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

FORM 20-F/A
(Amendment No. 1)

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

OR

[X] **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2020

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
5th Floor, 9 Bond Court
Leeds
LS1 2JZ
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Tel: +44 (0) 113 895 0130
Email: legal@4dpharma.com
(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, 2020
Ordinary Shares, nominal value £0.0025 per	131,467,935

Share

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.

Yes [ ] No [X]

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 [X]

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 [X]

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 [X] 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 [X]
		Emerging growth company [X]

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 [X]	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 [X]

† 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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EXPLANATORY NOTE

The Registrant is filing this Amendment No. 1 on Form 20-F/A (this "Amended Filing") to its Annual Report on Form 20-F for the fiscal year ended December 31, 2020 (the "Original Filing") to (1) include audited consolidated financial statements for the fiscal year ended December 31, 2018 omitted from the Original Filing, (2) include in Part I—Item 3.A. selected financial data for the fiscal year ended December 31, 2018 omitted from the Original Filing, and (3) incorporate by reference in Part I—Item 5.A. the corresponding comparison of results of operations for the fiscal years ended December 31, 2019 and 2018 previously filed with the SEC in Amendment No. 5 to the Registrants registration statement on Form F-4 (File No. 333-250986). For the convenience of the reader, this Amended Filing sets forth the Original Filing, as modified where necessary to reflect the foregoing revisions.

For clarity, the audited consolidated financial statements as of and for the fiscal years ended December 31, 2020 and 2019 included in this Amended Filing are unchanged from the audited consolidated financial statements included in the Original Filing.

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 own or have rights to trademarks, trade names and service marks that they use in connection with the operation of their 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 2020 and 2019 and for the years ended December 31, 2020, 2019 and 2018 (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 26, 2021, 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 $1.3794 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 the Exchange Act. Forward looking terms such as "may," "will," "could," "should," "would," "plan," "potential," "intend," "anticipate," "project," "target," "believe," "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. From time to time, oral or written forward-looking statements may also be included in other materials released to the public.

Forward-looking statements are based on the current beliefs and assumptions of the management of 4D Pharma and on information currently available to such management. While the management of 4D Pharma 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, Blautix, Thetanix or MRx-4DP0004 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 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 of the COVID-19 pandemic on our operations, including 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 or the research collaboration and option to license agreement with Merck Sharp & Dohme Corp.;
- our ability to raise any additional funding we will need to continue to pursue our business and product development plans;
- 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 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;
- 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

4D Pharma is a corporation organized under the laws of England and Wales. A substantial portion of 4D Pharma's assets and most of its directors and executive officers are located and reside, respectively, outside the United States. Because of the location of 4D Pharma's assets and board members, it may not be possible for investors to serve process within the United States upon 4D Pharma or such persons with respect to matters arising under the United States federal securities laws or to enforce against 4D Pharma 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.

4D Pharma understands 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.

4D Pharma has 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

The selected historical consolidated financial information for the years ended December 31, 2020, 2019 and 2018 and the selected statements of financial position data as of December 31, 2020 and 2019 have been derived from, and should be read in conjunction with, our audited consolidated financial statements and notes thereto appearing elsewhere in this annual report.

Our historical results do not necessarily indicate results expected for any future periods. The selected consolidated financial data should be read in conjunction with, and are qualified in their entirety by reference to, our audited consolidated financial statements and related notes set forth elsewhere in this annual report and "Item 5. Operating and Financial Review and Prospects" included elsewhere in this annual report.

We have not included selected historical consolidated financial data for the years ended December 31, 2017 and 2016 or as of December 31, 2018, 2017 and 2016 in the table below as we qualify as an emerging growth company as defined in Section 2(a)(19) of the Securities Act (an "**Emerging Growth Company**" or "**EGC**"), we make use of an accommodation for reduced reporting.

	Year ended December 31,		
U.S. dollars in thousands, except share and per share data	**2020**	**2019**	**2018**
Revenues	$ 690	$ 269	$ —
Operating expenses:			
Research and development expenses	23,384	29,193	27,830
General and administrative expenses	13,015	10,380	11,294
Foreign currency losses (gains)	(699)	957	(234)
Total operating expenses	35,700	40,530	38,890
Loss from operations	(35,010)	(40,261)	(38,890)
Other income (expense), net:			
Interest income	6	78	379
Interest expense	—	—	(3)
Other income	4,496	6,883	6,378
Change in fair value of contingent consideration payable	—	2,967	(465)
Total other income (expense), net	4,502	9,928	6,289
Net loss before income tax benefit	$ (30,508)	$ (30,333)	$ (32,601)
Income tax benefit	13	—	—
Net loss	$ (30,495)	$ (30,333)	$ (32,601)
Other comprehensive loss:			
Foreign currency translation adjustment	1,566	1,113	(3,995)
Comprehensive loss	$ (28,929)	$ (29,220)	$ (36,596)
Basic and diluted net loss per common share	$ (0.27)	$ (0.46)	$ (0.50)
Weighted average common shares used in computing basic and diluted net loss per common share	114,149,743	65,493,842	65,493,842

U.S. dollars in thousands	Years ended December 31, 2020	2019
Balance Sheet Data:		
Cash and cash equivalents	$ 11,990	$ 5,031
Total assets	49,099	40,826
Total liabilities	10,128	9,639
Accumulated deficit	(148,235)	(117,740)
Total stockholders' equity	38,971	31,187

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 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 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 the COVID-19 pandemic in the United Kingdom, United States and the rest of the world.

- 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**”). Our net loss was $30.5 million for the year ended December 31, 2020, $30.3 million for the year ended December 31, 2019 and $32.6 million for the year ended December 31, 2018. As of December 31, 2020, we had an accumulated deficit of $148.2 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.

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 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, 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, 2020, we had $12.0 million in cash and cash equivalents. We expected our current cash and cash equivalents, including the sales of ordinary shares in March 2021, and after giving effect to the Merger and a €1 million ($1.1 million) overdraft facility, will be sufficient to fund our current operating plan through the second quarter of 2022. Our estimate as to how long we expect the net proceeds of the merger with Longevity and from the sales of ordinary shares in March 2021, together with 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 who 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. 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. In our respiratory program, our therapeutic candidate, MRx-4DP0004, is being assessed in patients with partly controlled asthma and to prevent or reduce the hyperinflammatory response in patients hospitalized with COVID-19. 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 in Parkinson’s disease, MRx0006 in rheumatoid arthritis and MRx0002 in multiple sclerosis. 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, 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.

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, 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. 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 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 remain viable in the gastrointestinal tract of humans. If these bacteria exert a pathogenic effect, despite this not having been observed in any 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 remerge. 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 seven 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 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.

The regulatory approval processes of the MHRA, FDA, EMA and other comparable foreign regulatory authorities are lengthy, time consuming and 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, we do not know how it will perform in current or future clinical trials as it has in prior preclinical 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.

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 COVID-19 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 has been impacted due to factors associated with the COVID-19 pandemic, potentially delaying 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 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.

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 the University of Texas MD Anderson Cancer Center. To date, we have initiated two clinical trials as part of this strategic alliance. For additional information on our relationships with MSD and the University of Texas MD Anderson Cancer Center, 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 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 United States Patent and Trademark Office, or 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 October 2039 (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.

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 few if any therapeutic 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 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 EPO. Currently three of our European patents have been challenged by third parties in Opposition proceedings before the EPO. 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 common stock. 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 common stock. 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.

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, or 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 PTE and PTA, 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. 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 Patent Term Extension (PTE) 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 common stock. 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.

In December 2019, COVID-19 was reported to have surfaced in Wuhan, China, resulting in significant disruptions to Chinese manufacturing and travel. COVID-19 has now spread to numerous other countries, including the United Kingdom and United States, resulting in the World Health Organization characterizing COVID-19 as a 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. As the COVID-19 pandemic continues to spread around the globe, we may experience disruptions that could severely impact our business and clinical trials, 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.

We are still assessing the impact that COVID-19 may have on our ability to effectively conduct our business operations as planned and there can be no assurance that we will be able to avoid a material impact on our business from the spread of COVID-19 or its consequences, including disruption to our business and downturns in business sentiment generally or in our industry. A significant proportion of our employees are currently telecommuting, which may impact certain of our operations over the near term and long term.

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 experience 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 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, 2020, we had 92 employees, including 40 employees in the United Kingdom and one employee in the United States. Of these employees, 78 were engaged in research and development activities and 14 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, 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, 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, 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, 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, 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, MRx0029, Blautix and Thetanix or any of our other therapeutic candidates;

- the level of demand for MRx0518, MRx-4DP0004, 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, MRx0029, Blautix and Thetanix and any of our other therapeutic candidates;
- our ability to commercialize MRx0518, MRx-4DP0004, 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.

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 common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated guidance we may provide.

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 phishing and social engineering attacks from third parties in connection with the COVID-19 pandemic. 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 (the "GDPR") which became effective and enforceable across all then-current member states of the EU on May 25, 2018. 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, imposing limitations on retention of personal data, creating mandatory data breach notification requirements in certain circumstances, and establishing onerous new obligations on services providers who process personal data simply on behalf of others, as well as obligations regarding the security and confidentiality of the personal data. The 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 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. This expansion would incorporate any clinical trial activities in EU member states. The GDPR imposes special protections for "sensitive information" which includes health and genetic information of data subjects residing in the EU. The GDPR also grants individuals the opportunity to object to the processing of their personal information, allows them to request deletion of personal information 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 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.

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 GDPR has been modified to reflect the fact that the UK is no longer a member of the EU.

Businesses based in the United Kingdom who operate in the EU are now subject to both the GDPR ("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 UK and EU countries.

In respect of data transfers from the EU to the UK, the EU-UK Trade and Cooperation Agreement provides for a transitional period permitting the continuation of such transfers until 30 June 2021. After such date, transfers to the UK may continue freely if the European Commission issues an adequacy decision in favour of the UK. A draft decision has been issued but still needs to be approved. In the absence of such decision, transfers may only continue if the parties to the transfer put in place appropriate safeguards as required by the EU GDPR, which would involve additional costs.

Data transfers from the UK to the EU are permitted by UK law. Such permission will be reviewed in 4 years.

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 UK 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, 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 data transfers, UK and EU entities are now required to assess the local laws which will apply to the data after it is transferred.

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.

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**") on December 24, 2020 to regulate their post-Brexit trade relationship. The TCA has already been ratified by the UK. In the EU, the TCA was applied initially on a provisional basis until 28 February 2021, pending a decision by the European Parliament to assent to the ratification of the TCA by the Council of the EU. The UK-EU Partnership Council has since agreed to an extension of the period for the provisional application of the TCA by the EU to 30 April 2021. It is possible that this time period could be extended beyond 30 April 2021 if the European Parliament has not assented to the ratification before that date.

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 after January 1, 2021, 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.

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

We do not know whether listing in the Nasdaq will increase liquidity for our shareholders. We do not know whether an active, liquid and orderly trading market will develop for our ADSs or what the market price of our ADSs will be and as a result it may be difficult for you to sell your ADSs at or above the price you pay for them, if at all.

Our ADSs were approved to list on the Nasdaq and began trading on March 22, 2021 . However, prior to March 22, 2021, while our ordinary shares have been traded on AIM since February 2014, no public market has previously existed for our ADSs or ordinary shares in the United States. We have undertaken the Merger because we believe that the Merger will provide us and our shareholders, with a number of advantages, including providing our shareholders with securities that we expect will enjoy greater market liquidity than the securities these shareholders currently hold. However, the Merger may not accomplish these objectives. We cannot predict whether a liquid market for 4D Pharma ADSs and existing 4D Pharma Shares will be maintained.

The lack of an active market for ADSs may impair your ability to sell your shares at the time you wish to sell them or at a price that you consider reasonable. 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 price of our ADSs may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our ADSs, and we could be subject to securities class action litigation as a result.

Our stock price is likely to be volatile. 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 market price for our 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;
- 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 other factors described in this "Risk Factors" section.

These and other market and industry factors may cause the market price and demand for our shares and ADSs to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from selling their shares or ADSs at or above the price paid for the shares or ADSs and may otherwise negatively affect the liquidity of our 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 managements' 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 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. All of our outstanding shares are freely tradeable on AIM. The ADSs are freely tradeable on Nasdaq. 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 Jumpstart Our Business Startups Act of 2012 (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 and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- 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, 2021.

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. In connection with the listing, we intend to improve the process of documenting, reviewing and improving our internal controls and procedures for compliance with Section 404, which will require annual management assessment of the effectiveness of our internal control over financial reporting. We have begun recruiting additional finance and accounting personnel with certain skill sets that we will need 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 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 21.9% of our issued and outstanding ordinary shares, based on the number of ordinary shares issued and outstanding as of March 23, 2021. 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 2021 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 2021 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 2021 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 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, 2020, we had gross cumulative carryforward tax losses of $53.9 million, $6.1 million and $1.0 million respectively in the UK, Ireland and Spain. With our U.S. and BVI entities having been recently formed there are no such carryforward losses. 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, or SMEs, or in some instances we access the 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). 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 are scheduled to begin for years commencing from April 2021, will cap the available claim under the schemes to a multiple of payroll taxes. This cap is likely to 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 do not have provisions for current tax liabilities arising in the normal course of business as we anticipate that any such liabilities would be covered by our losses to date. 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 $18 thousand at December 31, 2020.

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 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 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 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 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 or ($1.53) per share.

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, Central Nervous System ("CNS") and gastrointestinal diseases. In recent months, we believe this approach has been validated by clinical results in our programs in immune-oncology and gastrointestinal disease.

Our LBPs are a novel class of biologics 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 peptide 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 drugs' modalities such as small molecules or to 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 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, MRx0006 targeting rheumatoid arthritis and MRx0002 targeting multiple sclerosis. We have completed three clinical trials and currently have five more ongoing. Our clinical and preclinical Live Biotherapeutic development programs are illustrated below.

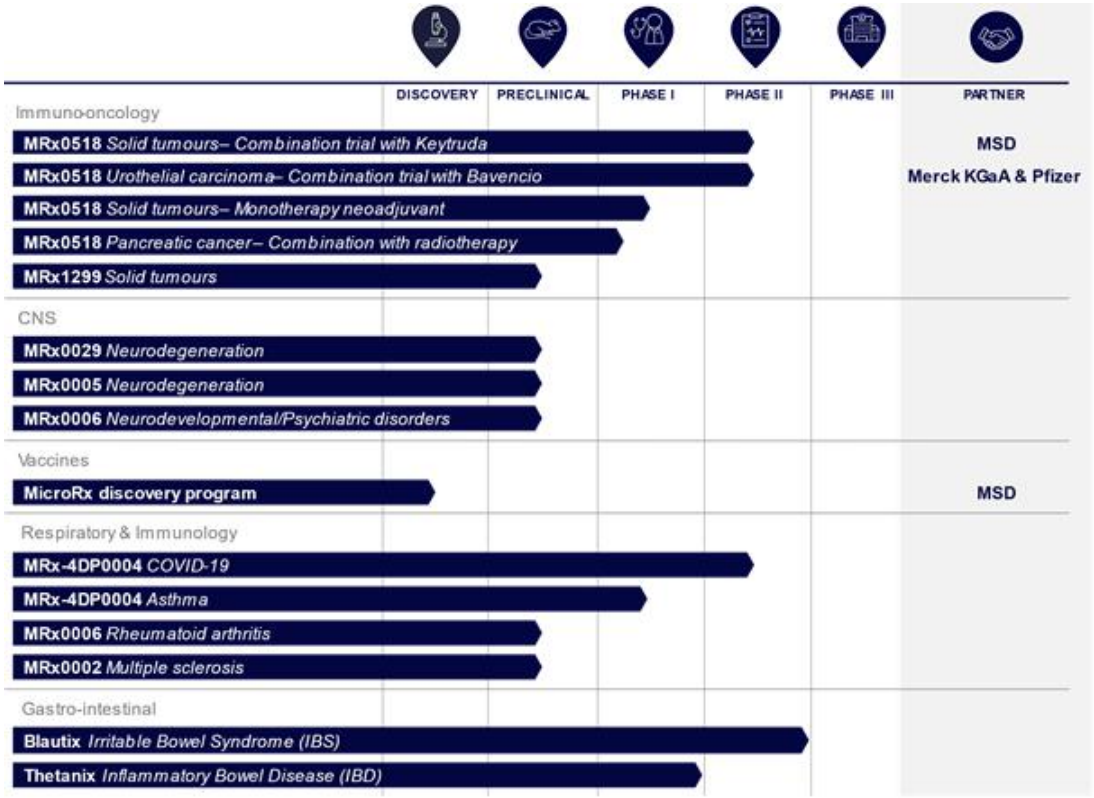


Figure 1 - 4D Pharma's pipeline of LBP therapeutic candidates.

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 in patients with metastatic NSCLC, RCC and UC 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, enrolling 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 to be 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. Encouraged by the results of Part A of this clinical trial, we have expanded enrollment for Part B to additional trial sites to help accelerate recruitment and delivery of the clinical readout of Part B of this clinical trial.

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. 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 the University of Texas MD Anderson Cancer Center, for which we expect clinical data in 2021. 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.

After the period end, 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 intends to commence a clinical trial in 2021 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.

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 candidate, MRx0029, in Parkinson's disease patients. 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. 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. This trial is ongoing and, due to COVID-19 related delays, it is anticipated that the results of this study will be available Q3 2021.

A critical stress factor facing healthcare systems as a result of the COVID-19 global pandemic is the inflammatory response to infection, particularly in the lungs, leading to the need for oxygen therapy, ventilation or other critical care. In addition to effective vaccines, there is an urgent need for rapid development of therapeutics to reduce harmful lung and/or systemic inflammation induced by SARS-CoV-2 infection without impairing the appropriate anti-viral immune response. Our understanding of the functionality and unique immunomodulatory profile of MRx-4DP0004, paired with the patient immunological data generated since the outset of the pandemic, allowed us to recognize the potential of the candidate to treat patients with COVID-19. We are now investigating MRx-4DP0004 in a Phase II clinical trial as an oral therapeutic to prevent or reduce the hyperinflammatory response in patients hospitalized with COVID-19. The Phase II trial of MRx-4D0004 received expedited approval from the MHRA in April 2020, and we expect to report preliminary clinical data in 2021.

In our gastro-intestinal disease portfolio, we currently have two LBP candidates that have completed early-stage clinical evaluation, Blautix and Thetanix. Blautix is being developed as the first therapeutic to 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 candidate 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

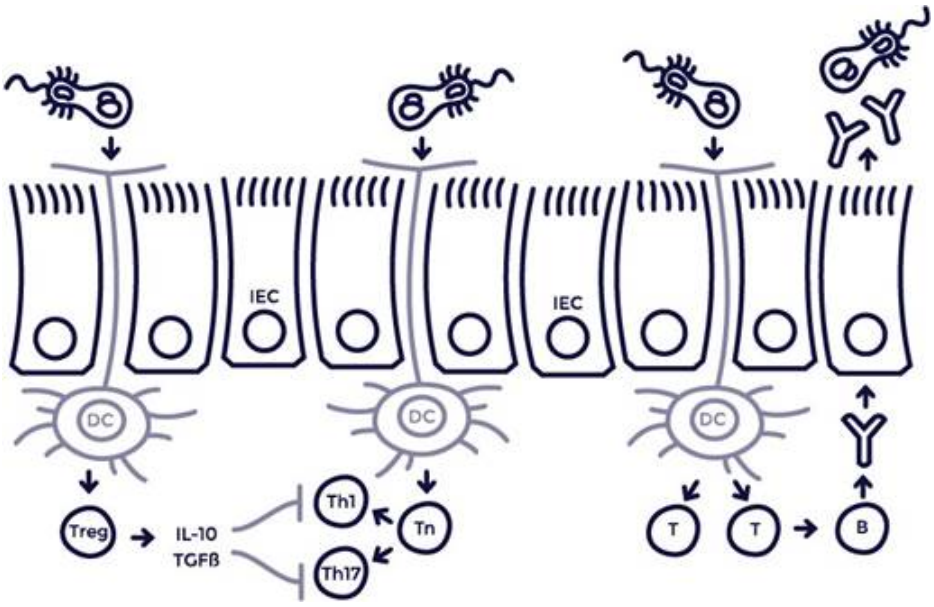


Figure 2. LBPs interact with the host by a variety of mechanisms. Although typically initiated in the gut, the resulting changes in downstream pathways are diverse and can produce effects in distal areas of the body. IEC = intestinal epithelial cell; DC = dendritic cell; Treg = T regulatory cell; IL-10 = 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 commensal human bacteria found in the 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 particularly 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 250 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 seven 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 2021, 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

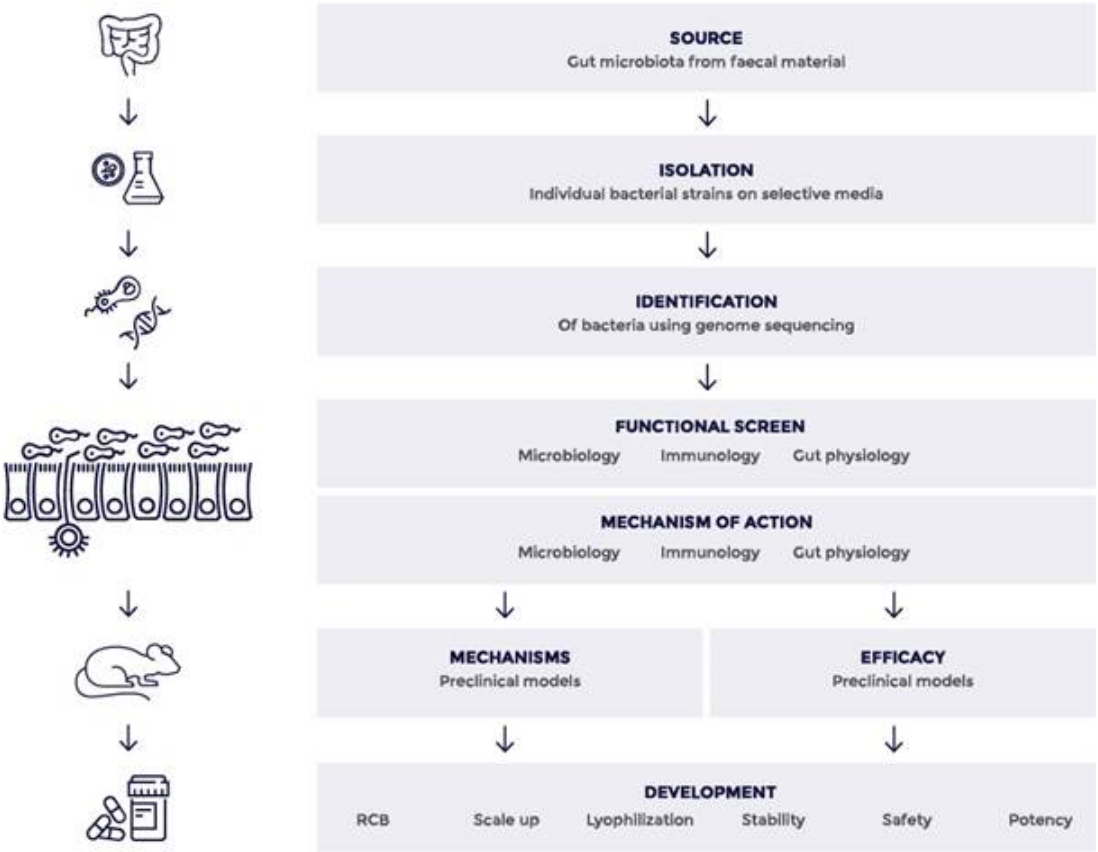


Figure 3. A high-level overview of the processes that underpin the MicroRx discovery platform

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 is 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 with single strain LBPs in multiple disease areas, and provide valuable data on safety, tolerability, pharmacodynamic responses and immune biomarkers. Additionally, we have an in-house team of bioinformaticians that provide microbiome 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 the University of Texas MD Anderson Cancer Center to evaluate 4D'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 three 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 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

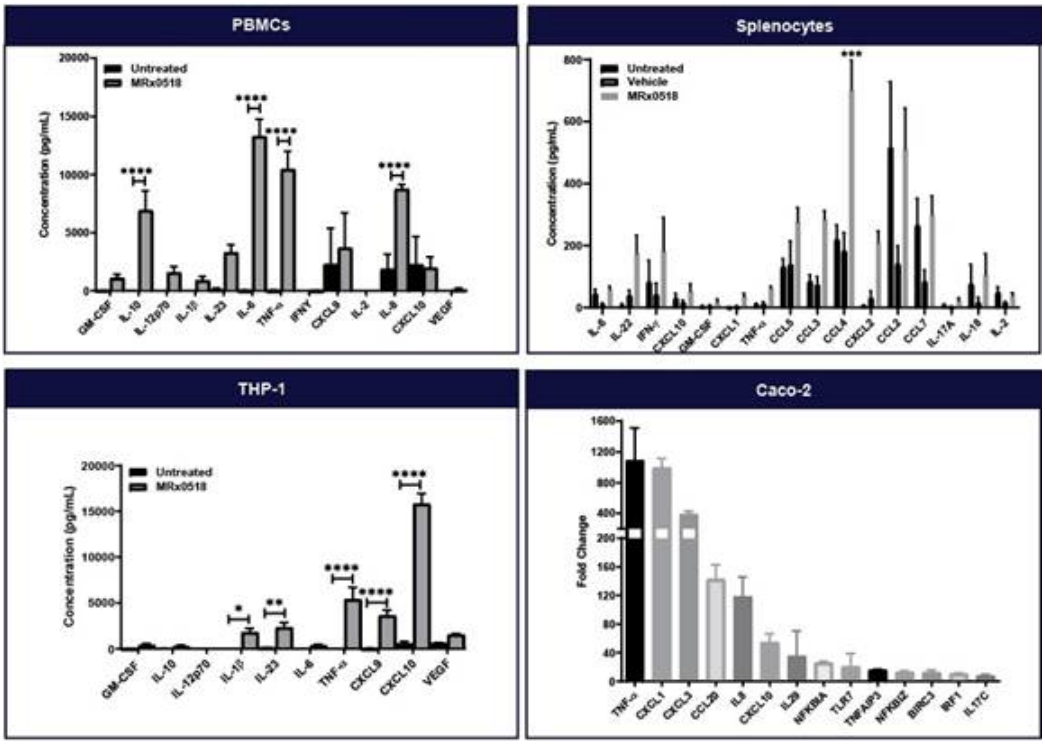


Figure 4. Results of *in vitro* assays, demonstrating the effects of MRx0518 on peripheral blood mononuclear cells (PBMCs), splenocytes, THP-1 cells (cell-line derived from an acute monocytic leukemia patient) and Caco-2 cells (cell-line derived from a patient with colon carcinoma). Significance relative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

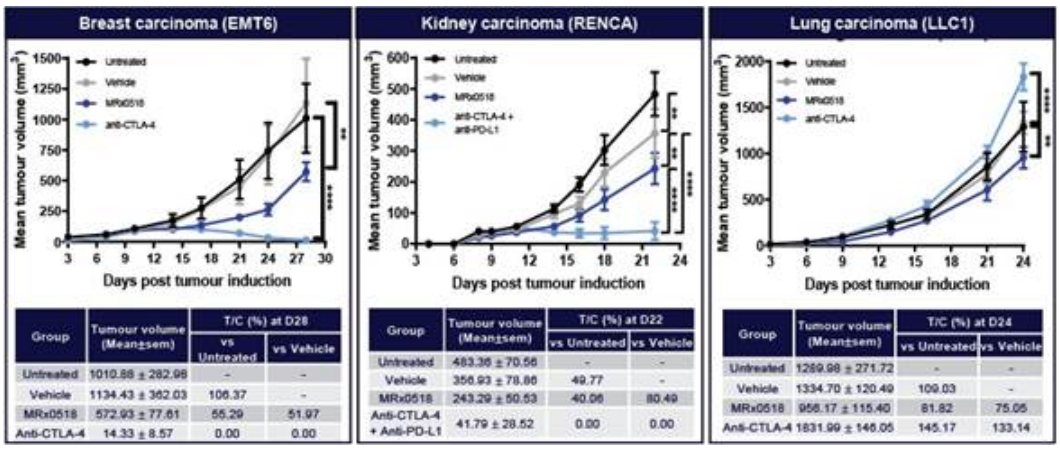
Screening of our proprietary library against a variety of *in vitro* assays enabled the discovery of MRx0518, a single strain of *Enterococcus gallinarum*. MRx0518 was able to induce a strong innate immune response in a range of *in vitro* assays (see Figure 4), in addition to a strong adaptive immune 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	T/C (%) at D28 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	T/C (%) at D22 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	T/C (%) at D24 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.

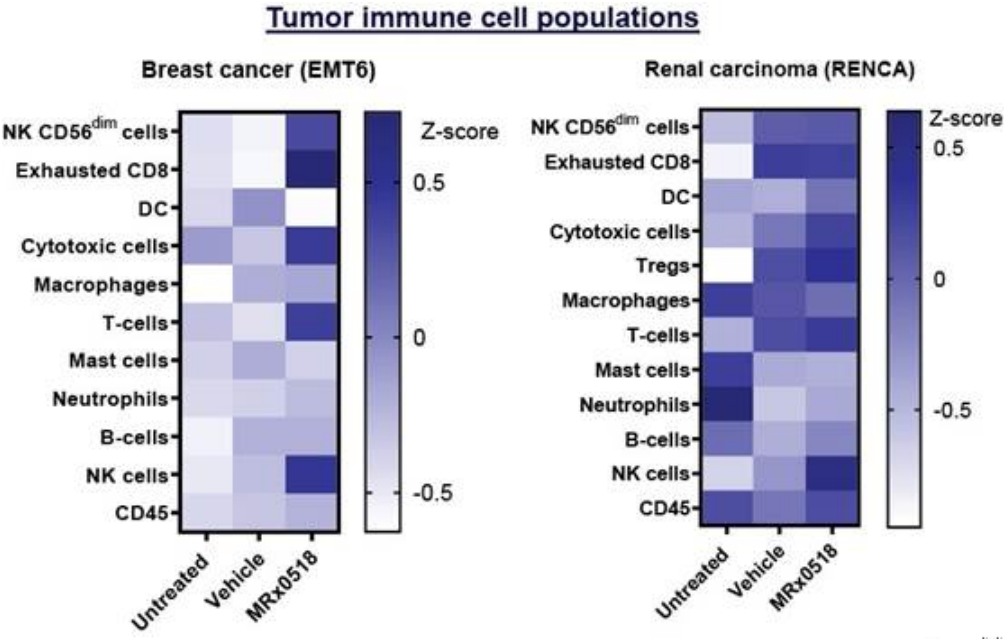


Figure 6 - Quantification of cell subsets utilizing tumor tissues and analysis via NanoString PanCancer IO360 Gene Expression Profile showed that MRx0518 administration in animal models led to increased intra-tumor populations of cytotoxic cells, T cells, CD8+ T cells and NK cells.

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.

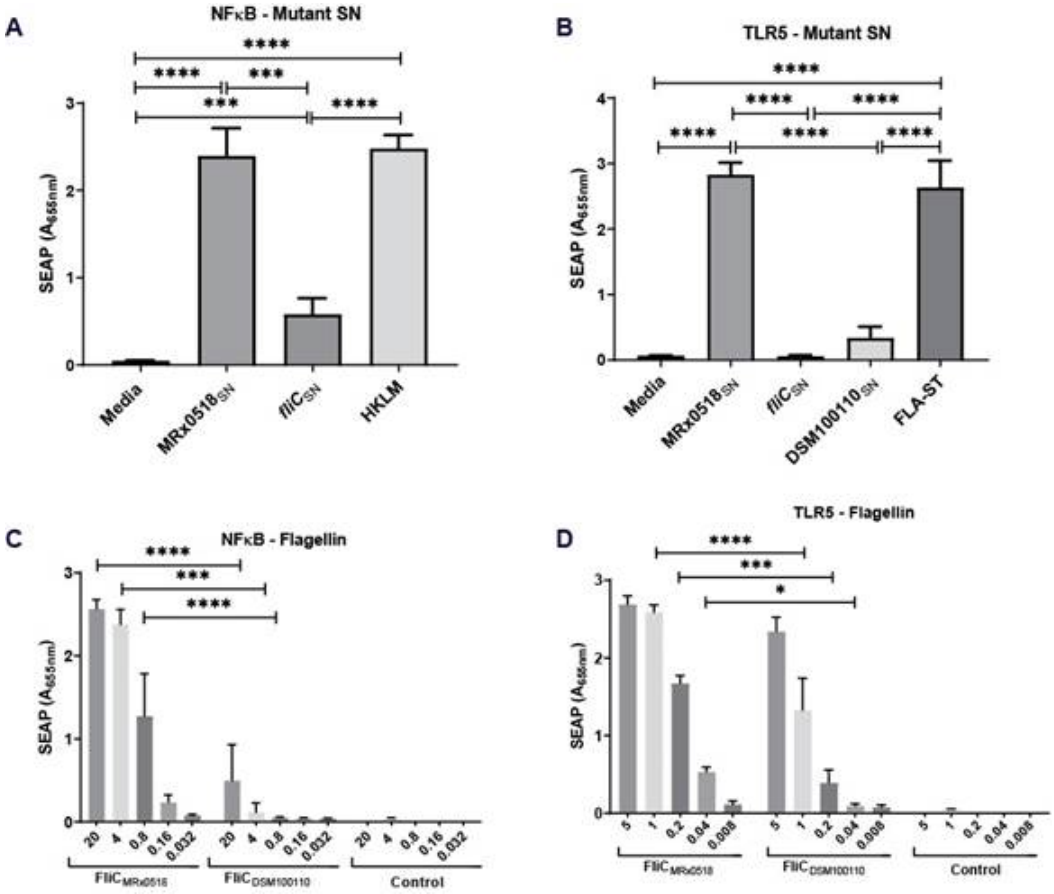


Figure 7. Activation of NF-κB and TLR5 pathway by *E. gallinarum* MRx0518 treatments. NF-κB (A) and TLR5 (B) activation after 22 h incubation with *E. gallinarum* MRx0518 (MRx0518LV), heat-killed MRx0518 (MRx0518HK) and culture supernatant (MRx0518SN) in HEK-Blue hTLR5 and THP1-Blue NF-kB reporter cell 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

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 and UC that are refractory to prior anti-PD-1/PD-L1 therapy. Additionally, new cohorts of 10 patients with new tumor types are to be 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. 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, 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, 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 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 .

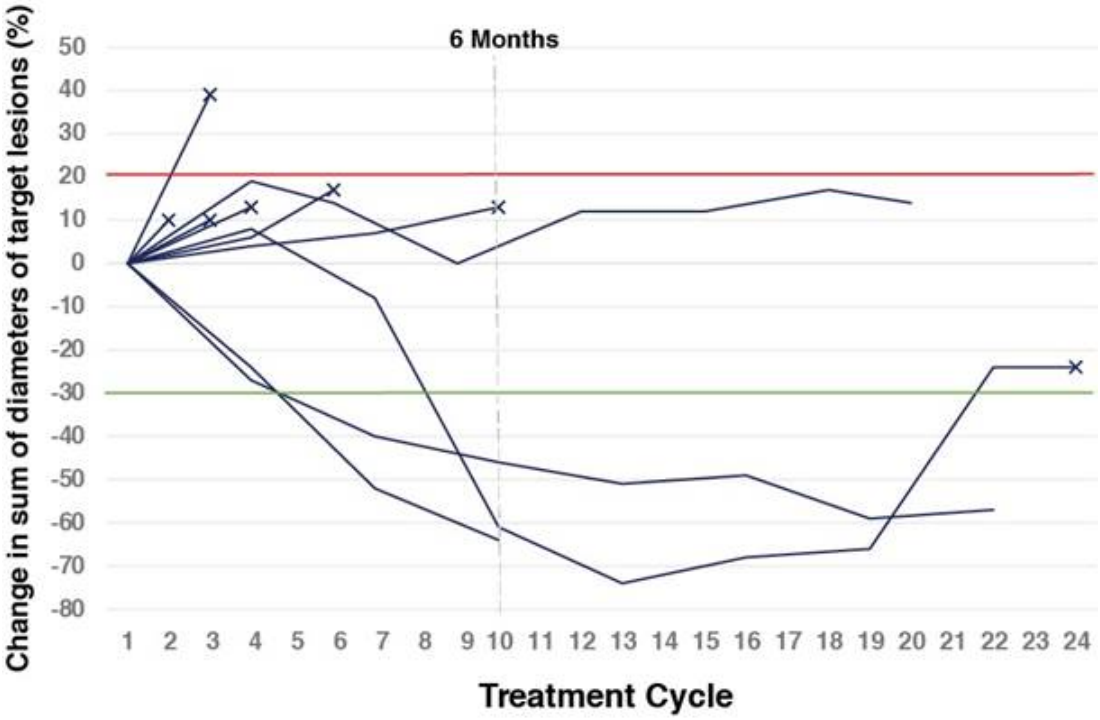


Figure 8. **Percentage change in sum of diameters of target tumors per RECIST v1.1 in patients enrolled in Part A of Phase I/II MRx0518 and Keytruda combination trial (NCT03637803), as of October 23, 2020. Radiological assessment was not possible for two patients who were withdrawn from the study due 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 approved alternative treatment options 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 to be 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.

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 is taken at baseline. MRx0518 is then dosed as a monotherapy for two to four weeks prior to resection, at which point another tumor sample is taken. Changes in systemic immune and intratumoral biomarkers are then analyzed to assess the effect of MRx0518 monotherapy on immune cell populations over the dosing period. Results of this trial are expected to develop our understanding of the mechanism of action of MRx0518 in the clinical setting which could inform the clinical development strategy for this candidate.

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. We are currently designing Part B of this Phase I clinical trial and expect to begin enrollment and dosing 2021.

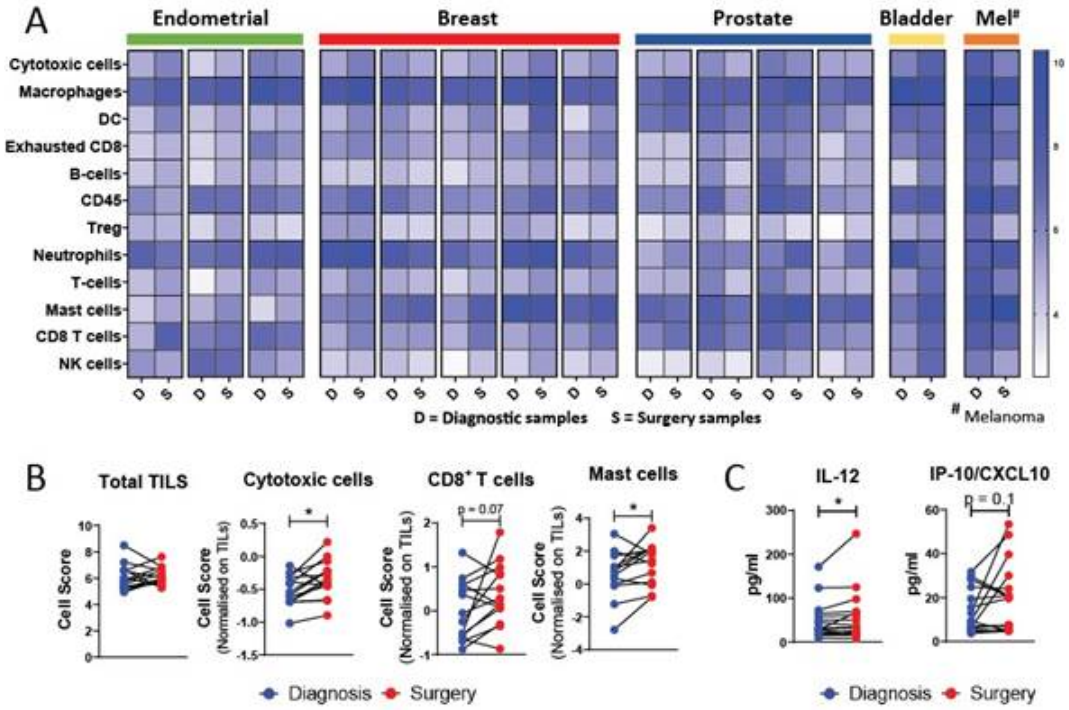


Figure 9. Relative frequency of immune cell subsets in diagnostic and surgery tumour samples were evaluated in the Phase I MRx0518 neoadjuvant monotherapy trial, evaluated using the NanoString IO360 platform and nSolver (A-B). Systemic cytokine concentrations were evaluated in plasma (Luminex) (C). P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

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 the University of Texas MD Anderson Cancer Center. 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 receiving initial data from this Phase I clinical trial in 2021.

Exploring new settings and combinations

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 and 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 our LBPs at 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 remain the sponsor of any studies and clinical trials. Merck KGaA and Pfizer are providing Bavencio without cost to us for the clinical trials.

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* (**Figure 10**).

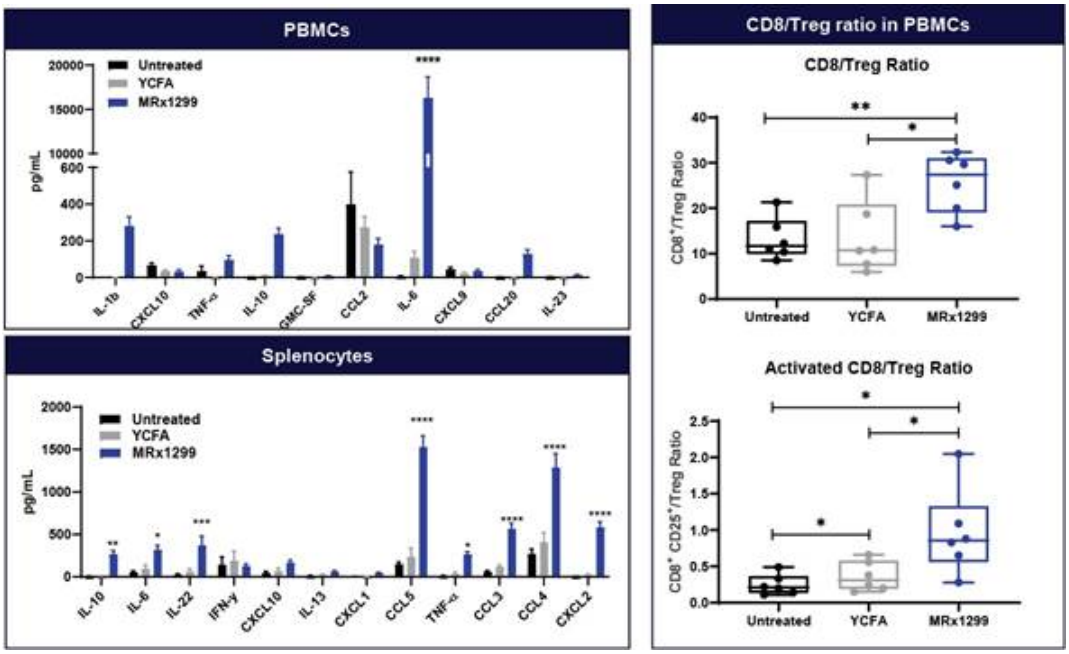


Figure 10. **MRx1299-induced immune activation was investigated in different cell types. MRx1299 induces a cytokine/chemokine signature in peripheral blood mononuclear cells (PBMCs) and splenocytes *in vitro* that includes IL-6, IL-22, IL-10, TNF-α, CXCL2, CXCL10, CCL3, CCL4 and CCL5, and increases the 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 (**Figure 11** and **Figure 12**). 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.

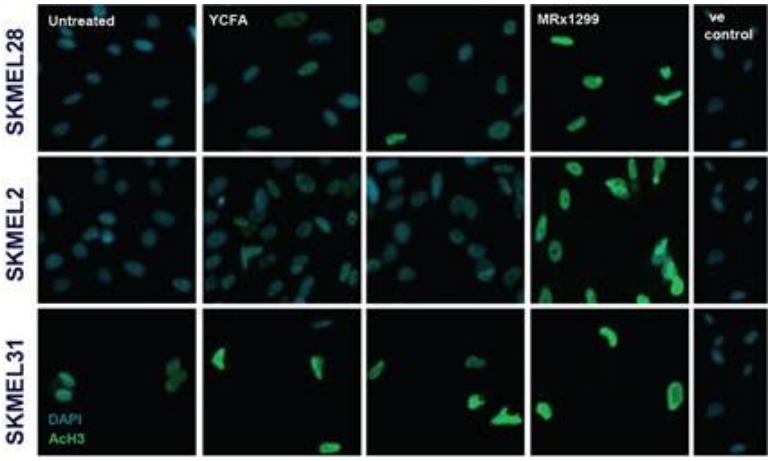


Figure 11. **MRx1299 increased acetylated H3 and H4 nuclear staining in melanoma cell lines. YCFA = Yeast extract-Casein hydrolysate-fatty acid medium.**

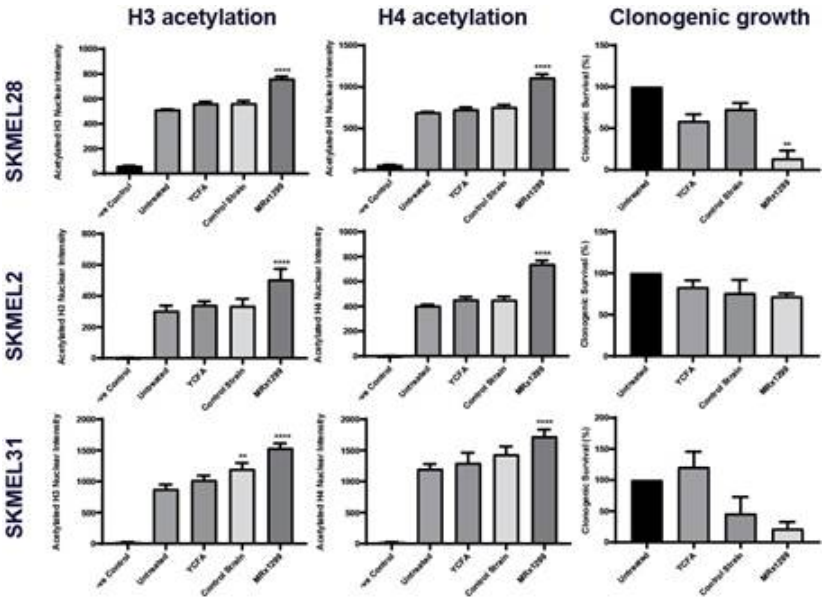


Figure 12. **MRx1299-induced histone acetylation correlated with reduced clonogenic growth in preclinical models of melanoma and colon carcinoma. YCFA = Yeast extract-Casein hydrolysate-fatty acid medium. Significance relative to vehicle: * ($p < 0.05$), ** ($p < 0.01$), *** ($p < 0.001$), **** ($p < 0.0001$).**

Respiratory Disease Portfolio

Asthma

A significant number of patients with asthma are poorly controlled by current treatments, leading to exacerbations, hospitalization and mortality. 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 in a clinical setting via 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, something not possible with existing approved asthma therapies. The candidate is currently being evaluated in two clinical trials, a Phase I/II study in patients with uncontrolled asthma, and a Phase II study in patients with COVID-19.

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 14**). 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**).

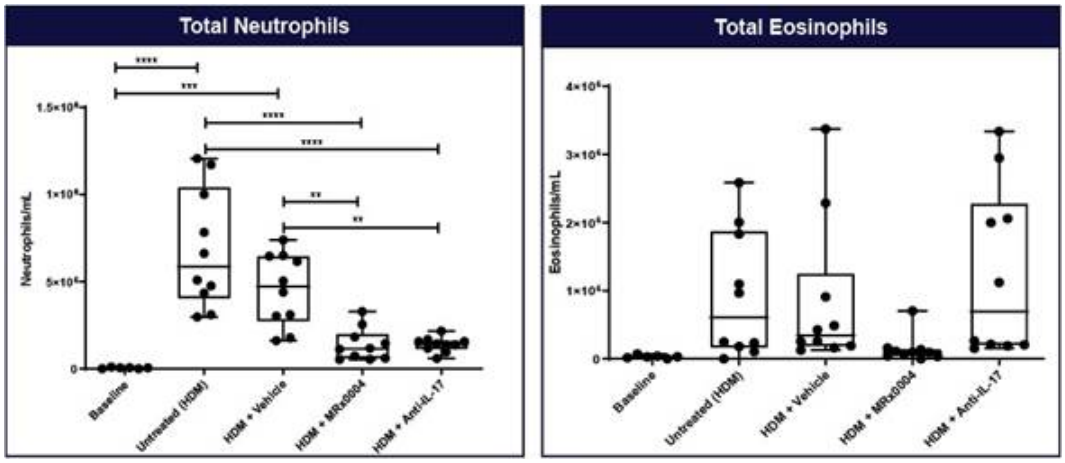


Figure 14. **Bronchoalveolar lavage fluid (BALF) cell counts of mice exposed to HDM, and treated therapeutically with MRx-4DP0004, anti-IL-17 or vehicle, with samples collected 24 h after final exposure. MRx-4DP0004 significantly reduced airway neutrophils, in addition to eosinophils. Significance relative to vehicle: Significance relative to vehicle: * (p < 0.05), ** (p < 0.01), *** (p < 0.001), **** (p < 0.0001).**

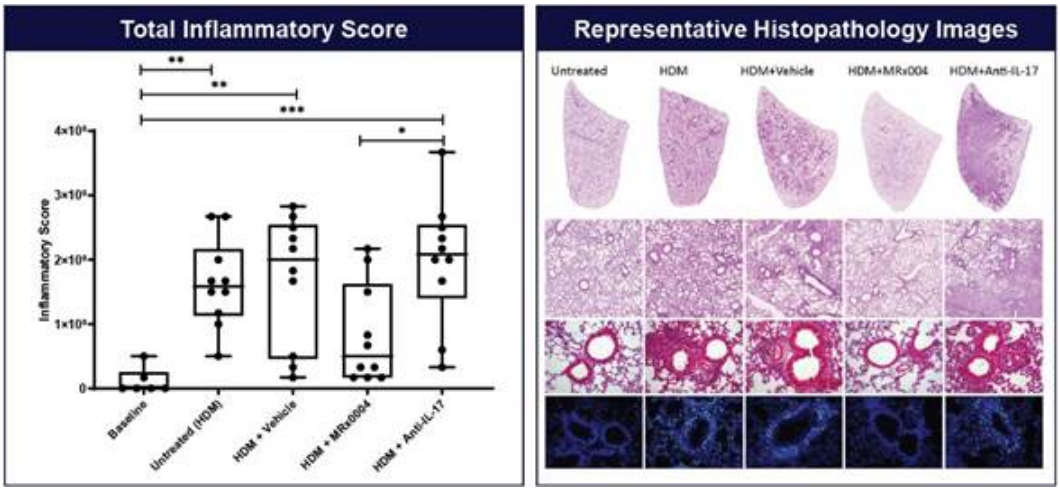


Figure 15. MRx-4DP0004 lowered inflammation in the lung, strongly reducing peribronchiolar and perivascular infiltrates, and lung IL-1α, IL-1β, CXCL2. In contrast, anti-IL-17 treated animals were comparable to vehicle-treated groups. Histopathological analysis of lungs of mice exposed to HDM, and treated 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

In July 2019, we launched a Phase I/II clinical trial first-in-human study of MRx-4DP0004 in 90 patients with partly controlled asthma. Patients on the study receive MRx-4DP0004 daily in addition to their long-term maintenance asthma medication. The clinical trial assesses the safety and tolerability of MRx-4DP0004, in addition to clinical endpoints relating to exacerbations, lung function and quality of life. A wide panel of host and microbiome biomarkers are also being assessed, that will contribute to mechanistic understanding of the candidate.

To our knowledge, this is the world's first clinical trial of a single strain Live Biotherapeutic in this indication. COVID-19 has had an impact on enrollment for the trial, delaying expected preliminary data to Q3 2021, with the study expected to be completed in H1 2022.

Phase II clinical trial in patients hospitalized with COVID-19

The most critical stress facing healthcare systems because of the COVID-19 global pandemic is the inflammatory response to infection, particularly in the lungs, leading to the need for oxygen therapy, ventilation or other critical care. Thus, there is an urgent need for rapid development of a therapeutic to reduce harmful lung and/or systemic inflammation induced by SARS-CoV-2 infection without impairing the appropriate anti-viral immune response. We are utilizing the unique immunomodulatory profile of MRx-4DP0004 as a therapeutic to prevent or reduce the hyperinflammatory response in patients hospitalized with COVID-19.

Based on peer-reviewed data emerging from China early in 2020 regarding the immune response to the novel coronavirus SARS-CoV-2, we were able to recognize the potential of MRx-4DP0004 to impact multiple components of the immune system implicated in the worsening of disease as a result of the body's hyperinflammatory response. As a result, in April 2020 we received MHRA acceptance for a UK Phase II clinical trial of LBP MRx-4DP0004 to treat 90 patients hospitalized with COVID-19. The clinical trial assesses the impact of treatment on mean clinical status score as measured by the WHO Ordinal Scale for Clinical Improvement and also the safety and tolerability of MRx-4DP0004. We expect preliminary data from the study in 2021 , with the study expected to be completed in H1 2022.

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 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 (**Figure 16**).

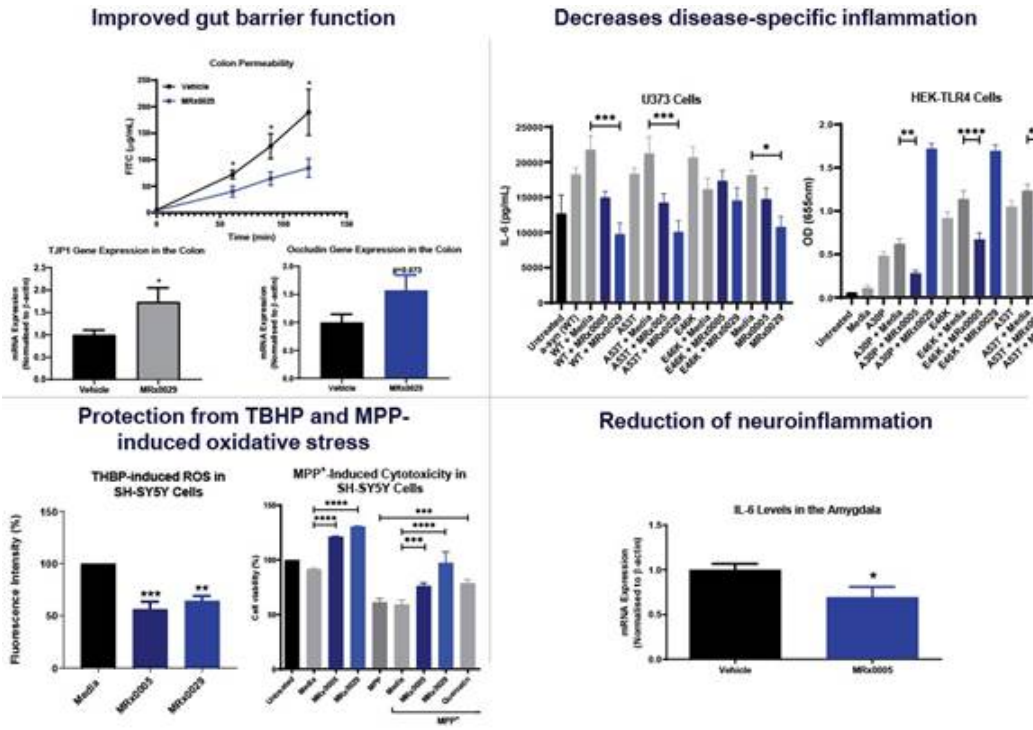


Figure 16. ***In vitro*****, MRx0029 was able to decrease gut permeability as measured by FITC/Ussing chambers, and increase gene expression of proteins associated with gut barrier functions such as Tight Junction Protein 1 and Occludin. The candidates also demonstrated neuroprotection from TBHP and 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 (**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.

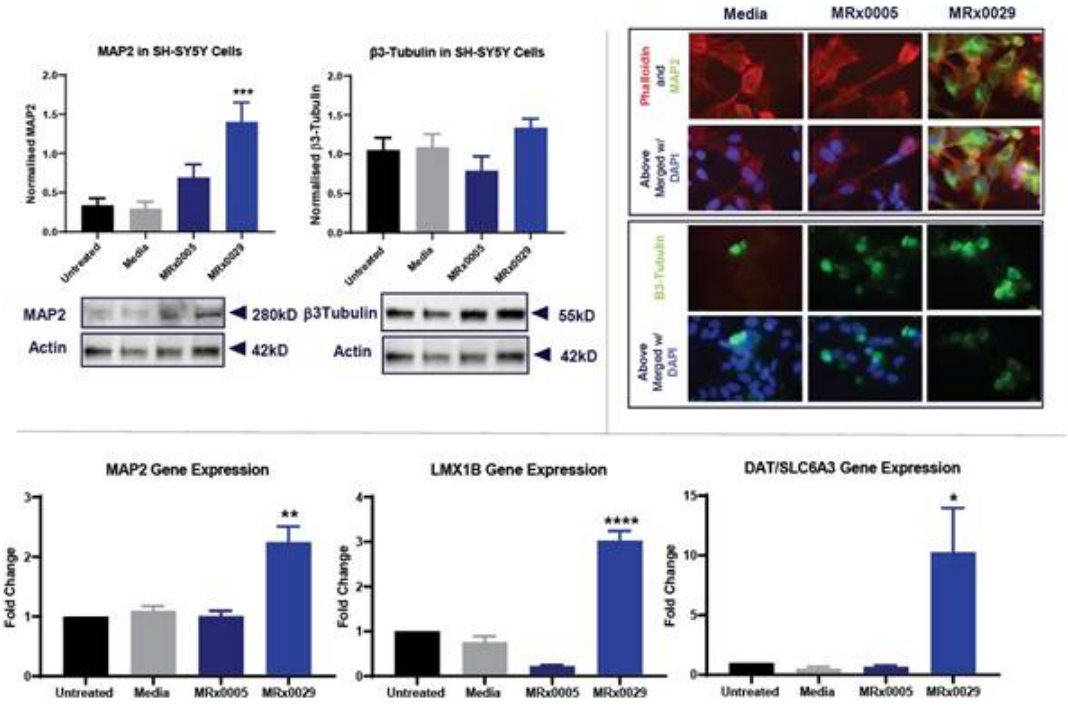


Figure 17. *In vitro* treatment of neuroblastoma cells with MRx0029 demonstrated differentiation to a dopaminergic-like neuronal phenotype, and significantly upregulated expression of numerous markers of dopaminergic neurons, including MAP2, LMX1B and DAT. MPTP = 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine; 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 (**Figure 18).**

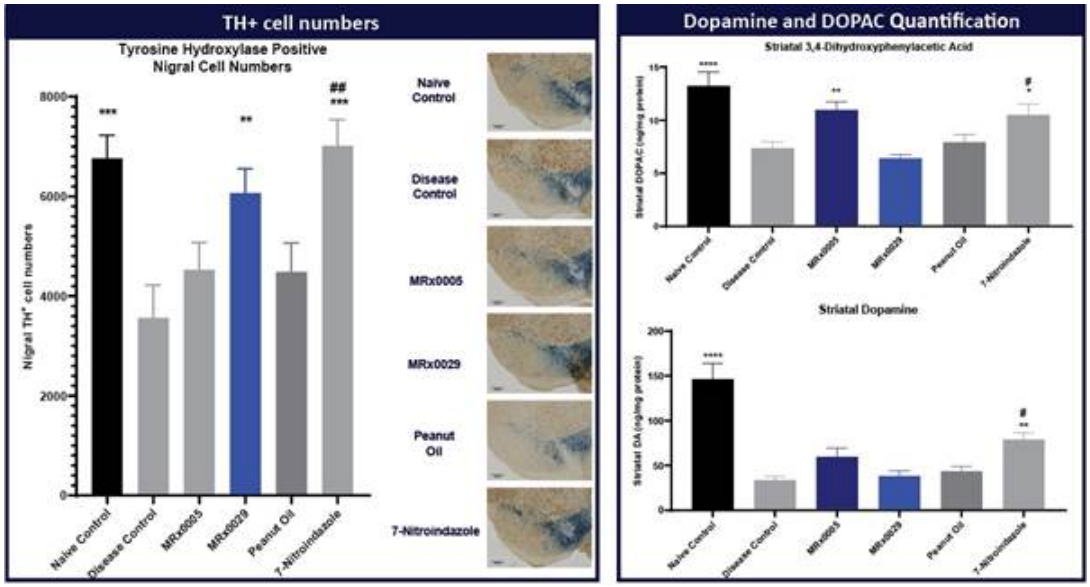


Figure 18. In the MPTP-induced animal model of PD, MRx0029 protected from the loss of TH+ neurons in MPTP-induced brain lesions, offering comparable neuroprotection to the 7-NI positive control. MRx0005 protected from loss of striatal dopamine and DOPAC in MPTP-treated mice, with a similar effect to 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 are in the process of evaluating designs for a potential first-in-human clinical trial of MRx0029 in patients with PD and have enlisted the help of key opinion leaders in PD clinical study design to assist in planning.

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.

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 19**).

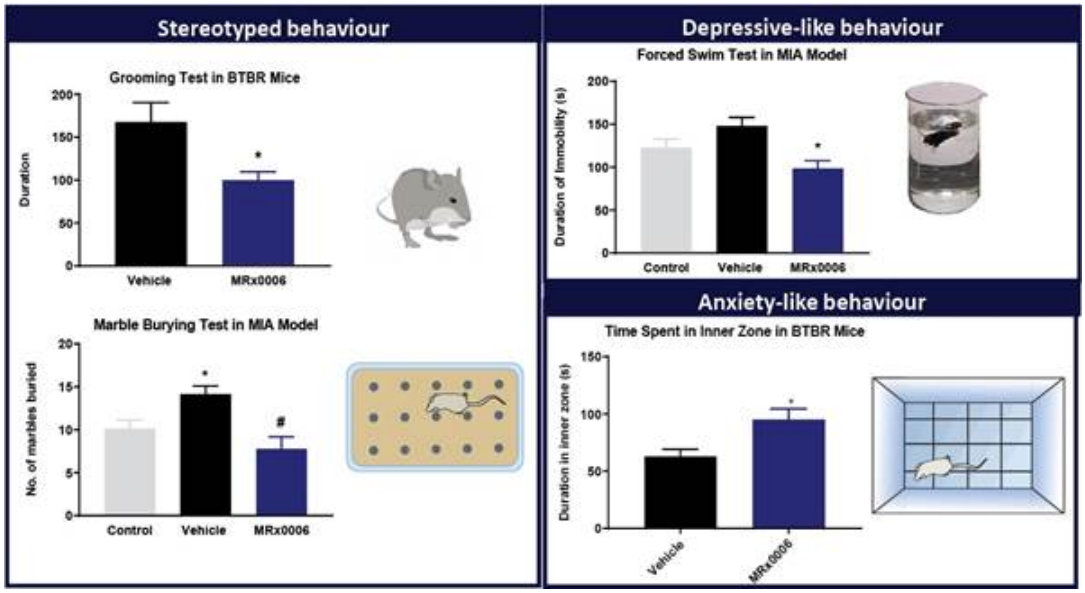


Figure 19. MRx0006 effect on social behaviors assessed in several models, including three-chamber test and urine sniffing test. BTBR = inbred BTBR T+tf/J mouse model of autism; MIA = maternal immune activation. Significance relative to vehicle: * ($p < 0.05$), ## (no significant difference from vehicle + 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 (**Figure 20**).

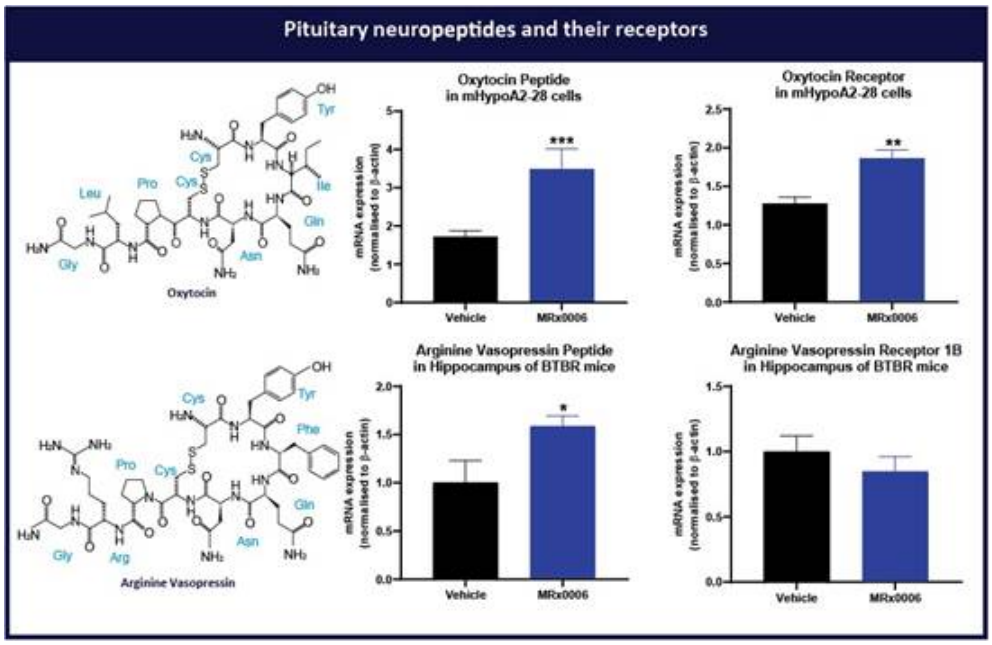


Figure 20. MRx0006 significantly increased oxytocin and oxytocin receptor mRNA expression in mHypoA2-28 cells. MRx0006 also significantly increased hippocampal arginine vasopressin mRNA expression in BTBR mice. Significance relative to vehicle: * (p < 0.05), ** (p < 0.01), * (p < 0.001).**

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 (**Figure 21**).

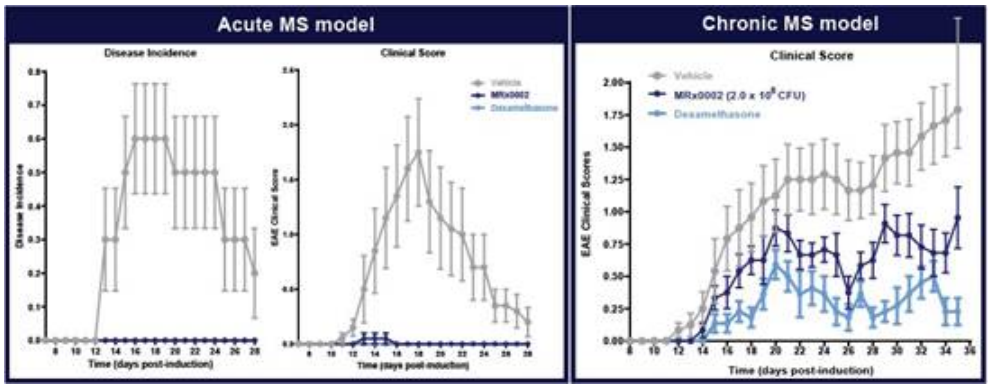


Figure 21. **In an acute experimental autoimmune encephalomyelitis (EAE) mouse model, MRx0002 completely prevented the onset of disease. In a chronic EAE model, MRx0002 also led to a significant reduction in clinical scores. PBS = Phosphate buffered saline; CFU = colony-forming unit.**

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 22**). MRx0006 also showed a distinct protection of joint architecture from inflammatory damage in histopathological assessment and scoring (see **Figure 23**).

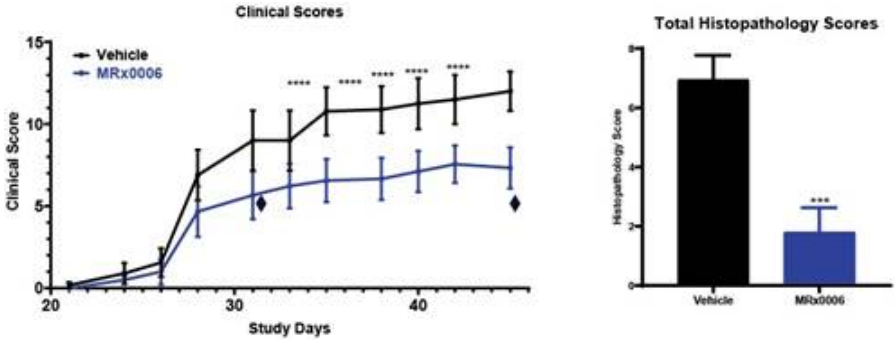


Figure 22. MRx0006 significantly reduced clinical scores (swelling of paws and joints), compared to vehicle following type II-collagen (CII) induction; and significantly reduced all hind limb histopathological scores, including joint inflammation, and cartilage and bone damage. Significance relative to vehicle: ♦ (p<0.05 compared to vehicle on given day), ** (p<0.0001 compared to Day 21 in vehicle); *** (p < 0.001).**

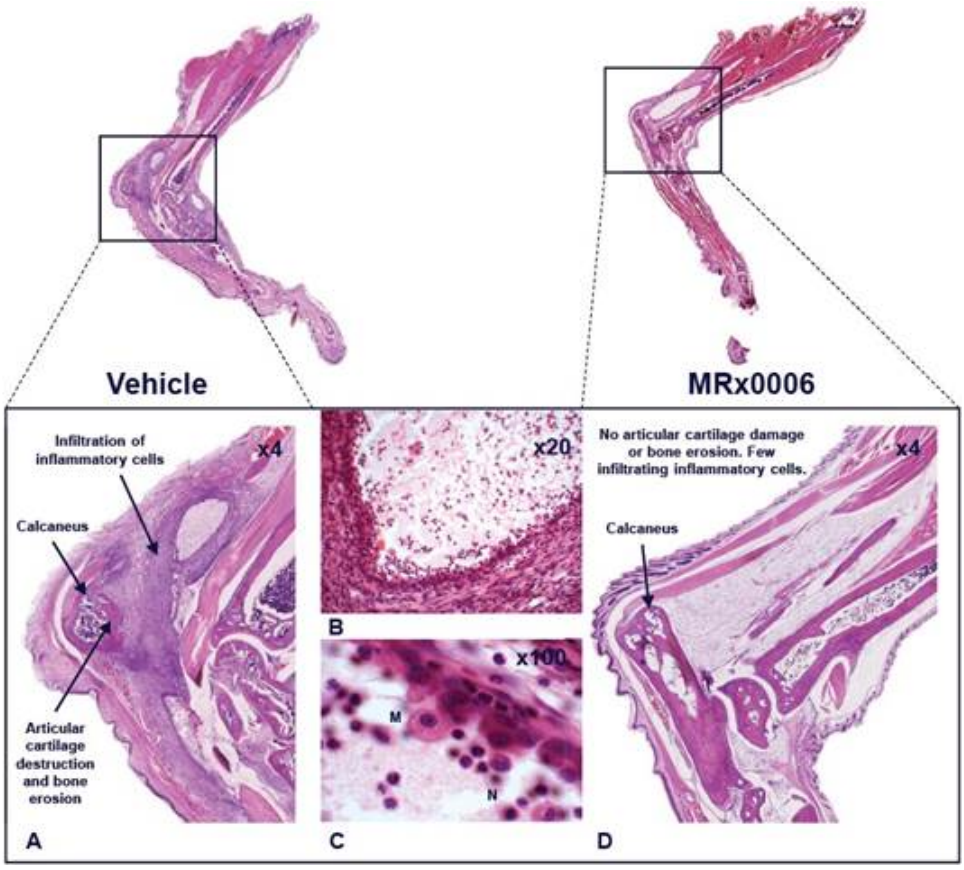


Figure 23. Representative H&E stained saggital sections of arthritic mouse hind limbs derived from subjects in the type II collagen (CII)-induced arthritis model of RA. Cartilage destruction, bone erosion and infiltration of inflammatory cells including macrophages (M) and neutrophils (N) were visible 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 and pediatric Crohn's disease.

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 is the largest clinical trial of a Live Biotherapeutic conducted to date, enrolling 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 Phase III pivotal program towards registration.

Blautix achieved a statistically significant overall response rate compared to placebo in the combined IBS-C/D group Efficacy Evaluable Analysis Set ($p = 0.037$) and demonstrated positive, although not statistically significant, trends in improving overall response for both the IBS-C and IBS-D subgroups independently. Interestingly, and highly supportive of the potential for Blautix to treat both IBS-C and IBS-D subtypes, a statistically significant effect on improvement in bowel habit was shown in both IBS-C ($p = 0.038$) and IBS-D patients ($p = 0.05$) and in the combined IBS-C/D group ($p = 0.0045$). Blautix was well tolerated, with a safety profile comparable to placebo with respect to adverse events and severe adverse events.

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. Additional analysis of the BHT-II-002 clinical trial data is ongoing. 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 14**). 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.*

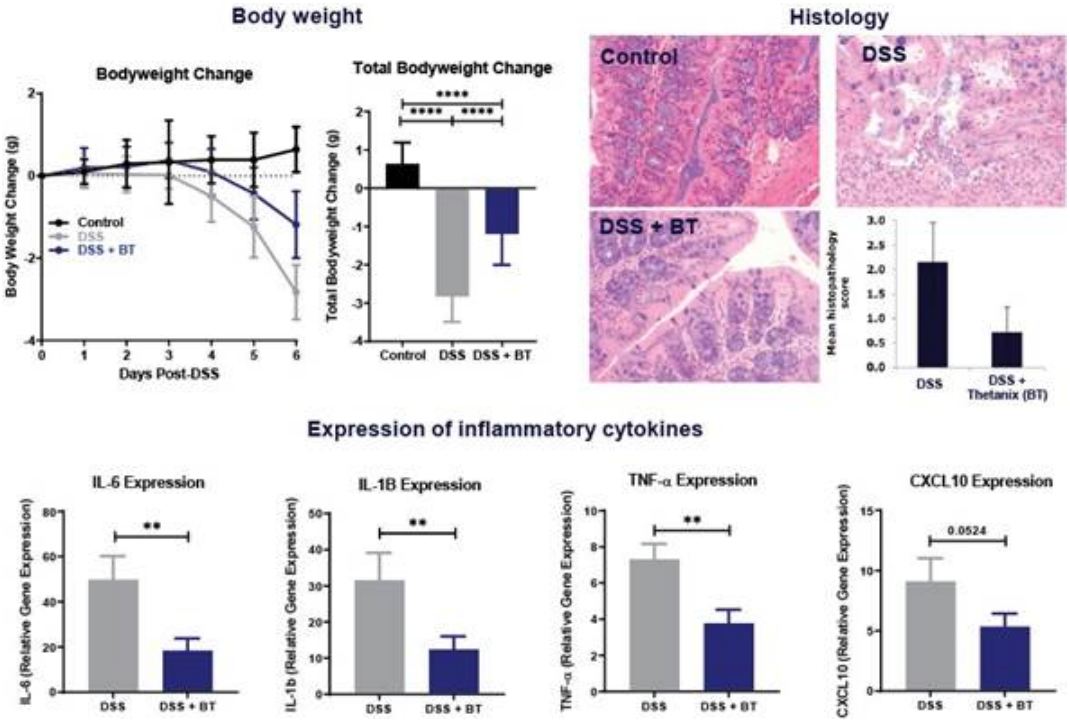


Figure 24. Thetanix protects against intestinal inflammation in dextran sodium sulfate (DSS) mouse models of colitis, reducing disease-associated bodyweight loss, downregulating inflammatory signals, and improving histopathology scores. BT = Thetanix. Significance relative to vehicle: ** ($p < 0.01$), ** ($p < 0.0001$).**

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 and evenness was observed across the dosing period. 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. 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.

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 seven 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. 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 Serono 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, Bausch Health Companies Inc and Ardelyx.

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, 2020, our patent portfolio included approximately 37 issued U.S. patents, approximately 46 pending U.S. provisional or non-provisional patent applications, approximately 1130 foreign patents, and approximately 588 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 2021 and 2040, without taking into account any possible patent term adjustments or extensions.

With regard to MRx0518, as of December 31, 2020, we have approximately 3 issued U.S. patents, approximately 7 pending U.S. provisional or non-provisional patent applications, approximately 53 foreign patents, and approximately 145 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 2039, without taking into account any possible patent term adjustments or extensions.

With regard to MRx-4DP0004, as of December 31, 2020, we have approximately 2 issued U.S. patents, approximately 1 pending U.S. provisional or non-provisional patent application, approximately 89 foreign patents, and approximately 20 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, 2020, we have approximately 10 issued U.S. patents, approximately 7 pending U.S. provisional or non-provisional patent applications approximately 214 foreign patents, and approximately 95 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 2021 and 2040, without taking into account any possible patent term adjustments or extensions.

With regard to Thetanix, as of December 31, 2020, we have approximately 1 issued U.S. patent, approximately 1 pending U.S. provisional or non-provisional patent application, approximately 69 foreign patents, and approximately 20 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 United States Patent and Trademark Office (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, 2020, 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 the University of Texas MD Anderson Cancer Center (“MD Anderson”). 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. 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 a maximum of $10 million and have paid $4 million to date. The agreement expires six 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.

Research Collaboration and Option to License Agreement with Merck

In October 2019, we entered into a research collaboration and option to license agreement with Merck to discover and develop vaccines in up to three indications derived from our proprietary gut microbiome-derived commensal bacteria selected from our culture collection. The collaboration brings together MSD’s experience in the development of vaccines with our expertise in developing LBPs. 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.

The parties granted each other licenses under their intellectual property to conduct the research under the agreement. Each party owns the inventions that it invents solely under the research collaboration, but we jointly own inventions that are jointly developed between the parties. Merck has the first right to file and prosecute patents covering inventions developed under the research, until Merck's selection of its preferred LBPs, upon which time Merck's first right will be limited to those patents that cover inventions related to those preferred LBPs or vaccine products comprising those preferred LBPs. We granted Merck an exclusive option with respect to each indication to obtain exclusive licenses to develop and commercialize products as therapeutic agents useful in the treatment of such indication. For the term of the research collaboration, which expires on October 7, 2022, and for six months thereafter (the "Option Period"), we cannot research, develop or commercialize any vaccine product comprising a live bacteria and an exogenous antigen. In addition, during the term, and provided that Merck exercised at least one option, we cannot conduct certain activities that would lead to developing a competitive vaccine product. Under the agreement, Merck granted us a license under its intellectual property that specifically claim or cover LBPs for all purposes other than developing or commercializing a vaccine product. Under the terms of the agreement, we received a $2.5 million upfront cash payment, a $5 million equity investment, and we 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 and expire upon the later of (i) the last-to-expire valid patent claim or (ii) 10 years after the first commercial sale of such product in the applicable country. If Merck does not exercise one of its options during the Option Period, the agreement will expire at the end of the research collaboration. If Merck does exercise an option under the agreement, the agreement expires upon the expiration of Merck's royalty obligations. Merck can terminate the agreement without cause with 90 days' written notice. Either party can terminate the agreement in the event that the other party materially breaches the agreement and fails to cure such breach within 90 days of receiving notice from the non-breaching party, or if the other party becomes bankrupt and such proceeding is not dismissed within 90 days. If Merck terminates the agreement for convenience, or the agreement terminates because Merck does not exercise an option, Merck has a fully paid-up non-exclusive license under our interest in the intellectual property developed under the agreement for internal research purposes only. If Merck terminates the agreement due to our material breach, we will assign to Merck all interest that we have in the intellectual property generated by the research, as well as the LBPs that were the subject of and included in the research. If we terminate the agreement due to Merck's breach before Merck exercises an option, Merck grants us a non-exclusive license under Merck's interest in the intellectual property generated from the research for all purposes.

In the near-term we look forward to advancing our research with our world-leading partners at MSD and MD Anderson. Beyond these partnerships, we are actively pursuing additional research collaborations to enable us to realize the true value of the MicroRx platform and expand into new therapeutic areas.

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 a guidance, which the FDA subsequently updated, on conducting clinical trials during the pandemic, which 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 a 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 a 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.

There have been legislative and judicial efforts to repeal, replace, or change some or all of the ACA, including measures taken during the Trump administration. In November 2020, the United States Supreme Court held oral arguments on the Fifth Circuit U.S. Court of Appeals decision that held that the individual mandate is unconstitutional. It is uncertain how the United States Supreme Court will rule on this case or how healthcare measures of the Biden administration will impact the ACA and our business. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results. 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. Until the ACA is fully implemented or there is more certainty concerning the future of the ACA, it will be difficult to predict its full impact and influence on our business. We cannot predict whether current or future efforts to repeal or modify these laws and/or adopt new healthcare legislation will be successful, nor can we predict the impact that such a development would have on its business and operating results. 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 will remain in effect through 2030, with the exception of a temporary suspension implemented under various COVID-19 relief legislation from May 1, 2020 through March 31, 2021, unless additional Congressional action is taken. 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. At the federal level, the Trump administration's budget for fiscal year 2021 includes allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. On July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that seek to implement several of the administration's proposals. The FDA also released a final rule in September 2020 providing guidance for states to build and submit importation plans for drugs from Canada. Further, in November 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. The CMS also issued an interim final rule implementing President Trump's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. On December 28, 2020, the United States District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. In December 2020, CMS issued a final rule implementing significant manufacturer price reporting changes 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. It is unclear to what extent these new regulations and any future regulations and legislation by the Biden administration will have on our business, including our ability to generate revenue and achieve profitability, and the business of our customers.

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.

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, 2020, 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.
Dolphin Merger Sub 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 in December 2021 with rolling one-year extensions, lease 14,100 square feet of manufacturing facilities in Leòn, Spain that expires in April 2026; and lease 2,028 square feet of office and laboratory space in Cork, Ireland that expires June 2021. 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, 2020.

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 $38 thousand at December 31, 2020.

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. This discussion and other parts of the 20-F contain forward-looking statements based upon current expectations that involve risks and uncertainties. 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. Please also see "Cautionary Statement Regarding Forward-Looking Statements." For a comparison of our results of operations for the fiscal years ended December 31, 2019 and 2018, see Management's Discussion and Analysis of Financial Condition and Results of Operations of 4D Pharma included in Amendment No. 5 to our registration statement on Form F-4 (File No. 333-250986), filed with the SEC on February 24, 2021, and incorporated herein by reference.

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 and respiratory disease, with preclinical candidates targeting CNS and autoimmune conditions. We have completed three clinical trials and currently have five more 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 advance 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 to be 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 expressed 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. 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. Following the year end, in February 2021, we entered into agreement with Merck KGaA and Pfizer, who co-developed and co-commercialized Bavencio (avelumab) to supply Bavencio free of charge in a future clinical trial.

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. A Phase I/II clinical trial of MRx-4DP0004 in partly controlled asthma is ongoing, and to our knowledge the world's first clinical trial of an LBP in the indication. We are also investigating MRx4DP0004 in a Phase II clinical trial as an oral therapeutic to prevent or reduce the hyperinflammatory response in patients hospitalized with COVID-19. The Phase II trial of MRx-4D0004 received expedited approval from the MHRA in April 2020.

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 candidate, MRx0029, in Parkinson's disease patients. 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 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 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 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.

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 "Item 4. Information on the Company—B. Business Overview—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. 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. For the year ended December 31, 2020, we had one clinical trial completed through Phase II. For each of the years ended December 31, 2019 and 2018, we had two clinical trials completed through Phase I/Phase II.

2. Clinical trials initiated by phase – Clinical trials are essential in converting the productivity and potential of our MicroRx platform and early-stage research into long-term value. In the last year we commenced two new clinical trials, of which one Phase I and one Phase II. Shortly after the year ended 31 December 2019, we had initiated seven clinical trials: four Phase I clinical trials; two Phase I/II clinical trials and one Phase II clinical trial. There were three clinical trials that we initiated for year ended 31 December 2018 of two Phase I clinical trials and one Phase II clinical trials.

3. Strategic collaborations – Collaborations enable us to realize the potential of our platform, leveraging the complementary expertise of our partners. For the year ended December 31, 2020, we had four strategic collaborations and three strategic collaboration for the year ended December 31, 2019. In December 2020 we became an industry partner of the 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. Our representatives will join the Partner Scientific Advisory Board closely involved in the design and execution of the study, as well as a variety of PPMI Working Groups. After the period end, 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 intend to commence a clinical trial in 2021 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. These partnerships are in addition to an ongoing strategic collaboration with the University of Texas MD Anderson Cancer Center, to evaluate our Live Biotherapeutic oncology pipeline across a range of cancer settings, 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 tumors that are refractory to prior anti-PD-1/PD-L1 therapy, 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 MicroRxplatform with MSD's world-leading expertise in vaccine development. See "Item 4. Information on the Company—Business Overview—Collaborations" for more information on our strategic collaborations.

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, 2020, had initiated 65 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.

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. Our unique approach allows rapid translation from bench to bedside. For the year ended December 31, 2020, our R&D spend was $23.4 million compared to $29.2 million for the year ended December 31, 2019. While maintaining our strategy to invest in our clinical development programs on a long-term basis, the decrease is reflective of the effects COVID-19 has had on both our clinical trials and structure of the business after management took quick action 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, 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, and our subsidiaries (other than the non-UK subsidiaries mentioned below), functional currency is the GPB. 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 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. 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.

Our, and our subsidiaries, 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, 2020 and 2019, we had $13.5 million and $12.7 million of goodwill accounting for 27% and 31% of our total assets, respectively, and $6.2 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, 2020, 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 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, 2020, we had a valuation allowance of $16.0 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, 2020 and 2019, we have recognized $0.7 million and $0.3 million in collaboration revenues, respectively. Associated costs of sale of $1.3 million and $0.3 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 20-F. 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, 2020, we have current deferred revenues of $1.3 million and long-term deferred revenues of $0.3 million, which will be recognized as the research and development costs and labor effort are incurred, which is expected to be a three-year period.

MD Anderson Collaboration Agreement

In November 2017 we established 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. Under the agreement, we provide funding and in-kind support for pre-clinical and clinical studies in solid tumors and radiation oncology.

For the years ended December 31, 2020 and 2019, we have recognized $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 generally 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 incurs additional expenses related to an expansion of our research and development activities and our operation as a public company, including higher legal, accounting, insurance, compliance, compensation and other expenses.

Patent spend has reduced overall since 2018 as we implemented various cost saving measures including limiting the territorial protection for patents protecting non-core assets and making direct contact with suppliers in foreign territories therefore bypassing intermediary markup costs.

Staff costs increased in 2019 in line with increases in staff numbers before the COVID-19 pandemic occurred in 2020 which resulted in the 4D Pharma's Board taking decisive action, reducing staffing levels.

Our research and development expenses consist primarily of salaries and related personnel expenses, contractual commitments, depreciation and 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, 2020	2019
Contractual commitments	$ 12,080	$ 16,190
Staff costs	5,823	6,414
Depreciation and amortization	1,278	1,171
Other MRx research costs	3,032	1,572
Other MDx research costs	79	658
Other manufacturing research and development costs	1,092	3,187
Total	$ 23,384	$ 29,193

Over the last year we have continued to lead the development of LBPs, 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 2020 we made significant progress in the clinical development of lead immuno-oncology candidate MRx0518, launching our third clinical trial, in resecrable pancreatic cancer. We also generated data from the two ongoing clinical trials of MRx0518 in different treatment settings, completing Part A of a Phase I/II combination study of MRx0518 with Keytruda in solid tumors refractory to prior anti-PD-1/PD-L1 therapy, and completing Part A of our Phase I study of MRx0518 as a neoadjuvant monotherapy. Following successful completion of Part A, we initiated, expanded and accelerated enrolment of Part B of the MRx0518 and Keytruda combination study, with the inclusion of additional tumor type cohorts and bringing additional clinical sites on board. We also launched a Phase II clinical trial of MRx-4DP0004 as an oral therapeutic to prevent or reduce the hyperinflammatory response in patients hospitalized with COVID-19. Enrollment for the ongoing Phase I/II trial of MRx-4DP0004 in partly controlled asthma was impacted by the COVID-19 pandemic. A Phase II clinical trial of Blautix for irritable bowel syndrome with constipation ("IBS-C") or IBS-D was completed in the period.

After the period end, 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 intend to commence a clinical trial in 2021 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.

With the clinical phase of the Blautix now complete, coupled with the three clinical trials of our therapeutic candidate, MRx0518, and the Phase I/II clinical trial of MRx-4DP0004 in partly controlled asthma and Phase II clinical trial of MRx-4DP0004 as an oral therapeutic to prevent or reduce the hyperinflammatory response in patients hospitalized with COVID-19. Despite the ongoing trials above and the anticipated launch of a fourth trial of MRx0518 in 2021 in combination with Bavencio, we anticipate that our research and development expenses for 2021 will remain at a similar level to that experienced in 2020.

The completion of the Blautix trial in the early part of 2021 and issues with patient recruitment created by COVID-19 in our Asthma trial reduced overall contractual commitments from $16.2 million in 2019 to $12.1 million in 2020, a decrease of $4.1 million. COVID-19 then provided a point of inflection, with management taking swift action to scale back operations and cut costs or redirect resources across to other areas of study, As such there was a decrease in a number of costs including other MDx research costs and other manufacturing, research and development costs; the latter of which being partly offset by an increase in other MRx research costs as, amongst other items, we furthered manufactured supply and development of MRx518 product

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

Results of Operations

	For the Year Ended December 31,	
	2020	2019
Revenues	$ 690	$ 269
Operating expenses:		
Research and development	23,384	29,193
General and administrative expenses	13,015	10,380
Foreign currency losses (gains)	(699)	957
Total operating expenses	35,700	40,530
Operating loss	(35,010)	(40,261)
Other income (expense), net		
Interest income	6	78
Other income	4,496	6,883
Change in fair value of contingent consideration payable	-	2,967
Total other income, net	4,502	9,928
Net loss before income tax benefit --	(30,508)	(30,333)
Income tax benefit	13	-
Net loss	$ (30,495)	$ (30,333)

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 totalled $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, 2020, we had $12.0 million in cash and cash equivalents.

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

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

Operating Activities

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 $0.2 million during the year ended December 31, 2020, 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 $34.5 million during the year ended December 31, 2020 was primarily related to the issuance of common stock 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.

In July 2020, we completed the sale of 21.9 million shares of common stock at £0.35 ($0.44) per share for a total of approximately £7.7 million ($10 million) or £7.3 million ($9.5 million) net of transaction costs.

In February 2020, we completed the sale of 44 million common stock at £0.50 ($0.65) per share for a total of £22 million ($28.6 million) or £20.8 million ($26.8 million) net of transaction costs. Warrants were issued on March 9, 2020 on the basis of one warrant for every two shares acquired. The warrants have an exercise price of £1.00 ($1.37) per share, are immediately exercisable, expire five years from issuance and cannot be traded on a regulated market.

Current Outlook

We have historically financed our 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.

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.

On March 22, 2021, we completed a merger with Longevity a publicly-traded special purpose acquisition company. Shareholders of Longevity received our ADSs, and Longevity became our wholly-owned subsidiary.

At closing, Longevity merged with and into 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) were 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 is outstanding immediately prior to the effective time of the merger was assumed by us and automatically be converted into a warrant to purchase our common stock and a right to receive our common stock, payable in our ADSs, respectively. The per share merger consideration consisted of 7.5315 common shares, payable in ADSs (each ADS representing 8 ordinary shares), for each issued and outstanding ordinary shares 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 common shares at a share price of £1.10 or ($1.53) per share, pursuant to the PIPE Investment. For more information, see Item 10. Additional Information—C. Material Contracts—PIPE Subscription Agreement,"

Additionally, in March 2021, our subsidiary in Spain, received a €1.0 million (£0.86 million or $1.2 million) overdraft facility supported by the Spanish government as part of its COVID-19 relief package. The overdraft is unsecured, incurs annual interest at a rate of 2.35% and is repayable in full at the end of three years. To date, we have not drawn down any funds from the overdraft facility.

As of December 31, 2020, our cash and cash equivalents were $12.0 million. We expect that our existing cash and cash equivalents, including the cash received in the merger with Longevity, the sale of our common shares and the receipt from an overdraft facility, all in March 2021, will be sufficient to fund our operations through the second quarter of 2022. For further information, see the Subsequent Events note that accompanies our audited consolidated financial statements included elsewhere in this Annual Report on Form 20-F.

We currently anticipate that we will require approximately $35.4 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 $23.6 million for general and administrative costs over such 18-month period, which consists primarily of expenditures for staff costs, legal and other professional fees, patent costs and other administrative expenses. We also estimate receiving approximately $9.0 million in cash for research and development tax credit refunds over this 18-month 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; and
- 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;
- 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.

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, 2020.

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 $38 thousand at December 31, 2020.

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. Off-Balance Sheet Arrangements

Except for standard operating leases, we did not engage in any off-balance sheet arrangements, such as the use of unconsolidated subsidiaries, structured finance, special purpose entities or variable interest entities before the year end.

We do not believe that our off-balance sheet arrangements and commitments have or are reasonably likely to have a current or future effect on our financial condition, changes in financial condition, revenues or expenses, results of operations, liquidity, capital expenditures or capital resources that is material to investors.

F. Contractual Commitments and Other Commitments

The following table sets forth certain information concerning our estimated fixed obligations and commitments to make future payments under existing contracts at December 31, 2020.

	Payments Due by Period			
Description	Total	Less Than One Year	1 – 3 Years	3 – 5 Years
Operating lease obligations	$ 1,914	$ 318	$ 994	$ 602
Total	$ 1,914	$ 318	$ 994	$ 602

G. Safe Harbor

Forward-looking information discussed in this Item 5 includes assumptions, expectations, projections, intentions and beliefs about future events. These statements are intended as "forward-looking statements." We caution that assumptions, expectations, projections, intentions and beliefs about future events may and often do vary from actual results and the differences can be material. Please see the section entitled "Forward-Looking Statements" at the beginning of this Annual Report on Form 20-F.

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	51	Chief Executive Officer, and Director
Dr. Alexander Stevenson	50	Chief Scientific Officer, and Director
John Beck	61	Chief Financial Officer
Richard Avison	43	Group Finance Director
Non-Executive Directors		
Prof. Axel Glasmacher	60	Non-Executive Director Chairman
Dr. Edgardo (Ed) Baracchini	61	Non-Executive Director
Dr. Alexander (Sandy) Macrae	58	Non-Executive Director
Dr. Katrin Rupalla	53	Non-Executive Director
Paul Maier	73	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 Beck was appointed as our Chief Financial Officer in March 2021. Mr. Beck serves on the board of directors of Artelo Biosciences, as a scientific advisor, and mentor to the University of San Diego's student-run TRITON fund. Prior to joining us, Mr. Beck served as Senior Vice President, Finance and CFO of Ritter Pharmaceuticals from May 2018 to May 2020. Mr. Beck also served as Executive Manager and CEO at Wellspring Water Technologies, LLC from October 2015 to May 2018 and CEO of West Tech Medical, LLC from October 2015 to May 2018. Mr. Beck also was the CFO and Senior Vice President of Finance and Operations of Ardea Biosciences from February 2008 to June 2012, and held positions as Senior Vice President of Finance, Treasurer and CFO of Metabasis Therapeutics from February 1998 to February 2008, and the Director of Finance at Neurocrine Biosciences from June 1992 to February 1998. Mr. Beck holds a B.A. in Accounting from the University of Washington, Seattle, a degree in theology from a Seattle-area seminary and is a licensed CPA (inactive status) in the state of California.

Richard Avison has served as our Finance Director since November 2017. Prior to joining us, Mr. Avison served as Accounting Services Manager for Summ.it Assist LLP, a financial consulting agency, from January 2009 to October 2017. Mr. Avison holds a B.Sc. (Hons) in Accountancy, Finance & Computer Science from Lancaster University.

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 Counsulting 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. 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 Chief Business Officer of Imago BioSciences, Inc., a biotechnology company, since April 2020.Prior to joining us, Dr. Baracchini served as 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. Baracchinicurrently serves on the board of INmune Bio, Inc., a Nasdaq listed company. Dr. Baracchini holds a B.S. inMicrobiology 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 SVP, Head Regulatory, MedDoc, R&D Quality at Lundbeck since October 2019. Prior to that, Dr. Rupalla served as 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 2015at Bristol-Myers Squibb. Ms. 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, 2020.

Name	Salary ($)	Bonus ($)[1]	All Other Compensation ($)[2]	Total ($)[3]
Duncan Peyton	129,254	-	2,538	131,792
Alexander Stevenson	129,254	-	2,517	131,771
John Beck(4)	-	-	-	-
Richard Avison	105,873	-	5,615	111,488

(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 in March 2021.

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. He is entitled to a base salary of $129,254 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. He is entitled to a base salary of $129,254 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 is currently engaged as our Chief Financial Officer under a service agreement entered into on March 1, 2021. He is entitled to a base salary of $330,000 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 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 Richard Avison

Richard Avison is currently engaged as Group Finance Director under a service agreement entered into on November 1, 2017 and amended and restated on August 29, 2019. He is entitled to a base salary of $92,850 per annum and is entitled to participate in our group personal pension scheme. In addition to the base salary, Mr. Avison is entitled to a participate in a private healthcare scheme and in our bonus scheme, in our sole and absolute discretion and to receive taxable travel expenses on a "tax free" basis.

The agreement may be terminated by either party on three months' written notice or immediately by us in the event of default, which includes, but is not limited to circumstances in which Mr. Avison is negligent, convicted of any criminal offence, declared bankrupt, found guilty of fraud, or conducted 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. Avison. The agreement includes certain restrictive covenants and, upon termination, Mr. Avison 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 2020 to the current non-employee directors, all of which was in the form of annual fees:

Name	Base Salary ($ in thousands)
Prof. Axel Glasmacher	64.6
Dr. Edgardo (Ed) Barachini	64.6
Dr. Alexander (Sandy) Macrae	64.6
Dr. Katrin Rupalla(1)	19.1
Paul Maier(2)	—

(1) Dr. Rupalla was appointed as a member of our board of directors on September 23, 2020.

(2) Mr. Maier was appointed as a member of our board of directors March 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 $64,627 per annum for service on our board of directors. 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, 2020: [9]

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)	—	—	—	—	—	—	
Richard Avison	—	51,316(4)	$ 0.003	—	—	July 5, 2019	July 4, 2029
Non-Executive Directors							
Prof. Axel Glasmacher	—	—	—	—	—	—	
Dr. Edgardo (Ed) Barachini	—	—	—	—	—	—	
Dr. Alexander (Sandy) Macrae	—	—	—	—	—	—	
Dr. Katrin Rupalla(2)	—	—	—	—	—	—	
Paul Maier(3)	—	—	—	—	—	—	

(1) Mr. Beck was appointed as Chief Financial Officer on March 1, 2021.

(2) Dr. Rupalla was appointed as a member of our board of directors on September 23, 2020.

(3) Mr. Maier was appointed as a member of our board of directors March 1, 2021

(4) Excludes a further 27,631 options which are expected to vest but did not meet the performance conditions. At December 31, 2020 no remuneration committee judgment had been passed and so they have been treated as lapsed in the Financial statements.

Equity Incentive Arrangements

We operate the 2015 Long Term Incentive Plan (the "LTIP"), which is the primary mechanism for attracting and retaining selected key employees through the grant of stock options. All of our employees are eligible to participate in the LTIP and receive stock options, although participation is normally limited to senior managers and employees. Although our directors are eligible to participate in the LTIP and receive stock options, they have not done so.

The LTIP is 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 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.

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, which is ordinarily an amount equal to the aggregate nominal value of the stock that may be acquired on exercise.

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. 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 LTIP are non-transferrable (except, on death, to the option holder's personal representatives) and may not be assigned or charged.

No stock options may be granted under the 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. 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.

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 against any liability they incur by reason of their directorship. 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. Glasmacher, 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 Mr. Macrae, assists the board of directors in determining executive officer compensation. Prof. Glasmacher 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, 2020, we had 92 employees, including 40 employees in the United Kingdom and one employee in the United States. Of these employees, 78 were engaged in research and development activities and 14 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 26, 2021 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 178,984,386 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 26, 2021 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]	9,522,593	5.7%
Alexander Stevenson[3]	9,366,295	5.6%
Axel Glasmacher[4]	30,000	*%
Richard Avison[5]	838	*%
Edgardo Baracchini	—	*%
Katrin Rupalla	—	*%
Sandy Macrae	—	*%
John Beck	—	*%
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) 8,359,835 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) 496,092 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. Does not include any shares issuable pursuant to Mr. Peyton's commitment to enter into a Subscription Agreement to purchase ordinary shares in connection with the PIPE.

(3) Consists of (i) 8,317,896 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) 381,733 shares issued to Mr. 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. Does not include any shares issuable pursuant to Dr. Stevenson's commitment to enter into a Subscription Agreement to purchase ordinary shares in connection with the PIPE.

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

(5) Consists of 838 shares held of record by Mr. Avison.

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 26, 2021 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 178,984,386 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 26, 2021 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 (%)**
Entities affiliated with Steven Olivera[2]	26,572,916	14.4%
Merck & Co.[3]	12,145,523	6.6%
Duncan Peyton[4]	9,522,593	5.7%
Alexander Stevenson[5]	9,366,295	5.6%

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

(2) Consists of (i) 10,000,000 shares of record and 5,000,000 warrants issued on March 9, 2020 exercisable for £1.00 per share at any time for 5 years after issuance held by South Ocean Capital Management LLC, (ii) 7,114,986 shares of record held by Nemean Asset Management LLC, (iii) 850,000 shares of record and 383,050 warrants issued on March 9, 2020 exercisable for £1.00 per share at any time for 5 years after issuance held by Steven Oliveira, (iv) 612,880 shares of record and 306,440 warrants issued on March 9, 2020 exercisable for £1.00 per share at any time for 5 years after issuance held by South Ocean Capital LLC and (v) 2,305,560 shares issued to Nemean Asset Management LLC 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. The address for these entities is c/o 225 Via Palacio, Palm Beach Gardens, Florida, 33418, United States of America.

(3) 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.

(4) Consists of (i) 8,359,835 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) 496,092 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. Does not include any shares issuable pursuant to Mr. Peyton's commitment to enter into a Subscription Agreement to purchase ordinary shares in connection with the PIPE.

(5) Consists of (i) 8,317,896 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) 381,733 shares issued to Mr. 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. Does not include any shares issuable pursuant to Dr. Stevenson's commitment to enter into a Subscription Agreement to purchase ordinary shares in connection with the PIPE.

As of March 26, 2021, approximately 92% of our issued share capital was held in the U.K. (86% including warrants) and approximately 6% of our share capital was held in the United States (11% including warrants) with the remainder being held elsewhere.

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 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 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 $153 thousand and $51 thousand for the years ended December 31, 2020 and 2019, respectively. We charged Biomar $41 thousand and $35 thousand for services as of December 31, 2020 and 2019, respectively. As of December 31, 2020 and 2019, $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 common stock 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 common stock. 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 Indemnification."

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

On March 22, 2021, we consummated the Merger and applied for admission of 31,048,192 ordinary shares. In connection with the Merger, we have also issued new warrants convertible into ordinary shares (the "**New Warrants**") comprising 4,320,000 outstanding warrants that were previously issued by Longevity to holders of Longevity Shares at the time of the Longevity IPO and which will be converted into warrants to purchase up to 16,268,040 Ordinary Shares, payable in ADSs, warrants to be issued to the Backstop Investors to acquire up to 7,530,000 Ordinary Shares following Completion in connection with the Backstop Arrangements, and an option to acquire up to 2,892,096 Ordinary Shares to Cantor Fitzgerald, in its capacity as underwriter to Longevity at the time of the Longevity IPO.

On March 23, 2021, we issued 16,367,332 ordinary shares in connection with the private placement to raise approximately $25.03 million (£18.01 million). In connection with the private placement, certain directors have announced their intention to subscribe for, in aggregate, $2.0 million (£1.44 million) of new ordinary shares at the at a share price of £1.10 ($1.53) on release of the company's results for the year.

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 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 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 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;

- 6 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 defence 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 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.

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 or ($1.53) per share for an aggregate investment amount equal to £18.0 million ($25.0 million) (the "**PIPE Investment**").

The Subscription Agreements for the PIPE Investors provide for certain registration rights. In particular, we are 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 are 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.

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 U.S. Internal Revenue Code of 1986, as amended (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 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 2021 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. Holder's 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 2021 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, 2020, we had cash, cash equivalents and short-term deposits of $12.0 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, 2020, 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.

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, 2020.

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, 2020. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of December 31, 2020, 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.

B. Management's Annual Report on Internal Control over Financial Reporting

Not applicable.

C. Attestation Report of the Registered Public Accounting Firm

Not applicable.

D. Changes in Internal Control Over Financial Reporting

None.

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 two years ended December 31, 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 and 2020:

	Year Ended December 31,	
	2019(1)	2020
	(in thousands of dollars)	
Audit fees(2)	$ 375	$ 170
Audit related fees(3)	205	-
Other fees	5	-
Audit and other fees of affiliated entities(4)	$ 73	$ 80
Total fees	$ 658	$ 250

(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		20-F	04/02/21
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#	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
4.5	Lease Agreement between University Court of the University of Aberdeen and 4D Pharma Research Limited dated August 1, 2013		F-4/A	01/27/21
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
4.10+	Service Agreement between Richard Avison and 4D pharma plc, dated November 1, 2017		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+	4D pharma plc 2015 Long Term Incentive Plan and related forms		F-4/A	01/27/21
4.15+	Form of lock-up agreement by and among 4D pharma plc and certain of 4D pharma's shareholders		F-4/A	01/08/21
8.1	Subsidiaries of 4D pharma plc		20-F	04/02/21
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	XBRL Instance Document.	X		
101.SCH	XBRL Taxonomy Extension Schema.	X		
101.CAL	XBRL Taxonomy Extension Schema Calculation Linkbase.	X		
101.DEF	XBRL Taxonomy Extension Schema Definition Linkbase.	X		
101.LAB	XBRL Taxonomy Extension Schema Label Linkbase.	X		
101.PRE	XBRL Taxonomy Extension Schema Presentation Linkbase.	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.

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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, 2020 and 2019, 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, 2020, 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, 2020 and 2019, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2020, in conformity with accounting principles generally accepted in the United States of America.

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, Massachusetts
April 1, 2021

4D PHARMA PLC
CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share amounts)

	December 31,	
	2020	**2019**
ASSETS		
Current assets:		
Cash and cash equivalents	$ 11,990	$ 5,031
Research and development tax credits receivable	4,799	7,049
Prepayments and other current assets	4,055	2,705
Total current assets	20,844	14,785
Property and equipment, net	5,082	5,596
Right-of-use assets (operating leases)	1,129	1,251
Intangible assets, net	6,303	6,296
Goodwill	13,489	12,651
Deferred merger costs	2,010	-
Research and development tax credits receivable	242	247
Total assets	$ 49,099	$ 40,826
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 4,540	$ 1,641
Accrued expenses and other current liabilities	2,557	4,235
Current portion of operating lease liabilities	94	75
Deferred revenues, current	1,318	538
Total current liabilities	8,509	6,489
Long term operating lease liabilities, net	1,092	1,229
Deferred revenues, net	306	1,720
Deferred tax	18	31
Other liabilities	203	170
Total liabilities	10,128	9,639
Commitments and Contingencies (Note 7)		
Stockholders' equity:		
Common Stock, $0.003 par value, 167,991,442 authorized; 131,467,935 and 65,493,842 shares outstanding at December 31, 2020 and 2019, respectively	479	266
Additional paid in capital	210,876	174,376
Accumulated other comprehensive loss	(24,149)	(25,715)
Accumulated deficit	(148,235)	(117,740)
Total stockholders' equity	$ 38,971	$ 31,187
Total liabilities and stockholders' equity	$ 49,099	$ 40,826

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,		
	2020	**2019**	**2018**
Revenues	$ 690	$ 269	$ -
Operating expenses:			
Research and development	23,384	29,193	27,830
General and administrative expenses	13,015	10,380	11,294
Foreign currency losses (gains)	(699)	957	(234)
Total operating expenses	35,700	40,530	38,890
Loss from operations	(35,010)	(40,261)	(38,890)
Other income, net:			
Interest income	6	78	379
Interest expense	-	-	(3)
Other income	4,496	6,883	6,378
Change in fair value of contingent consideration payable	-	2,967	(465)
Total other income, net	4,502	9,928	6,289
Net loss before income tax benefit	(30,508)	(30,333)	(32,601)
Income tax benefit	13	-	-
Net loss	(30,495)	(30,333)	(32,601)
Other comprehensive income			
Foreign currency translation adjustment	1,566	1,113	(3,995)
Comprehensive loss	$ (28,929)	$ (29,220)	$ (36,596)
Net loss per common share, basic and diluted	$ (0.27)	$ (0.46)	$ (0.50)
Weighted-average number of common shares used in computing basic and diluted net loss per common share	114,149,743	65,493,842	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 Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance, December 31, 2017	65,493,842	$ 266	$ 173,673	$ (22,833)	$ (54,086)	$ 96,300
Other comprehensive income	-	-	-	(3,995)	-	(3,995)
Net loss	-	-	-	-	(32,601)	(32,601)
Share-based compensation	-	-	363	-	-	363
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	32,801	-	-	33,014
Issuance of warrants	-	-	3,270	-	-	3,270
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

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,		
	2020	**2019**	**2018**
Cash Flows from Operating Activities:			
Net loss	$ (30,495)	$ (30,333)	$ (32,601)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	1,572	1,644	1,614
Stock based compensation	331	340	363
Change in fair value of contingent consideration	-	(2,967)	465
Other non-cash expenses	13	74	1
Changes in assets and liabilities:			
Prepayments and other current assets	(1,168)	168	2,735
Research and development tax credits receivable	2,422	(939)	(1,678)
Accounts payable	2,677	(903)	163
Deferred revenues	(689)	2,197	-
Operating lease obligations	(185)	(148)	-
Other liabilities and accrued expenses	(1,748)	2,184	(1,220)
Net cash used in operating activities	(27,270)	(28,683)	(30,158)
Cash Flows from Investing Activities:			
Purchase of software	(19)	(73)	(5)
Purchase of property and equipment	(211)	(681)	(721)
Acquisition of subsidiary net of cash acquired	-	-	(887)
Proceeds on disposal of assets	-	55	-
Maturities of short-term investments	-	12,982	37,564
Net cash (used in) provided by investing activities	(230)	12,283	35,951
Cash Flows from Financing Activities:			
Net proceeds from issuance of common stock	33,014	-	-
Issuance of warrants	3,270	-	-
Warrant exercises	98	-	-
Deferred merger costs	(1,901)	-	-
Lease liability payments	(14)	(14)	(13)
Net cash provided by (used in) financing activities	34,467	(14)	(13)
Effect of exchange rate changes on cash and cash equivalents	(8)	1,000	(1,386)
Change in cash and cash equivalents	6,959	(15,414)	4,394
Cash and cash equivalents at beginning of year	5,031	20,445	16,051
Cash and cash equivalents at end of year	$ 11,990	$ 5,031	$ 20,445
Supplemental disclosures of non-cash investing and financing activities			
Cash paid for interest	$ 224	$ 230	$ 1
Lease liabilities from obtaining right-of-use assets	$ -	$ 1,446	$ -

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").

Merger Agreement

As discussed further in Note 14, on March 22, 2021 the Company completed a merger with Longevity Acquisition Corporation (NASDAQ: LOAC) a publicly-traded special purpose acquisition company ("SPAC"). Shareholders of LOAC received American Depositary Shares ("ADSs") of the Company, and LOAC became a wholly-owned subsidiary of the Company.

Transaction Details

At closing, LOAC merged with and into Dolphin Merger Sub 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 $11.6 million at the time of the merger after paying all of its debtors.

Immediately following the consummation of the merger, the shareholders of LOAC collectively own approximately 13.1% of outstanding ordinary shares of the combined entity based on the issued share capital of 4D Pharma and Longevity prior to consummation of the merger.

Concurrently with the completion of the merger, on March 22, 2021, the Company raised £18.0 million ($25.0 million) through the issuance of 16,367,332 common shares at a share price of £1.10 or ($1.53) per share.

Liquidity and capital resources

Since inception, the Company has incurred net losses and negative cash flows from operations. During the year ended December 31, 2020, the Company incurred a net loss of $30.5 million and used $27.3 million of cash in operations. As of December 31, 2020, the Company had an accumulated deficit of $148.2 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, 2020, the Company's cash and cash equivalents were $12.0 million. The Company expects that its existing cash and cash equivalents, including the cash received in the merger with LOAC, the sale of its common shares and the receipt from an overdraft facility, all in March 2021 (See Note 14 for further information), will be sufficient to satisfy its working capital needs, capital asset purchases, outstanding commitments and other liquidity requirements associated with our existing operations through the next 12 months following 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 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. 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) these 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 estimated fair value of the contingent consideration payable; 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, 2020 and 2019, the Company's cash, cash equivalents and short-term investments 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, 2020 from a collaboration partner. See Note 9, Revenues for additional information.

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. The Company had two suppliers that accounted for 27% of purchases for the period ended December 31, 2019. The accounts payable balance at December 31, 2019 contained two balances which constituted 21% of the total balance outstanding at that date.

(g) Deferred Merger 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.

(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 and cash deposits 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. We consider contingent considerations to be Level 3. We determine the fair value of Level 3 assets and liabilities utilizing various inputs, including contract terms. At December 31, 2020, the Company has no contingent consideration payable. At December 31, 2019, the contingent consideration payable on a business combination was measured at fair value. The method used to value this liability is a level 3 discounted expected cash flow model. The principal inputs to the model are:

- the probability of the liability occurring (2019 – 0%)
- the rate used to discount the estimated undiscounted liability (2019 – 17.5%).

The fair value is most sensitive to the probability of the liability occurring, which in turn depends on the achievement of milestones as described in Note 10. The greater the probability of the milestones being achieved, the greater the fair value of the contingent liability.

(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, 2020: UK $9,383, Spain $10,615 and Ireland $6,004. Long-lived assets by geography are as follows as of December 31, 2019: UK $9,733, Spain $10,246 and Ireland $5,815.

(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

On January 1, 2019, the Company adopted ASC 842 using a modified retrospective approach. In addition, we elected the package of practical expedients available for existing contracts, which allowed us to carry forward our historical assessments of lease identification, lease classification, and initial direct costs. As a result of adopting ASC 842, we recognized right-of-use assets and lease liabilities of approximately $1.5 million.

The Company enters into operating lease arrangements for real estate assets related to office space and finance lease arrangements for vehicles and other equipment. 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, 2020 and 2019 was $203 and $165, 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, 2020, 2019 and 2018 accretion expenses were $27, $22 and Nil, 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. Early application is permitted.

Patents

Acquired patents are initially recorded at cost (or if initially recognized 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 recognized 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 10.

(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.

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.

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 .

(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, 2020, 2019 and 2018, the Company excluded the outstanding securities summarized below, 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,		
	2020	2019	2018
Common stock warrants	21,924,307	-	-
Common stock options	485,056	925,589	1,047,332
Total	22,409,363	925,589	1,047,332

(t) Recently adopted accounting pronouncements

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework – Changes to the Disclosure Requirements for Fair Value Measurement*, which adds and modifies certain disclosure requirements for fair value measurements. Under the new guidance, entities will no longer be required to disclose the amount and reasons for transfers between Level 1 and Level 2 of the fair value hierarchy, or valuation processes for Level 3 fair value measurements. However, public business entities will be required to disclose the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements, and related changes in unrealized gains and losses included in other comprehensive income. ASU 2018-13 is effective for public and non-public business entities for fiscal years beginning after December 15, 2019, including interim periods. The adoption of ASU 2018-13 did not have a material impact on the Company's consolidated financial statements.

(u) Recent issued accounting pronouncements not yet adopted

Accounting Standards Update (ASU 2016-13), Financial Instruments – Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments – The amendments included in ASU 2016-13 require the measurement of all expected credit losses for financial assets held at the reporting date based on historical experience, current conditions, and reasonable and supportable forecasts. Financial institutions and other organizations will now use forward-looking information to better evaluate their credit loss estimates. Many of the loss estimation techniques applied today will still be permitted, although the inputs to those techniques will change to reflect the full amount of expected credit losses. In addition, the ASU amends the accounting for credit losses on available-for-sale debt securities and purchased financial assets with credit deterioration. ASU 2016-13 was originally effective for public companies for fiscal years beginning after December 15, 2019. In November of 2019, the FASB issued Accounting Standards Update No. 2019-10, which delayed the implementation of ASU 2016-13 to fiscal years beginning after December 15, 2022 for smaller reporting companies. The Company is currently evaluating the impact that the adoption of this guidance will have on its consolidated financial statements.

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740)*: *Simplifying the Accounting for Income Taxes*. The Board issued this update as part of its Simplification Initiative to improve areas of GAAP and reduce cost and complexity while maintaining usefulness of the financial statements. The main provisions remove certain exceptions, including the exception to the general methodology for calculating income taxes in an interim period when a year-to-date loss exceeds the anticipated loss for the year. In addition, the amendments simplify income tax accounting in the areas such as income-based franchise taxes, eliminating the requirements to allocate consolidated current and deferred tax expense in certain instances and a requirement that an entity reflects the effect of enacted changes in tax laws or rates in the annual effective tax rate computation in the interim period that includes the enactment date. ASU 2019-12 is effective for non-public companies beginning after December 15, 2021 and interim periods within fiscal years beginning after December 15, 2022. Because the Company's deferred tax assets and liabilities are fully reserved, it does not expect a material impact from the adoption of this standard.

(v) 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 14 for further information on subsequent events.

NOTE 3 – PREPAYMENTS AND OTHER CURRENT ASSETS

Prepayments and other current assets consisted of the following:

	December 31,	
	2020	**2019**
Prepayments	$ 2,394	$ 1,465
VAT receivables	1,263	980
Other assets – goods to be consumed in R&D activities	398	260
	$ 4,055	$ 2,705

NOTE 4 – PROPERTY AND EQUIPMENT

Property and equipment, net, consisted of the following:

	December 31,	
	2020	2019
Cost		
Property and machinery	$ 8,728	$ 7,852
Fixtures, fittings and office equipment	294	282
Land and buildings	1,674	1,549
Total cost	10,696	9,683
Accumulated depreciation	5,614	4,087
Total property and equipment, net	$ 5,082	$ 5,596

Depreciation and related amortization expense was $1,111, $1,368, and $1,216 for the years ended December 31, 2020, 2019 and 2018 respectively.

NOTE 5 – GOODWILL AND INTANGIBLE ASSETS

Goodwill:

Balance at December 31, 2018	$ 12,625
Translation differences	26
Balance at December 31, 2019	12,651
Translation differences	838
Balance at December 31, 2020	$ 13,489

Intangible assets, net, consisted of the following:

	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

	December 31, 2019			
	Software	Patents	Intellectual Property	Total
Gross amount beginning of period	$ 428	$ 1,377	$ 5,740	$ 7,545
Additions	73	-	-	73
Translation differences	4	41	170	215
Gross amount end of period	505	1,418	5,910	7,833
Disposals	(140)			(140)
Accumulated amortization	(232)	(1,165)	-	(1,397)
Net Book value	$ 133	$ 253	$ 5,910	$ 6,296

Estimated amortization expense for each of the next five years is:

Year		
2021	$	119
2022		22
2023		2
2024		1
2025		1
Total	$	145

Amortization expense was $262, $276 and $398 for the years ended December 31, 2020, 2019 and 2018, 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 commercialize LBPs.

NOTE 6 – Leases

Operating Lease obligations

Effective January 1, 2019, the Company adopted new guidance for the accounting and reporting of leases. The Company has two real estate leases classified as operating leases (one on Spain and one in the UK). No additional leases were entered into during 2019.

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 $165 and $136 at December 31, 2020 and 2019, 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 $38 and $29 at December 31, 2020 and 2019, 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 costs were $311 and $307 for the years ended December 31, 2020 and 2019, respectively. Cash paid for amounts included in the measurement of operating lease liabilities was $301 and $262 for the years ended December 31, 2020 and 2019, respectively. Short term lease costs were $174 and $199 for the years ended December 31, 2020 and 2019, respectively. Cash paid for short term leases was $155 and $169 for the years ended December 31, 2020 and 2019, respectively.

	December 31, 2020	December 31, 2019
Assets		
Right of use assets	$ 1,129	$ 1,251
Liabilities		
Current portion of operating lease liabilities	94	75
Long term operating lease liabilities, net	1,092	1,229
	$ 1,186	$ 1,304
Weighted-average remaining lease term (years)	6	7
Weighted-average discount rate	13.6%	13.6%

Maturities of operating leases liabilities are as follows:

	December 31, 2020
2021	$ 318
2022	320
2023	336
2024	339
2025	340
Thereafter	262
Total lease payments	1,915
Less: Imputed interest	(729)
	$ 1,186

NOTE 7 – ACCRUED EXPENSES AND OTHER CURRENT LIABLITIES

Accrued expenses and other current liabilities consisted of the following:

	December 31,	
	2020	2019
Clinical trials expenses	$ 231	$ 2,561
Patents and other research expenses	302	428
Payroll expenses	149	122
Building and office expenses	337	274
Professional consultants expenses	839	156
Tax expenses	305	334
Deferred grant income	82	52
Short-term finance lease	5	14
Other expenses	307	294
	$ 2,557	$ 4,235

NOTE 8 – COMMITMENTS AND CONTINGENCIES

We enter 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 the costs are material, 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 organizations, 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 9 – 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 ($1.37) 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.

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 ($1.37) 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 $3,270 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.

The following table summarizes the common stock warrant activity for the year ended December 31, 2020:

Balance at January 1, 2020	-
Issuances	22,000,000
Exercises	(75,693)
Balance at December 31, 2020	21,924,307

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.

The reconciliation of movement in share options in the years ended December 31, 2020 and 2019 is as follows:

	Number of Options	Weighted Average Exercise Price	Non-Vested Options	Weighted Average Grant date Fair Value
Outstanding at December 31, 2018	1,047,332	$ 0.0033	1,017,332	$ 2.88
Granted	538,596	0.0033	538,596	1.16
Vested and exercised		0.0033	(9,686)	11.18
Expired/cancelled	(660,340)	0.0033	(660,340)	3.01
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
Options exercisable	234,635	$ 0.0033		
Options vested	234,635	$ 0.0033		
Options expected to vest	73,715	$ 0.0033		

The weighted average remaining contractual life of options outstanding, options vested and options expected to vest at December 31, 2020 was 8.24 years, 7.04 years and 8.17 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, 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. The share price for December 31, 2019, was £1.00 ($1.3114) and the intrinsic value for options outstanding, exercisable and expected to vest was $1,211, $13 and $96, 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 remuneration 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 non-employee consultant to the Company. For the employee, the Company's remuneration 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.

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 a 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 13, 2020	July 22, 2020	December 31, 2019	December 31 2018
Risk-free interest rate	0.09%	0.08%	0.57%	0.72%
Expected volatility	35.74%	40.11%	69.62%	54.95%
Expected dividend yield	0.00%	0.00%	0.00%	0.00%
Expected term (in years)	1.56 year	0.77 years	3 years	3 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.

On July 5, 2019, the Company issued options to purchase 538,596 shares of common stock to its management and key staff at an exercise price of $0.0033. The options vest in three years based on based on market parameters and non-market performance measures and expire ten years from the date of grant. The aggregate fair value of the options granted was $626.

Stock-based compensation expense for the years ended December 31, 2020, 2019 and 2018 was $331, $340 and $363, respectively. As of December 31, 2020, total unrecognized stock-based compensation expense relating to unvested stock options was $344. This amount is expected to be recognized over a weighted-average period of 1.32 years.

NOTE 10 – 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, 2020, 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, 2020, 2019 and 2018, the Company has recognized $690, $269 and Nil respectively, in collaboration revenues. Associated development costs and labor effort of $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, 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, 2020, the Company has $1,318 as current deferred revenues and $306 as long-term deferred revenues.

NOTE 11 –CONTINGENT CONSIDERATION

Contingent consideration relates to the amounts due on the remaining milestones which form part of the original contingent acquisition costs for the entire issued share capital in Tucana Health Limited (now 4D Pharma Cork Limited) on February 10, 2016.

The contingent consideration is based on milestones in the development of the MicroDx diagnostic platform which has been designed to diagnose, stratify and monitor the treatment of patients based on their gut microbiome, the bacteria which colonize the human gastrointestinal tract.

The Company has provided for the contingent consideration on the achievement of three time-based milestones for the validation of the MicroDx platform by 4D Pharma Cork Ltd.

The contingent liability was calculated upon the acquisition of 4D Pharma Cork Limited and was based on the discounted probability of the liability at that time. The probability of future milestones is re-assessed as the timepoints for the milestones are reached; these milestones are:

1) *Technical validation of a diagnostic platform for IBS dysbiosis*

   The milestone was achieved by August 23, 2017 and triggered the issue of 635,692 shares for an aggregate market value of €2.6 million ($3.06 million) (at £3.7575 ($4.8095) per 4D pharma plc share, being the average mid-market price of a 4D share for the five business days immediately preceding the date of allotment).

2) *Clinical validation of the optimal IBS dysbiosis diagnostic platform based on more than 1,000 patients in a multicenter trial*

Whilst there are no adverse indicators relating to the clinical validation of the platform at December 31, 2019, the time-based criteria for the completion of the milestone, which required completion of this phase by August 23, 2019, was not achieved and the fair value of the contingent consideration has been adjusted by $2,094 to bring the balance at December 31, 2019 to $0.

3) *Regulatory approval of a diagnostic platform for IBS dysbiosis*

The third milestone is also time based and linked to regulatory approval being achieved by August 23, 2020. The fair value of the contingent consideration was adjusted as of December 31, 2019 to $0, releasing $873 of the contingent consideration. There was no contingent consideration for this milestone as of December 31, 2020. Based on the patient recruitment at milestone two it was anticipated that regulatory approval would not be achieved in 2021 meaning that achieving milestone three by the required date didn't occur; as a result the fair value was reduced to $0 as for year ended December 31, 2019.

Recurring Level 3 Activity and Reconciliation

The table below provides a reconciliation of the beginning and ending balances for the liability measured at fair value using significant unobservable inputs (Level 3).

	Current Portion	Long-term Portion	Total Contingent Consideration
Balance, January 1, 2019	$ 2,090	$ 871	$ 2,961
Change in fair value	(2,094)	(873)	(2,967)
Translation differences	4	2	6
Balance, December 31, 2019	$ -	$ -	$ -

NOTE 12 – 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 approximately 30%. At December 31, 2019, 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 19%.

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, 2020 and 2019.

For the years ended December 31, 2020 and 2019 loss before income tax benefit is as follows:

	December 31,		
	2020	**2019**	**2018**
Loss before income taxes arising in UK	$ 29,938	$ 27,751	$ 30,364
Loss before income taxes arising in Ireland	918	1,539	1,693
(Profit)/loss before income taxes arising in Spain	(340)	1,043	544
(Profit) before income taxes arising in United States	(8)	-	-
Total loss before income tax	$ 30,508	$ 30,333	$ 32,601

The provision for income taxes includes income taxes currently payable and deferred taxes resulting from net operating loss carry forwards 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:

	For the Years Ended December 31,					
	2020		**2019**		**2018**	
Loss before income taxes	$ (30,508)	%	$ (30,333)	%	$ (32,601)	%
Expected tax benefit	(5,797)	(19.0)%	(5,763)	(19.0)%	(6,087)	(18.7)%
Costs included in R&D tax credit	2,255	7.4%	4,070	13.4%	-	0.0%
Non-taxable income	(846)	(2.8)%	(1,299)	(4.3)%	-	0.0%
Foreign tax differential	(248)	(0.8)%	69	0.2%	4	0.0%
Change in valuation allowance	4,504	14.8%	3,111	10.3%	6,057	18.6%
Other	119	0.4%	(188)	(0.6)%	26	(0.1)%
Income tax benefit	$ (13)	0%	$ -	0%	$ -	0%

	Years Ended December 31,		
	2020	2019	2018
Current tax expense	$ 2	$ -	$ -
Deferred tax benefit	(15)	-	-
Income tax benefit	$ (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,	
	2020	**2019**
Deferred tax assets/(liabilities):		
Net operating tax loss carry forwards	$ 17,025	$ 10,847
Property and equipment, net	(179)	(247)
Right of use assets	(90)	(99)
Intangible assets	(1,166)	(1,006)
Stock-based compensation expense	319	218
Operating lease liabilities	103	102
Valuation allowance	(16,030)	(9,846)
Net deferred tax liability	$ (18)	$ (31)

For each of the years ended December 31, 2020 and 2019 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, 2020, the Company has net operating losses (NOLs) of approximately $83,852, $1,007 and $6,124 in the UK, Spain and Ireland respectively. NOLs may be carried forward indefinitely.

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,	
	2020	**2019**
UK research and development tax credits	$ 4,315	$ 6,565
Irish research and development tax credits	453	373
Translation differences	273	358
Total	5,041	7,296
Less: current portion	(4,799)	(7,049)
Research and development tax credits receivable, net	$ 242	$ 247

For the years ended December 31, 2020 and 2019, the Company has recorded other income of $4,457 and $6,840, respectively for the research and development tax credits.

NOTE 13 – 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 $153, $51 and $24 for the years ended December 31, 2020, 2019 and 2018, respectively. The Company charged Biomar $41, $35 and $44 for services as of December 31, 2020, 2019 and 2018, respectively. As of December 31, 2020 and 2019, $4 and $54, respectively, was due from Biomar for these services.

MSD purchased 7,661,000 shares of the Company's common stock in February 2020 and currently holds 5.8% 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 tumors who progressed on prior PD-1 inhibitor therapy. Under the terms of the agreement MSD will provide KEYTRUDA free of charge to the trial.

NOTE 14 – SUBSEQUENT EVENTS

Merger with Longevity Acquisition Corporation

On March 18, 2021 (the "Closing Date"), the transaction (the "Closing") contemplated by the previously announced Merger Agreement and BVI Plan of Merger (the "Merger"), dated as of October 21, 2020 (as amended, the "Merger Agreement"), by and among Longevity Acquisition Company ("Longevity"), the Company, and Dolphin Merger Sub Limited, a British Virgin Islands company and a wholly-owned subsidiary of the Company (the "Merger Sub"), and the other parties named therein, was approved by the shareholders' of both Company and 4D Pharma and the transaction was completed on March 22, 2021. The Merger Sub is the surviving entity. As a result of the Merger, each Longevity share issued and outstanding immediately prior to the completion of the Merger was converted into the right to receive 7.5315 common shares of the Company payable in 4D Pharma American Depository Shares ("ADS") at a rate equal to one 4D Pharma ADS for every eight shares of the Company. The Company issued no fractional shares or 4D Pharma ADSs in the Merger. Each warrant to purchase Longevity Shares and right to receive Longevity Shares that was outstanding immediately prior to the Closing was assumed by the Company and automatically converted into a warrant to purchase the Company's common shares and a right to receive the Company's common shares, payable in 4D Pharma ADSs, respectively.

In connection with the Closing, certain holders of Longevity common shares exercised their right to redeem those shares in accordance with Longevity's organizational documents, as amended, for cash at a price of approximately $11 per common share, for an aggregate of approximately $3,000. Accordingly, pursuant to a Backstop Agreement previously entered into between Longevity, the Company, Longevity's sponsor (Whale Capital Management the "Sponsor") and certain current Company shareholders and new investors (such current Company shareholders and new investors, collectively, the "Buyers"). The Buyers provided financial backing of approximately $14.7 million to Longevity immediately prior to the Closing, to cover against redemptions by Longevity Shareholders. In view of the *de minimis* redemptions, the backstop was not called upon. The consideration paid to the Buyers pursuant to the Backstop Agreements consisted of 700,000 newly issued Ordinary Longevity Shares, the transfer by Longevity's sponsor of 200,000 outstanding Longevity Shares, the grant of an option to acquire up to an additional 400,000 outstanding Longevity Shares from the Sponsor , and the Company's commitment to grant to the Buyers, following the closing of the Merger, warrants to acquire up to 1,000,000 Longevity shares (equivalent to 7,530,000 common shares of the Company) for 0.25 pence ($0.35) per common share. In connection with the Closing, and pursuant to the Merger Agreement, (a) an aggregate of 28,298,192 common shares of the Company were issued to Longevity shareholders and the Buyers, (b) the Company assumed Longevity warrants to acquire and rights to receive an aggregate of 16,268,040 common shares of the Company, and (c) 2,750,000 common shares of the Company were issued to a bank as an advisor fee.

At the Closing, the Company entered into a Lock-up Agreement with the Sponsor and certain shareholders of Company. Pursuant to the Lock-Up Agreement, each holder agreed that, subject to certain exceptions, during the period ending twelve months after the Closing, it will not (i) lend, offer, pledge, hypothecate, encumber, donate, assign, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares received as consideration in the Merger (the "Restricted Securities"), (ii) enter into any swap, short sale, hedge or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the Restricted Securities, or (iii) publicly disclose the intention to effect any transaction specified in clause (i) or (ii), or (iv) make any demand for or exercise any right with respect to the registration of any Longevity Shares.

Management of 4D Pharma has concluded the Merger is a recapitalization through an asset acquisition and not a business combination as Longevity does not meet the definition of a business pursuant to ASC 805. According to the guidance in ASC 805, the Company obtained control as: (i) it owns 100% of the issued and outstanding shares of Longevity; (ii) Longevity merged with and into a wholly-owned subsidiary of the Company, the separate existence of Longevity ceased, and the wholly-owned subsidiary of the Company will be the surviving company; and (iii) the Company's board of directors and officers are the initial board of directors and officers of the Company following the Closing. The Company was the accounting acquirer and issued equity in exchange for the net assets of Longevity with no goodwill or intangible assets recorded in the Merger. At Closing, Longevity had approximately $14.8 million of gross cash in hand, $11.6 million net of costs and payment of liabilities, which has been transferred to the Company.

NASDAQ Listing

On March 22, 2021, with the completion of the Longevity transaction, the Company completed its NASDAQ Global Market listing using ADSs under the ticker 'LBPS'. The Company's common shares can be converted at any time to ADSs at a ratio of eight common shares for one ADS. J.P Morgan Chase bank, N.A. is acting as depositary bank for the ADSs and the Company's common shares will continue to be admitted to trading on AIM under the ticker 'DDDD'.

Private Placement Financing

On March 17, 2021, the Company announced that it had entered into securities purchase agreements with certain US and UK institutional and accredited investors raised approximately £18.0 million ($25.0 million) in gross proceeds (£16.87 million ($23.5 million) net of fees) through the sale of 16,367,332 common shares at a price of £1.10 ($1.53) per share including a late subscription from Merck Sharp & Dohme.

Overdraft Facility

In March 2021, the Company's subsidiary in Spain, received a €1.0 million (£0.86 million or $1.2 million) overdraft facility supported by the Spanish government as part of its COVID-19 relief package. The overdraft is unsecured, incurs annual interest at a rate of 2.35% and is repayable in full at the end of three years.

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

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: April 30, 2021

/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 Beck, 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: April 30, 2021

/s/ John Beck

Name: John Beck
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, 2020 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: April 30, 2021

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, 2020 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, John Beck, 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: April 30, 2021

By: */s/ John Beck*
Name: John Beck
Title: Chief Financial Officer