to those above,

and for the purposes of this rule, the terms "Participant", "Group Company" and "business unit" include any former Participant, Group Company or business unit.

8.2 If Shares or cash are yet to be delivered to a Participant to satisfy their Award, the Committee may, at any time before the end of the Recovery Period, in its absolute discretion, reduce (including to nil) the number of Shares to which the Award relates and/or impose additional conditions on the Award.

8.3 If Shares or cash have been delivered to a Participant to satisfy their Award, the Committee may, in its absolute discretion, at any time before the end of the Recovery Period, require the Participant to make a cash payment to the Company in respect of some or all of the Shares and/or cash delivered to them (before or after any applicable Tax Liability) or to transfer Shares of an equivalent value to the Company or another person free of charge.

8.4 In order to effect the recovery of Shares and/or cash from a Participant under rule 8.3 the Committee may, in its absolute discretion:

(a) reduce (including to nil) the number of Shares to which an Award under the Plan relates, if Shares or cash have not yet been delivered to the Participant to satisfy such Award; and/or

(b) reduce any remuneration that a Participant would be entitled to receive from a Group Company under any bonus or incentive plan.

8.5 The Committee may apply rule 8.4(a) to give effect to any provisions similar to those in this rule 8 that are included in any other incentive plan operated by a Group Company.

8.6 If, at the time the Recovery Period is due to end, the conduct of any Participant, Group Company or business unit is being investigated in connection with this rule 8 (or an equivalent provision in another incentive plan operated by a Group Company) and such investigation has not been concluded, the Committee may determine that the Recovery Period will instead continue until such investigation concludes and any reduction or recovery in accordance with this rule 8 (or equivalent provision) has been applied.

9. AMENDMENTS

9.1 General

(a) The Committee may amend the rules of the Plan or the terms of any Award at its discretion subject to rules 9.1(b) and 9.1(c).

(b) No amendment to the material disadvantage of existing rights of Participants (except in respect of a Performance Condition) may be made unless every Participant who may be affected has been invited to indicate whether they approve the amendment and it is approved by a majority of those who respond.

(c) Notwithstanding rule 9.1(b), the Committee may, at any time alter the terms of a Conditional Award such that it becomes a Nil-cost Option or vice versa.

(i) .

(d)No amendment may be made under this rule 9 if it would prevent the Plan from being an employees' share scheme within the meaning of section 1166 of the Companies Act.

9.2 Performance Conditions

The Committee may amend or substitute an existing Performance Condition if an event occurs which it considers would make it appropriate to do so, provided that the amended or new condition would not, taking into account all the circumstances, be materially easier to satisfy than the original condition would have been but for the event.

10. MISCELLANEOUS

10.1 No disposal of Award

An Award must not be sold, transferred, assigned, charged or otherwise disposed of in any way (except to a Participant's personal representatives if the Participant dies) and will lapse immediately on any such purported action.

10.2 Bankruptcy

An Award will lapse immediately if the Participant is declared bankrupt (or, where the Participant is located outside the UK, if any equivalent event occurs).

10.3 Not pensionable

No benefits received under the Plan will be pensionable.

10.4 Ranking of Shares

Shares issued or transferred from treasury under the Plan will rank equally in all respects with the Shares then in issue, except that they will not rank for any voting, dividend or other rights attaching to Shares by reference to a record date preceding the date of issue or transfer from treasury.

10.5 Relationship to employment

(a) Rules 10.5(b) to 10.5(c) apply during a Participant's employment with any Group Company and after the termination of such employment, whether or not the termination is lawful.

(b) A Participant's employment with any Group Company is separate from their participation in the Plan. A Participant's participation in the Plan does not create any right to continued employment or to be granted further Awards, either at all or on any particular terms, including the number of Shares to which an Award relates.

(c) By participating in the Plan, a Participant waives any claim for compensation for any loss under or in connection with the Plan, whether such loss is claimed by way of damages for breach of any contract, compensation for loss of office or otherwise.

(d) The exclusion included in rule 10.5(c) applies (without limitation) to any loss arising from:

(i) the lapse of any Award or the loss or reduction of any rights or expectations in any circumstances or for any reason, including (without limitation) the termination, whether lawful or otherwise, of the Participant's employment, the application of rule 6 or the application of rule 8;

(ii) any exercise of or failure to exercise any discretion in relation to an Award and/or the Plan; and

(iii) the operation of the Plan, including its suspension or termination, or any Award.

10.6 Data protection

The personal data of any Eligible Employee, Participant or former Participant will be processed in accordance with the Group's data protection policy as notified to Eligible Employees and, except for the purposes of the EU General Data Protection Regulation 2016/679 (including as such legislation is retained under UK law), by participating in the Plan, each Participant consents to the processing of their personal data for the purposes of the Plan.

10.7 Regulatory consent

If the Committee determines that the grant of an Award was contrary to any relevant laws or regulations, it may, in its absolute discretion, determine that the grant of such Awards was void and that they should be treated for all purposes as never having been granted.

10.8 Administration of the Plan

(a) The Committee has authority to administer the Plan, including the appointment of a third party administrator, and to interpret and apply its terms, provided that, where any act or decision would be beyond the scope of the authority delegated to the Committee by the Board, the Committee shall refer such act or decision to the Board and act or decide in accordance with the Board's determination.

(b) The decisions of the Committee will be final and bind all parties.

10.9 Construction

If any provision of the Plan or any Award would be unenforceable because it contains certain wording and the terms are capable of being construed without such wording the Committee may apply the provision on that basis.

10.10 Notices

(a) Any notice or other communication in connection with the Plan may be delivered personally or sent by electronic means or post.

(b) A notice or other communication will be deemed to have been received:

(i) where it is delivered personally, immediately (if delivered during working hours on a Dealing Day) or on the opening of the next Dealing Day (otherwise);

(ii) 72 hours after it was put into the post properly addressed and stamped; and

(iii) where it is given by electronic means, immediately (if delivered during working hours on a Dealing Day) or on the opening of the next Dealing Day (otherwise) in either case, unless the sender receives an electronic automatic reply to the contrary.

10.11 Termination of the Plan

The Plan will terminate on the Termination Date. The existing rights of Participants will not be affected by such termination.

10.12 Rights of third parties

No third party other than a Group Company will have any rights under the UK Contracts (Rights of Third Parties) Act 1999 to enforce any term of the Plan.

10.13 Governing law and jurisdiction

The rules of the Plan and all Awards made under it will be governed by and construed in accordance with the laws of England and Wales and any person referred to in the Plan submits to the exclusive jurisdiction of the Courts of England and Wales.

10.14 Overseas territories

The Committee may establish further plans or sub-plans (as schedules to the Plan or otherwise) based on the Plan but modified to take account of local tax, exchange control or securities laws in overseas territories provided that any Awards or similar rights granted under any such plans or sub-plans will count towards the limits on the total number of Shares in rule 2.2.

SCHEDULE 1: AWARDS SUBJECT TO A HOLDING PERIOD

This schedule 1 shall apply to any Award granted under the Plan that the Committee has determined will be subject to a Holding Period (as defined below). Awards that are subject to a Holding Period shall be subject to the rules of the Plan, except as amended by this schedule 1.

1. Definitions and interpretation

1.1 Unless otherwise stated, the words and expressions below have the following meanings:

"Holding Period" means a period beginning on the Normal Vesting Date and ending on the Normal Release Date; and

"Normal Release Date" means the second anniversary of the Normal Vesting Date (or such other period as the Committee may determine on or before the Grant Date),

and, in each case, the rules of the Plan will be construed accordingly.

1.2 References in this schedule 1 to:

(a) a "rule" relate to a rule of the Plan; and

(b) a "paragraph" relate to a paragraph of this schedule 1.

1.3 Where there is any conflict between the rules of the Plan and this schedule 1, the terms of this schedule 1 will prevail.

2. Grant

2.1 An Award that is subject to a Holding Period may not be granted to any US Taxpayer (as defined in schedule 2).

2.2 As soon as reasonably practicable after the Grant Date, a Participant will be notified:

(a) that their Award is subject to a Holding Period; and

(b) of the Normal Release Date.

3. Release

Unless otherwise prescribed in the rules of the Plan, an Award that is subject to a Holding Period will be Released on its Normal Release Date, unless the Committee determines in its absolute discretion in relation to any Unreleased Award that it shall be Released early in whole or in part.

4. Good Leavers before the Normal Vesting Date

If a Participant is a Good Leaver, their Award will, subject to paragraph 3 and rule 5.2(b), continue to be subject its Holding Period and Normal Release Date.

5. Leaving on or after the Normal Vesting Date

If a Participant Leaves on or after the Normal Vesting Date of their Award, their Award will, subject to paragraph 3 and rule 5.4, continue to be subject its Holding Period and Normal Release Date.

6. International transfers

If rule 7 applies, the Committee may determine that the Holding Period shall cease to apply, provided that the Committee may make the Release of the Award subject to such conditions as it determines appropriate, which may include restrictions on the disposal of Shares acquired before the Normal Release Date of the Award.

SCHEDULE 2: US TAXPAYERS

This schedule 2 shall apply to any Award granted to or held by a US Taxpayer (as defined below) (a **"US Award"**). US Awards shall be subject to the rules of the Plan, except as amended by this schedule 2. It is intended that US Awards shall qualify as short-term deferrals exempt from the requirements of Section 409A (as defined below), and the rules of the Plan will be interpreted and construed accordingly.

1. Definitions and interpretation

1.1 Unless otherwise stated, the words and expressions below have the following meanings: **"Section 409A"** means Section 409A of the US Code;

"US Code" means the United States Internal Revenue Code of 1986, as amended from time to time, including any regulations or authoritative guidance promulgated thereunder and successor provisions thereto;

"US Conditional Award" means a US Award granted in the form of a Conditional Award ; and

"US Taxpayer" means any Eligible Employee or Participant who is or will be subject to a tax or social security liability under the US Code in connection with an Award,

and, in each case, the rules of the Plan will be construed accordingly.

1.2 References in this schedule 2 to:

(a) a "rule" relate to a rule of the Plan; and

(b) a "paragraph" relate to a paragraph of this schedule 2.

1.3 Where there is any conflict between the rules of the Plan and this schedule 2, the terms of this schedule 2 will prevail.

2. Grant

A US Award may only be granted in the form of a Conditional Award or a Market Value Option.

3. Vesting

3.1 If a US Conditional Award will Vest on or after its Normal Vesting Date in accordance with rule 3.1, the Committee shall in any event determine the extent to which any Performance Condition has been satisfied in accordance with rule 3.2(a) and whether any reduction should be made under rule 3.2(c) no later than 15 March in the calendar year following the Normal Vesting Date.

3.2 If a US Conditional Award will Vest under the rules of the Plan before its Normal Vesting Date, the Committee shall in any event determine the extent to which any Performance Condition has been satisfied in accordance with rule 3.2(b)(i), the degree to which the Vesting level will be reduced in accordance with rule 3.2(b)(ii) and whether any reduction should be made under rule 3.2(c) no later than 15 March in the calendar year following the Early Vesting Trigger.

4. Release

Unless rule 3.5(a) applies, a US Conditional Award may not in any event be Released later than 15 March in the calendar year following the Normal Vesting Date.

5. Settlement

5.1 Unless rule 4.2 applies, any Shares to be delivered to the Participant under rule 4.1(a) or cash to be paid to the Participant under rule 4.1(b) following the Release of a US Conditional Award may not in any event be delivered or paid later than 15 March in the calendar year following the Normal Vesting Date.

6. Good Leavers

6.1 Rule 5.2(a)(ii) shall not apply to a US Conditional Award.

6.2 Rule 5.2(b)(ii) shall be deleted and replaced with the following:

"If a Participant is a Good Leaver, their US Conditional Award will Vest and be Released when they Leave or on such other date before the Normal Vesting Date as the Committee may determine, provided that their US Conditional Award may not in any event Vest or be Released later than 15 March in the calendar year following the date they Leave. Rule 3.2(b) shall apply to such US Award and the Participant Leaving will be the Early Vesting Trigger."

6.3 If any delivery of Shares or payment of cash made under the Plan in connection with the termination of a Participant's employment is determined, in whole or in part, to constitute "nonqualified deferred compensation" within the meaning of Section 409A, and the Participant is a specified employee within the meaning of section 409A(2)(B)(i) of the US Code, no such Shares may be delivered or cash paid before the day that is six months and one day after the date of termination or, if earlier, ten Dealing Days following the Participant's death.

7. Adjustment of US Awards

7.1 Any adjustment made under rule 6.4(a) will only be effective to the extent that it is consistent with the short-term deferral exemption to Section 409A.

8. Amendments

8.1 Any amendment made under rule 9.1 will only be effective to the extent that it is consistent with the short-term deferral exemption to Section 409A.

9. Liability

9.1 In no event whatsoever will any Group Company be liable for any additional tax, interest or penalties that may be imposed on any Participant under Section 409A or any damages for the terms of the Plan failing to comply with Section 409A.

Exhibit 8.1

SUBSIDIARIES OF 4D PHARMA PLC.

Name of Subsidiary	Jurisdiction of Incorporation or Organization
4D Pharma Research Limited	Scotland
4D Pharma Leon Sociedad Limitada Unipersonal	Spain
4D Pharma Cork Limited	Ireland
4D Pharma Delaware Incorporated	Delaware
4D Pharma (BVI) Limited	British Virgin Islands

Exhibit 12.1

Certification by the Chief Executive Officer
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Duncan Peyton, certify that:

1. I have reviewed this annual report on Form 20-F of 4D pharma 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(s) 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 generally accepted accounting principles;

    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(s) 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.

Date: March 31, 2022

/s/ Duncan Peyton
Name: Duncan Peyton
Title: Chief Executive Officer

Exhibit 12.2

Certification by the Chief Financial Officer
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, John Doyle, certify that:

1. I have reviewed this annual report on Form 20-F of 4D pharma 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(s) 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 generally accepted accounting principles;

   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(s) 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.

Date: March 31, 2022

/s/ John Doyle
Name: John Doyle
Title: Chief Financial Officer

Exhibit 13.1

Certification by the Chief Executive Officer
Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

In connection with the annual report of 4D pharma plc (the "Company") on Form 20-F for the year ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Duncan Peyton, Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 31, 2022

By: */s/ Duncan Peyton*
Name: Duncan Peyton
Title: Chief Executive Officer

Exhibit 13.2

Certification by the Chief Financial Officer
Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

In connection with the annual report of 4D pharma plc (the "Company") on Form 20-F for the year ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, John Doyle, Chief Financial Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 31, 2022

By: */s/ John Doyle*
Name: John Doyle
Title: Chief Financial Officer