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

FORM 20-F

(mark one)

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

OR

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

For the fiscal year ended January 31, 2019

OR

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

For the transition period from _____ to_____

OR

☐ **SHELL COMPANY 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: 001-36866

Summit Therapeutics plc

(Exact name of Registrant as specified in its charter)

England and Wales
(Jurisdiction of incorporation or organization)
136a Eastern Avenue
Milton Park, Abingdon
Oxfordshire OX14 4SB
United Kingdom
(Address of principal executive offices)

Glyn Edwards, Chief Executive Officer
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(Name, Telephone, E-mail and/or Facsimile number and Address of Company Contact Person)

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

Title of each class	Name of each exchange on which registered
American Depositary Shares, each representing 5 Ordinary Shares, par value £0.01 per share	**The Nasdaq Stock Market LLC**

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.

160,389,881 ordinary shares, par value £0.01 per 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 ☒

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 ☒

Note—checking the box above will not relieve any registrant required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934 from their obligations under those Sections.

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

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

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

Large accelerated filer ☐ Accelerated filer ☒ Non-accelerated filer ☐

Emerging growth company ☒

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

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

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

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

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

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GENERAL INFORMATION

In this Annual Report on Form 20-F, references to "Summit," "we," "us," and "our" or to the "Group" or the "company" refer to Summit Therapeutics plc and its consolidated subsidiaries, except where context otherwise requires.

The trademarks, trade names and service marks appearing in this Annual Report on Form 20-F are the property of their respective owners.

PRESENTATION OF FINANCIAL AND OTHER DATA

The consolidated financial statement data as of January 31, 2019 and 2018 and for the years ended January 31, 2019, 2018 and 2017 have been derived from our consolidated financial statements, as presented at the end of this Annual Report, which have been prepared in accordance with International Financial Reporting Standards, or IFRS, as issued by the International Accounting Standards Board, or IASB, and as adopted by the European Union and audited in accordance with the standards of the Public Company Accounting Oversight Board (United States).

All references in this Annual Report to "$" are to U.S. dollars and all references to "£" are to pounds sterling. Solely for the convenience of the reader, unless otherwise indicated, all pounds sterling amounts as of and for the year ended January 31, 2019 have been translated into U.S. dollars at the rate at January 31, 2019, the last business day of our fiscal year ended January 31, 2019, of £1.00 to $1.3135. These translations should not be considered representations that any such amounts have been, could have been or could be converted into U.S. dollars at that or any other exchange rate as of that or any other date.

FORWARD-LOOKING STATEMENTS

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

- the timing and conduct of our clinical trials of ridinilazole (formerly SMT19969) for the treatment of patients with *Clostridium difficile* infection, including statements regarding the timing of initiation and completion of the clinical trials and the period during which the results of the clinical trials will become available;
- the timing of and our ability to obtain marketing approval of ridinilazole, and the ability of ridinilazole to meet existing or future regulatory standards;
- the timing and conduct of clinical trials for any other product candidates;
- the potential benefits of our acquisition of Discuva Limited, or Discuva, including the operations of the acquired bacterial genetics-based discovery and development platform, which we refer to as our Discuva Platform;
- our plans to conduct research and development and advance potential new mechanism antibiotic compounds identified and developed under our Discuva Platform;
- the cost-share arrangement under our license and collaboration agreement with Sarepta Therapeutics, Inc.;
- the potential benefits and future operation of our collaboration with the Biomedical Advanced Research and Development Authority, or BARDA;
- the potential benefits and future operation of our collaboration with the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator Program, or CARB-X;
- the potential benefits and future operation of our license and commercialization agreement with Eurofarma Laboratórios SA;
- our plans with respect to possible future collaborations and partnering arrangements;

- our plans to pursue research and development of other future product candidates;
- the potential advantages of ridinilazole and our other new mechanism antibiotics;
- the rate and degree of market acceptance and clinical utility of ridinilazole and our other new mechanism antibiotics;
- our estimates regarding the potential market opportunity for ridinilazole and our other new mechanism antibiotics;
- our sales, marketing and distribution capabilities and strategy;
- our ability to establish and maintain arrangements for manufacture of ridinilazole;
- our intellectual property position;
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- the impact of government laws and regulations; and
- our competitive position.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report, particularly in the "Risk Factors" section in this Annual Report, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this Annual Report and the documents that we have filed as exhibits to this Annual Report completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements.

PART I

Item 1: Identity of Directors, Senior Management and Advisers

Not applicable.

Item 2: Offer Statistics and Expected Timetable

Not applicable.

Item 3: Key Information

A. Selected Financial Data

The following table summarizes our consolidated financial data as of the dates and for the periods indicated. The consolidated financial statement data as of January 31, 2019 and 2018 and for the years ended January 31, 2019, 2018 and 2017 have been derived from our consolidated financial statements, as presented at the end of this Annual Report, which have been prepared in accordance with IFRS, as issued by the IASB, and audited in accordance with the standards of the Public Company Accounting Oversight Board (United States). The consolidated financial statement data as of January 31, 2017, 2016 and 2015 and for the years ended January 31, 2016 and 2015 have been derived from our consolidated financial statements, which are not presented herein, which have also been prepared in accordance with IFRS as issued by the IASB, and audited in accordance with the standards of the Public Company Accounting Oversight Board (United States).

Our consolidated financial statements are prepared and presented in pounds sterling, our presentation currency. Solely for the convenience of the reader, our consolidated financial statements as of and for the year ended January 31, 2019 have been translated into U.S. dollars at £1.00 to $1.3135 based on the foreign exchange rates published by the Federal Reserve Bank of New York for January 31, 2019. Such convenience translations should not be construed as a representation that the pound sterling amounts have been or could be converted into U.S. dollars at this or at any other rate of exchange, or at all.

Our historical results are not necessarily indicative of the results that may be expected in the future. The following selected consolidated financial data should be read in conjunction with our audited consolidated financial statements included at the end of this Annual Report and the related notes and Item 5, “Operating and Financial Review and Prospects” below.

Selected Consolidated Income Statement Data

	Year Ended January 31,					
	2019	2019	2018	2017	2016	2015
			(Adjusted*)			
	(in thousands, except per share data)					
Revenue	$ 56,496	£ 43,012	£ 12,360	£ 2,304	£ —	£ —
Other operating income	19,907	15,156	2,725	72	1,281	1,888
Operating profit / (loss)	3,503	2,667	(25,884)	(24,853)	(20,346)	(12,233)
Finance income	3,662	2,788	3,096	8	30	51
Finance cost	(557)	(424)	(1,164)	(862)	(2,879)	(499)
Income tax credit	3,278	2,496	3,762	4,336	3,058	1,297
Profit / (loss) for the period	9,886	7,527	(20,190)	(21,371)	(20,137)	(11,384)
Basic and diluted earnings / (loss) per ordinary share from continuing operations	$ 0.12	£ 0.09	(0.31)	(0.35)	(0.34)	(0.29)
Weighted average number of shares outstanding (in thousands)	85,702	85,702	65,434	61,549	59,102	39,599

Selected Consolidated Balance Sheet Data

	As of January 31,					
	2019	2019	2018	2017	2016	2015
			(Adjusted *)			
			(in thousands)			
Cash and cash equivalents	$ 35,278	£ 26,858	£ 20,102	£ 28,062	£ 16,304	£ 11,265
Working capital[(1)]	9,205	7,007	(6,978)	(5,621)	1,327	359
Total assets	78,504	59,767	53,962	37,587	25,057	19,396
Accumulated losses reserve	(99,947)	(76,092)	(93,957)	(73,767)	(52,396)	(32,259)
Total equity / (deficit)	$ 55,880	£ 42,542	£ (3,184)	£ (3,493)	£ 16,080	£ 12,962

(1) We define working capital as prepayments and other receivables (including current tax receivables) less current liabilities.

* See Note 3 - 'Changes to accounting policies - Adoption of IFRS 15 Revenue from contracts with customers' within the financial statements filed as part of this Annual Report.

B. Capitalization and Indebtedness

Not applicable.

C. Reasons for the Offer and Use of Proceeds

Not applicable.

D. Risk Factors

Our business has significant risks. You should consider carefully the risks described below, together with the other information contained in this Annual Report, including our financial statements and the related notes. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks Related to our Financial Position and Need for Additional Capital

We have incurred significant losses since our inception. We expect to incur losses for at least the next several years and may never generate profits from operations or maintain profitability.

Since inception, we have incurred significant operating losses. Our net profit was approximately £7.5 million for the year ended January 31, 2019, our net loss was approximately £20.2 million for the year ended January 31, 2018, and £21.4 million for the year ended January 31, 2017. As of January 31, 2019, we had an accumulated deficit of £76.1 million. The profit recorded for the year ended January 31, 2019, was due to the recognition of all remaining deferred revenue related to our license and collaboration agreement with Sarepta Therapeutics, Inc., or Sarepta, following our decision to discontinue the development of ezutromid in June 2018. This recognition of deferred revenues did not impact our cash flows. To date, we have financed our operations primarily through issuances of our ordinary shares and American Depositary Shares, or ADSs, payments to us under our license and collaboration agreement with Sarepta, a payment to us under our license and commercialization agreement with Eurofarma Laboratórios SA, or Eurofarma, and development funding and other assistance from government entities, philanthropic, non-government and not for profit organizations and patient advocacy groups for our product candidates. We have devoted substantially all of our efforts to research and development, including clinical trials. We have not completed development of any drugs. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. The net losses we incur may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially in connection with conducting clinical trials for our lead product candidate, ridinilazole (formerly SMT19969), for the treatment of patients with *Clostridium difficile* infection, or CDI, and seeking marketing approval for ridinilazole in the United States, as well as other geographies. In addition, if we obtain marketing approval of ridinilazole in the United States or other jurisdictions where we retain commercial rights, we expect to incur significant sales, marketing, distribution and outsourced manufacturing expenses, as well as ongoing research and development expenses.

In addition, our expenses will increase if and as we:

- continue the research and development of ridinilazole, as well as our preclinical program targeting infections caused by *Neisseria gonorrhoeae*;
- seek to identify and develop additional product candidates, including through our bacterial genetics-based discovery and development platform, which we refer to as our Discuva Platform, for discovering and developing new mechanism antibiotics, and specifically our discovery stage program against a group of bacteria that collectively are known as the ESKAPE pathogens;
- seek marketing approvals for any product candidates that successfully complete clinical development;
- ultimately establish a sales, marketing and distribution infrastructure in jurisdictions where we have retained commercialization rights and scale up external manufacturing capabilities to commercialize any product candidates for which we receive marketing approval;
- acquire or in-license other product candidates and technology;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, regulatory and scientific personnel;
- expand our physical presence; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts.

Our ability to generate profits from operations and remain profitable depends on our ability to successfully develop and commercialize drugs that generate significant revenue. Based on our current plans, we do not expect to generate significant product sales revenue unless and until we obtain marketing approval for, and commercialize, ridinilazole for the treatment of CDI or any other product candidates we develop. This will require us to be successful in a range of challenging activities, including:

- successfully initiating and completing clinical trials of ridinilazole for the treatment of CDI and any other product candidates we develop;
- obtaining approval to market ridinilazole for the treatment of CDI and any other product candidates we develop;
- protecting our rights to our intellectual property portfolio related to ridinilazole and any other product candidates we develop;
- contracting for the manufacture of clinical and commercial quantities of ridinilazole and any other product candidates we develop;
- negotiating and securing adequate reimbursement from third-party payors for ridinilazole and any other product candidates we develop; and
- establishing sales, marketing and distribution capabilities to effectively market and sell ridinilazole and any other product candidates we develop in the United States, as well as other geographies.

We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to generate profits from operations. Even if we do generate profits from operations, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to generate profits from operations and remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

Our operations to date have been limited to organizing and staffing our company, developing and securing our technology, raising capital and undertaking preclinical studies and clinical trials of our product candidates. We have not yet demonstrated our ability to successfully complete development of any product candidates, obtain marketing approvals, 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. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

Assuming we obtain marketing approval for any of our product candidates, we will need to transition from a company with a research and development focus to a company capable of supporting commercial activities. We may encounter unforeseen expenses, difficulties, complications and delays and may not be successful in such a transition.

We will need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we initiate and continue clinical trials of ridinilazole for the treatment of CDI, continue our research activities and initiate preclinical programs for other product candidates. In addition, if we obtain marketing approval for ridinilazole where we retain commercial rights or any other product candidates we develop, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. Furthermore, we expect to continue to incur additional costs associated with operating as a public company in the United States in addition to in the United Kingdom. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

We believe that our existing cash and cash equivalents, as well as the remaining amounts receivable under the $44.0 million we have been awarded under our contract with the Biomedical Advanced Research and Development Authority, or BARDA, for the development of ridinilazole, the remaining amounts receivable under the $2.0 million we have been awarded under our sub-award from the Trustees of Boston University under the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator program, or CARB-X, for our gonorrhea program, and the cost-sharing arrangement under our license and collaboration agreement with Sarepta, will be sufficient to enable us to fund our operating expenses and capital expenditure requirements through January 31, 2020. While these capital resources have allowed us to initiate our two Phase 3 clinical trials of ridinilazole, we do not expect to be able to complete these trials without additional capital. We have based the foregoing estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. This estimate assumes, among other things, that we do not obtain any additional funding through grants and clinical trial support or through new collaboration arrangements. Our future capital requirements will depend on many factors, including:

- the progress, costs and results of clinical trials of ridinilazole for CDI;
- the number and development requirements of other product candidates that we pursue;
- the costs, timing and outcome of regulatory review of ridinilazole and other product candidates we develop;
- the costs and timing of commercialization activities, including product sales, marketing, distribution and manufacturing, for any of our product candidates that receive marketing approval;
- subject to receipt of marketing approval, revenue received from commercial sales of ridinilazole or any other product candidates;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property-related claims;
- our contract with BARDA and whether BARDA elects to pursue its designated options beyond the base period and first exercised option;
- our contract with CARB-X and whether CARB-X elects to pursue its designated options beyond the base period;
- the amounts we receive from Eurofarma under our license and commercialization agreement, including for the achievement of development, commercialization and sales milestones and for product supply transfers;
- our ability to establish and maintain collaborations, licensing or other arrangements and the financial terms of such arrangements;
- the extent to which we acquire or invest in other businesses, products and technologies;
- the rate of the expansion of our physical presence; and
- the costs of operating as a public company in the United States and in the United Kingdom.

Conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we are not planning to have commercially available for several years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. Additional financing may not be available to us on acceptable terms, or at all.

Raising additional capital may cause dilution to our investors, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, collaborations, strategic alliances, grants and clinical trial support from government entities, philanthropic, non-government and not for profit organizations and patient advocacy groups, debt financings, and marketing, distribution or licensing arrangements. We do not have any committed external source of funds other than the amounts we are entitled to receive from BARDA under our contract with them to fund, in part, the clinical development of ridinilazole, from Eurofarma under our license and commercialization agreement with them and from CARB-X. 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 an equity holder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends or other distributions.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Risks Related to the Development and Commercialization of our Product Candidates

We depend heavily on the success of our lead product candidate, ridinilazole, which we are developing for the treatment of CDI. All of our other programs are still in the preclinical or discovery stage. If we are unable to commercialize ridinilazole, or experience significant delays in doing so, our business will be materially harmed.

We have invested a significant portion of our efforts and financial resources in the development of ridinilazole for CDI, which is still in clinical development. Our ability to generate product revenues, which may not occur for several years, if ever, will depend heavily on the successful development and commercialization of ridinilazole. The success of this product candidate will depend on a number of factors, including the following:

- successful completion of clinical development;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity;
- protecting our rights in our intellectual property portfolio;
- establishing sales, marketing and distribution capabilities;
- launching commercial sales of ridinilazole, if and when approved, whether alone or in collaboration with others;
- acceptance of ridinilazole, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies; and
- maintaining a continued acceptable safety profile of ridinilazole, following approval.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize ridinilazole, which would materially harm our business.

If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of the U.S. Food and Drug Administration, or the FDA, or the European Medicines Agency, or the EMA, or do not otherwise produce favorable results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of ridinilazole or any other product candidate.

In connection with obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. In particular, the small number of patients in our early clinical trials may make the results of these clinical trials less predictive of the outcome of later clinical trials. The design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced or completed. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

For example, in June 2018, we announced that our Phase 2 clinical trial of ezutromid, our then-lead utrophin modulator for the treatment of the neuromuscular disease Duchenne muscular dystrophy, or DMD, which we referred to as PhaseOut DMD, failed to meet its primary and secondary endpoints. PhaseOut DMD was a 48-week open label clinical trial conducted at trial sites in the United Kingdom and the United States. PhaseOut DMD enrolled a total of 40 ambulatory boys between their fifth and tenth birthday, inclusive, who had a genetically confirmed diagnosis of DMD. The primary objective of PhaseOut DMD was to investigate changes in magnetic resonance parameters from baseline in leg muscle health. The secondary objectives of PhaseOut DMD investigated changes in utrophin expression in muscle and muscle fiber regeneration through the examination of muscle fiber biopsies taken from patients at baseline and after 24 weeks or 48 weeks of treatment with ezutromid. We reported interim 24-week data from PhaseOut DMD in January 2018, with further findings reported in February 2018, and while these data showed positive changes in some of the primary and secondary endpoint measurements after 24 weeks of treatment, we did not see these effects after 48 weeks of treatment. We announced the discontinuation of the development of ezutromid in June 2018, and we have now substantially completed the activities related to the close-out of the PhaseOut DMD clinical trial.

If we are required to conduct additional clinical trials or other testing of ridinilazole or any other product candidate that we develop beyond those that we contemplate, if we are unable to successfully complete our clinical trials or other testing, if the results of these clinical trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as we intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements or restrictions; or
- have the product removed from the market after obtaining marketing approval.

If we experience any of a number of possible unforeseen events in connection with our clinical trials, potential marketing approval or commercialization of our product candidates could be delayed or prevented.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- we may be unable to enroll a sufficient number of patients in our clinical trials to ensure adequate statistical power to detect any statistically significant treatment effects;

- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators, institutional review boards or independent ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- we may have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks;
- regulators, institutional review boards or independent ethics committees may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate, which may occur if, for example, enrollment for our Phase 3 clinical trials were delayed and the clinical supply of ridinilazole manufactured for such trials was not utilized prior to its expiration and needed to be replaced; and
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators, institutional review boards or independent ethics committees to suspend or terminate the clinical trials.

Our product development costs will increase if we experience delays in testing or marketing approvals. We do not know whether any preclinical tests or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

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

We may not be able to initiate or continue clinical trials for our product candidates, if we are unable to locate and enroll a sufficient number of eligible patients to participate in these clinical trials. CDI is an acute infection that requires rapid diagnosis. For our Phase 3 clinical trials of ridinilazole, we need to identify potential patients, test them for CDI and enroll them within three days and prior to patients receiving other antibiotic treatments that may be active against CDI for greater than a 24-hour period. In addition, our competitors in CDI have ongoing clinical trials for product candidates that could be competitive with our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates.

Patient enrollment is affected by other factors, including:

- severity of the disease under investigation;
- eligibility criteria for the clinical trial in question;
- perceived risks and benefits of the product candidate under study;
- competition for patients, time and resources at clinical trials sites from other investigational therapies in clinical trials that target the same patient population;
- approval of other therapies to treat the indication that is being investigated in the clinical trial;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients.

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

If serious adverse or inappropriate side effects are identified during the development of ridinilazole or any other product candidate, we may need to abandon or limit our development of that product candidate.

All of our product candidates are in clinical or preclinical development and their risk of failure is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive marketing approval. If our product candidates are associated with undesirable side effects or have characteristics that are unexpected, we may need to abandon their development or limit development to certain 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.

Although ridinilazole has generally been well tolerated at all doses tested, patients who typically are diagnosed with CDI have a number of underlying illnesses, which means it is more likely that we will see adverse events and serious adverse events being reported even if these events are later deemed to be unrelated to treatment with ridinilazole. For example, in our Phase 2 proof of concept clinical trial of ridinilazole, a total of 180 adverse events were reported for ridinilazole, although the majority of these were considered unlikely to be related to treatment with ridinilazole, and the number of ridinilazole reported adverse events was similar to patients treated with vancomycin, the comparator drug used in this clinical trial, where a total of 183 adverse events were reported. Most of the adverse events occurred in the gastrointestinal system organ class with nausea, abdominal pain, abdominal distention and vomiting the most commonly reported events for both treatment groups. Often, it is not possible to determine conclusively whether or not the product candidate being studied caused a particular adverse event. Regulatory authorities may draw different conclusions or require additional testing to confirm these determinations, if they occur. In addition, it is possible that as we test ridinilazole in a larger clinical program, illnesses, discomforts and other adverse events that were observed in earlier clinical trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by clinical trial patients.

Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause side effects or other safety issues that prevented further development of the compound. If we elect or are forced to suspend or terminate any clinical trial of our product candidates, the commercial prospects of such product candidate will be harmed and our ability to generate product revenues from such product candidate will be delayed or eliminated. Any of these occurrences could materially harm our business.

Even if ridinilazole or any other product candidate receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If ridinilazole or any of our other product candidates receive marketing approval, such products may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenues or revenue from collaboration agreements, including our license and commercialization agreement with Eurofarma, or any profits from operations. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages compared to alternative treatments or competitive products;
- the prevalence and severity of any side effects;
- the ability to offer our product candidates for sale at competitive prices, including in the case of ridinilazole, which we expect, if approved, will compete with the antibiotics vancomycin and metronidazole, both of which are available in generic form at low prices, and fidaxomicin, and potentially other approaches to be used as an adjunctive therapy to antibiotics, such as the monoclonal antibody bezlotoxumab, vaccines or fecal biotherapy;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement;
- the timing of any such marketing approval in relation to other product approvals;
- support from patient advocacy groups; and
- any restrictions on concomitant use of other medications.

Our ability to negotiate, secure and maintain third-party coverage and reimbursement may be affected by political, economic and regulatory developments in the United States, the European Union and other jurisdictions.

Governments continue to impose cost containment measures, and third-party payors are increasingly challenging prices charged for medicines and examining their cost effectiveness, in addition to their safety and efficacy. These and other similar developments could significantly limit the degree of market acceptance of ridinilazole or any of our other product candidates that receive marketing approval.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may not be successful in commercializing ridinilazole or any other product candidate if and when such product candidates are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale or marketing of pharmaceutical products. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. If ridinilazole receives marketing approval, we intend to commercialize it in the United States with our own specialized sales force. We will rely on Eurofarma to commercialize ridinilazole in Argentina, Belize, Bolivia, Brazil, Chile, Colombia, Costa Rica, Ecuador, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Suriname, Dominican Republic, Uruguay and Venezuela, pursuant to the license and commercialization agreement we entered into with Eurofarma in December 2017. We are also currently exploring options to develop and commercialize this antibiotic in other territories. There are risks involved with establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to or persuade adequate numbers of physicians to prescribe any future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales and marketing services, our product revenues or the profitability of these product revenues to us are likely to be lower than if we were to market and sell any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are acceptable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

We face substantial competition, which may result in others discovering, developing or commercializing products before us or more successfully than we do.

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates and any products we may seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide.

Several pharmaceutical and biotechnology companies have established themselves in the market for the treatment of CDI, and several additional companies are developing products for the treatment of CDI. Currently the mostly commonly used treatments for CDI are the broad spectrum antibiotics vancomycin and metronidazole, both of which are available in generic form in the United States. Generic antibiotic therapies typically are sold at lower prices than branded antibiotics and generally are preferred by managed care providers of health services. The antibiotic fidaxomicin (Dificid™ in the United States and Dificlir™ in Europe), which is marketed in the United States by Cubist Pharmaceuticals, Inc., or Cubist, a wholly owned subsidiary of Merck & Co., Inc., or Merck, and in Europe by Astellas Pharma Inc., is approved for treatment of CDI in the United States and the European Union. Merck received approval from the FDA and EMA for bezlotoxumab (Zinplava™), a monoclonal antibody for the treatment of patients, in combination with an antibiotic, who have a high risk of disease recurrence. Other approaches in development for the treatment of CDI include vaccines and fecal biotherapy. For more information, see “Business—Competition” in this Annual Report.

Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are more effective, safer, have fewer or less severe side effects, are approved for broader indications or patient populations, or are more convenient or less expensive than any products that we develop and commercialize. Our competitors may also obtain marketing approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

We believe that many competitors are attempting to develop therapeutics for the target indications of our product candidates, including academic institutions, government agencies, public and private research organizations, large pharmaceutical companies and smaller more focused companies.

Many of our competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining approvals from regulatory authorities 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. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific 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.

Even if we are able to commercialize ridinilazole or any other product candidate that we develop, the product may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Our ability to commercialize ridinilazole or any other product candidate successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the E.U. and U.S. healthcare industries and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. 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.

For example, under Medicare, hospitals are reimbursed under an inpatient prospective payment system. This pricing methodology provides a single payment amount to hospitals based on a given diagnosis-related group. As a result, with respect to Medicare reimbursement for services in the hospital inpatient setting, hospitals could have a financial incentive to use the least expensive drugs for the treatment of CDI, generic antibiotics, which may significantly impact our ability to charge a premium for ridinilazole. We cannot be sure that coverage and reimbursement will be available for ridinilazole or any other product that we commercialize and, if coverage and reimbursement are available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. In addition, third-party payors are likely to impose strict requirements for reimbursement of a higher priced drug. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the applicable regulatory authority. Moreover, eligibility for coverage and reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, intellectual property, manufacture, sale and distribution expenses. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs, and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. In the United States, third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. In the European Union, reference pricing systems and other measures may lead to cost containment and reduced prices. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, particularly the member states of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidate to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on prices or reimbursement levels within the country of publication and other countries. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be adversely affected.

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

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

- reduced resources of our management to pursue our business strategy;
- decreased demand for any product 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 clinical trial participants or patients;
- loss of revenue;
- increased insurance costs; and
- the inability to commercialize any products that we may develop.

We have separate product liability insurance policies that cover our product candidates and each of our clinical trials. These policies each provide coverage of up to £20.0 million in the aggregate for clinical trials, or portions thereof, conducted worldwide. The insurance policies covering our clinical trials are subject to a per claim deductible. The amount of insurance that we currently hold may not be adequate to cover all liabilities that we may incur. We will need to increase our insurance coverage when and if we begin commercializing ridinilazole or any other product candidate that receives marketing approval. 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.

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 currently, and may in the future, involve the use of hazardous and flammable materials, including chemicals and medical and biological materials, and produce hazardous waste products. Even if we 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 or disposal of hazardous wastes, we could be held liable for any resulting damages, and any liability could exceed our resources.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We also maintain liability insurance for some of these risks, but our policy has a coverage limit of £10.0 million per occurrence.

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.

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

Because we have limited financial and managerial resources, we focus on specific product candidates. As a result, we may forego or delay pursuit of opportunities with other product candidates that later 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 development programs and product candidates may not yield any commercially viable products.

For example, in June 2018, we announced that our PhaseOut DMD clinical trial of ezutromid for DMD failed to meet its primary and secondary endpoints. We had reported interim 24-week data from PhaseOut DMD in January 2018, with further findings reported in February 2018, and while these showed positive changes in some of the primary and secondary endpoint measurements after 24 weeks of treatment, we did not see these effects after 48 weeks of treatment. We announced the discontinuation of the development of ezutromid in June 2018 and have also discontinued the development of our future generation utrophin modulators, despite our significant investment of resources into the development of our utrophin modulators for the treatment of DMD over a number of years.

We have based our research and development efforts for CDI on the antibiotic ridinilazole. Notwithstanding our large investment to date and anticipated future expenditures in proprietary technologies that we use in the discovery of product candidates for CDI and other infectious diseases, we have not yet developed, and may never successfully develop, any marketed drugs. As a result of pursuing the development of product candidates using our proprietary technologies, we may fail to develop product candidates or address indications based on other scientific approaches that may offer greater commercial potential or for which there is a greater likelihood of success. Research programs to identify new product candidates require substantial technical, financial and human resources. These research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development.

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.

The anticipated benefits of any acquisition that we consummate may not be fully realized, may take longer to realize than expected or may not be realized at all.

Any acquisition we consummate will involve the integration of the operations, product candidates and technology of the acquired business with our existing operations and programs, and there are uncertainties inherent in any such integration. Unexpected difficulties in the integration process for an acquisition or the failure to retain key management personnel from an acquired business could adversely affect our business, financial results and financial condition. In addition, any acquisitions are likely to require significant resources and management attention, including the resources and attention required to further the development of any acquired product candidates or other development programs, or the commercialization of any acquired product, and we may not realize the anticipated benefits from such an acquisition within the time period we expect, or at all. In addition, in any acquisition, the due diligence process may not identify all factors that could produce unintended or unexpected consequences for us. Undiscovered factors could cause us to incur potentially material financial liabilities and prevent us from achieving the expected benefits from the acquisition within our desired timeframe, or at all. In December 2017, we obtained a bacterial genetics-based platform, which we refer to as our Discuva Platform, for the discovery and development of new mechanism antibiotic compounds through our acquisition of Discuva Limited, or Discuva. While we expect to use the Discuva Platform to facilitate our discovery and development of new mechanism antibiotics, we may fail to do so. As a result, we may not obtain any value from our acquisition of Discuva.

The United Kingdom's withdrawal from the European Union could lead to increased market volatility and make it more difficult for us to do business in Europe, which could adversely impact the market price of our ordinary shares and ADSs.

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union (commonly referred to as "Brexit"). The withdrawal of the United Kingdom from the European Union will take effect either on the effective date of the withdrawal agreement or, in the absence of agreement, two years after the United Kingdom provides a notice of withdrawal pursuant to Article 50 of the E.U. Treaty, unless the European Council, in agreement with the United Kingdom, unanimously decides to extend this period. On March 29, 2017, the U.K. Prime Minister formally delivered the notice of withdrawal. The United Kingdom had a period of a maximum of two years from the date of its formal notification to negotiate the terms of its withdrawal from, and future relationship with, the European Union. Discussions between the United Kingdom and the European Union focused on finalizing withdrawal issues and transition agreements are ongoing. On March 21, 2019, the European Council, in agreement with the United Kingdom, unanimously agreed to extend the deadline to May 22, 2019, if the U.K. Parliament approves in an upcoming vote the withdrawal agreement agreed to between the United Kingdom and the European Union in November 2018, and to April 12, 2019, if the U.K. Parliament does not approve it. However, ongoing uncertainty within the U.K. Government and Parliament sustains the possibility of the United Kingdom leaving the European Union on April 12, 2019, without a withdrawal agreement and associated transition period in place, which is likely to cause significant market and economic disruption.

We may also face new regulatory costs and challenges that could have a material adverse effect on our operations. Lack of clarity about future U.K. laws and regulations as the United Kingdom determines which E.U.-derived laws and regulations to replace or replicate as part of a withdrawal, including financial laws and regulations, tax and free trade agreements, intellectual property rights, supply chain logistics, environmental, health and safety laws and regulations, immigration laws and employment laws, could further decrease foreign direct investment in the United Kingdom, increase costs, depress economic activity and restrict our access to capital. Depending on the terms of Brexit, the United Kingdom could lose the benefits of global trade agreements negotiated by the European Union on behalf of its members, which may result in increased trade barriers which could make our doing business in Europe more difficult. In addition, currency exchange rates in the pound sterling and the euro with respect to each other and the U.S. dollar have been and may continue to be adversely affected by Brexit. In the near term, there is a risk of disrupted import and export processes due to a lack of administrative processing capacity by the respective U.K. and E.U. customs agencies that may delay time-sensitive shipments and may negatively impact our clinical trial supply chain, which includes locations in both the United Kingdom and the European Union.

Recent and potential future changes to U.S. and non-U.S. tax laws could materially adversely affect our company and holders of our ordinary shares and the ADSs.

Legislation bringing about broad changes in the existing corporate tax system, commonly referred to as the Tax Cuts and Jobs Act (the "Tax Act"), was enacted in December 2017. Many aspects of the legislation are unclear at this time and remain subject to pending regulatory and accounting guidance as well as potential amendments and technical corrections, any of which could modify various aspects of the legislation in ways that are either positive or negative for us or holders of the ADSs. As a result, the overall impact of this legislation on us or on holders of our ordinary shares and the ADSs is uncertain and could be adverse. Other legislative or regulatory changes and judicial developments could also affect the taxation of our business or of holders of our ordinary shares and the ADSs.

Future changes in tax laws, regulations and treaties, or the interpretation thereof, in addition to initiatives related to the Base Erosion and Profit Shifting, or BEPS, Project of the Organisation for Economic Co-Operation and Development, or OECD; the European Commission's "state aid" investigations; and other developments could have an adverse effect on the taxation of international businesses, including our own. Furthermore, countries where we are subject to taxes, including the United States, evaluate their tax policies and rules on a regular basis, and we may see significant changes in legislation and regulations concerning taxation.

We are unable to predict what tax changes may be enacted in the future or what effect such changes would have on our business, but such changes could affect our effective tax rates in countries where we have operations and could have an adverse effect on our overall tax position in the future, along with increasing the complexity, burden and cost of tax compliance.

Our computer systems, or those of any collaborators or contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Despite the implementation of security measures, our computer systems and those of third parties with whom we contract are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Any system failure, accident or security breach that causes interruptions in our operations could result in a material disruption of our product development programs and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. For example, the loss of clinical trial data from completed clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we may incur liabilities and the further development of our product candidates may be delayed. In addition, we may not have adequate insurance coverage to provide compensation for any losses associated with such events.

We could be subject to risks caused by misappropriation, misuse, leakage, falsification or intentional or accidental release or loss of information maintained in the information systems and networks of our company, including personal information of our employees. In addition, outside parties may attempt to penetrate our systems or those of our vendors or fraudulently induce our employees or employees of our vendors to disclose sensitive information in order to gain access to our data. Like other companies, we may experience threats to our data and systems, including malicious codes and viruses, and other cyber-attacks. The number and complexity of these threats continue to increase over time. If a material breach of our security or that of our vendors occurs, the market perception of the effectiveness of our security measures could be harmed, we could lose business and our reputation and credibility could be damaged. We could be required to expend significant amounts of money and other resources to repair or replace information systems or networks. Although we develop and maintain systems and controls designed to prevent these events from occurring, and we have a process to identify and mitigate threats, the development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become more sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the European Union's General Data Protection Regulation 2016/679, or GDPR, and as enacted in the U.K. through the Data Protection Act 2018, imposes strict obligations on the processing of personal data, including personal health data, and the free movement of such data. The GDPR applies to any company established in the European Union as well as any company outside the European Union that processes personal data in connection with the offering of goods or services to individuals in the European Union or the monitoring of their behavior. The GDPR enhances data protection obligations for processors and controllers of personal data, including, for example, obligations relating to: processing health and other sensitive data; obtaining consent of individuals; providing notice to individuals regarding data processing activities; responding to data subject requests; taking certain measures when engaging third-party processors; notifying data subjects and regulators of data breaches; implementing safeguards to protect the security and confidentiality of personal data; and transferring personal data to countries outside the European Union, including the United States. The GDPR imposes additional obligations and risks upon our business and substantially increases the penalties to which we could be subject in the event of any non-compliance, including fines of up to €20 million or 4% of total worldwide annual turnover, whichever is higher. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages. Given the breadth and depth of changes in data protection obligations, preparing for and complying with the GDPR's requirements has required and will continue to require significant time, resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the European Union. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices or lead to government enforcement actions, private litigation or significant fines and penalties against us, reputational harm and could have a material adverse effect on our business, financial condition or results of operations.

Risks Related to our Dependence on Third Parties

Our reliance on government funding for ridinilazole and our gonorrhea program adds uncertainty to our research and commercialization efforts with respect to ridinilazole and uncertainty to our research efforts with respect to our gonorrhea program.

We expect that a significant portion of the funding for the development of ridinilazole will come from our contract with BARDA. BARDA is entitled to terminate our BARDA contract for convenience at any time, in whole or in part, and there can be no assurance that our BARDA contract will not be terminated. Changes in government budgets and research priorities may result in a decreased and de-prioritized emphasis on supporting the development of antibacterial product candidates such as ridinilazole. If our BARDA contract is terminated or BARDA declines to exercise options for the full research program, or if there is any reduction or delay in funding under our BARDA contract, we may be forced to seek alternative sources of funding, which may not be available on non-dilutive terms, terms favorable to us, or at all. If alternative sources of funding are not available, we may suspend or terminate development activities related to ridinilazole. In addition, a meaningful portion of the initial funding for the development of a lead clinical candidate in our gonorrhea program is supported by our award from CARB-X. If CARB-X terminates our award, we may suspend or terminate development activities related to our gonorrhea program.

BARDA could decide to delay certain of our activities, and we may elect to move forward with certain activities at our own risk and without BARDA reimbursement.

Under our BARDA contract, BARDA will regularly review our ridinilazole development efforts and clinical activities. Under certain circumstances, BARDA may direct us to delay certain activities and invest additional time and resources before proceeding. If we follow such BARDA direction, we may incur delays and additional costs for which we had not planned. In addition, even if BARDA does not direct us to delay certain activities, BARDA's review of our progress may take longer than we expect, which may result in overall program delays. Also, the costs associated with following BARDA's direction to delay certain activities may or may not be reimbursed by BARDA under our contract. Finally, if we decide not to follow the direction provided by BARDA and instead pursue activities that we believe are in the best interest of the development of ridinilazole, we might forgo reimbursement under our BARDA contract, and BARDA could assert that we are in default of our contractual commitments, potentially leading to the termination of our contract, and possibly suspension, debarment, or exclusion from eligibility for other U.S. government contracts, funding programs and regulatory approvals.

BARDA may elect not to pursue the remaining designated options beyond the base period.

Even if BARDA does not terminate the contract, the BARDA contract does not require BARDA to provide funding beyond the amount currently obligated under the base period and the first option of the existing contract. Our BARDA contract includes a base period providing for reimbursement of up to $32 million and three options that, if exercised in full by BARDA, would extend the contract until the year 2022 and increase the total potential reimbursement to $62 million. In August 2018, BARDA exercised the first of these three options with the $12 million in funding to be drawn down to specifically support drug manufacturing activities required for the submission of marketing approval applications and other regulatory activities related to ridinilazole. However, BARDA will decide in its sole discretion whether to pursue the remaining options under the contract, and there can be no assurance that BARDA will elect to pursue either of them. Changes in government budgets and research priorities may result in a decreased and de-prioritized emphasis on supporting the development of antibacterial product candidates such as ridinilazole. In such event, BARDA would have no obligation to exercise its remaining options or extend our existing contract. Any such decision by BARDA to end its support for our ridinilazole research program could materially adversely affect our business.

Our reliance on government funding for the clinical and regulatory development of ridinilazole and our gonorrhea program may impose requirements that increase the costs of commercialization and production of product candidates developed with the support of these government-funded programs.

Aspects of our development programs are currently being supported, in part, with funding from BARDA and CARB-X. Contracts and grants awarded by the U.S. government, its agencies and its partners, including our awards from BARDA and CARB-X, include provisions that implement the U.S. government's rights and remedies, many of which are not typically found in commercial contracts, including, for example, powers of the government to:

- terminate agreements, in whole or in part, at any time, for any reason or no reason;
- unilaterally modify the parties' obligations under such contracts, subject to government-determined equitable price adjustments;
- decline to exercise any option for work beyond the initial base period under multi-year contracts;
- suspend contract performance if Congressionally appropriated funding becomes unavailable;
- obtain rights to inventions and technical data made or first produced in the performance of such contracts;
- audit contract-related costs and fees, including allocated indirect costs;
- suspend or debar the contractor from receiving new contracts pending resolution of alleged violations of procurement laws or regulations in the event of wrongdoing by us;
- take actions that result in a longer development timeline than expected;
- direct the course of a development program in a manner not chosen by the government contractor;
- impose U.S. manufacturing requirements for products that embody or that are produced through the use of inventions conceived or first reduced to practice under such contracts;
- assert qualified march-in rights to grant licenses to third parties to practice contractor-owned inventions that are conceived or first reduced to practice under such contracts;
- pursue criminal or civil remedies under the False Claims Act, False Statements Act and similar remedy provisions specific to government agreements; and
- limit the government's financial liability to amounts appropriated by the U.S. Congress on a fiscal-year basis, thereby leaving some uncertainty about the future availability of funding for a program even after it has been funded for an initial period.

We may not have the right to prohibit the U.S. government from using certain inventions and technical data funded by the government and developed by us, and we may not be able to prohibit third-party companies, including our competitors, from using those inventions and technical data in providing products and services to the U.S. government. The U.S. government generally takes the position that it has the right to royalty-free use of inventions and technical data that are developed under U.S. government contracts. While we do not believe the intellectual property rights that we have granted to the U.S. government under the BARDA agreement will impact our rights to commercialize ridinilazole, the government's non-exclusive license to intellectual property developed under the agreement and the government's march-in to inventions made under the agreement may allow the government, or a third party on its behalf, to more easily and/or quickly develop a product that could compete with ridinilazole.

In addition, U.S. government contracts normally contain additional requirements that may increase our costs of doing business, reduce our profits, and expose us to liability for failure to comply with these terms and conditions. These requirements include, for example:

- specialized accounting systems unique to government contracts;
- potential liability for price adjustments or recoupment of government funds after such funds have been spent;
- mandatory disclosure of credible evidence of certain contractual or statutory violations occurring in connection with the contract;
- adhering to stewardship principals imposed by CARB-X as a condition of the award;
- public disclosures of certain contract information, which may enable competitors to gain insights into our research program; and
- mandatory socioeconomic compliance requirements, including labor standards, non-discrimination and affirmative action programs and environmental compliance requirements.

As an organization, we are relatively new to government contracting and the associated regulatory compliance obligations. If we fail to maintain compliance with those obligations, we may be subject to potential civil and/or criminal liability, termination of our BARDA contract, termination of our CARB-X award and/or suspension, debarment, or exclusion from eligibility for other U.S. government contracts, funding programs and regulatory approvals. As a U.S. government contractor, we are subject to financial audits and other reviews by the U.S. government of our costs and performance under our BARDA contract and CARB-X award, as well as our accounting and general business practices related to our BARDA contract and CARB-X award. Based on the results of its audits, the U.S. government may adjust our contract-related costs and fees, including allocated indirect costs.

Laws and regulations affecting government contracts, including our BARDA contract, make it more costly and difficult for us to successfully conduct our business. Failure to comply with these laws and regulations could result in significant civil and criminal penalties and adversely affect our business.

We must comply with numerous laws and regulations relating to the administration and performance of our government contracts, including our BARDA contract. Among the most significant government contracting regulations are:

- the Federal Acquisition Regulation, or FAR, and agency-specific regulations supplemental to the FAR, which comprehensively regulate the procurement, formation, administration and performance of government contracts;
- extensive U.S. government regulation of government-funded clinical research activities, including, for example, compliance requirements relating to protection of human and animal research subjects, restrictions on uses of human research materials, and conditions on dissemination of research results.
- business ethics and public integrity obligations, which govern areas such as conflicts of interest, the recruitment and hiring of former government employees, bribes and gratuities, and limitations on and mandatory disclosure of lobbying activities, pursuant to laws such as the Anti-Kickback Act, the Procurement Integrity Act, the False Claims Act and the Foreign Corrupt Practices Act; and
- export control and import laws and regulations.

In addition, U.S. government agencies such as the Department of Health and Human Services and the Defense Contract Audit Agency routinely audit and investigate government contractors for compliance with applicable laws and standards. These agencies review a contractor's performance under its contracts, including contracts with BARDA and CARB-X, cost structure and compliance with applicable laws, regulations and standards.

These agencies also review the adequacy of, and a contractor's compliance with, its internal control systems and policies, including the contractor's purchasing, property, estimating, compensation and management information systems. Any costs found to be unreasonable, unallowable under applicable reimbursement policies, or improperly allocated to a specific contract will not be paid, while such costs already paid must be refunded. Claims for costs that are expressly unallowable under applicable reimbursement policies may also be subject to administrative penalties. If we are audited and such audit uncovers improper or illegal activities, we may be subject to civil and criminal penalties and administrative sanctions, including:

- termination of any government contracts, including our BARDA contract;
- suspension of payments;
- administrative sanctions, such as long-term monitoring arrangements;
- fines; and
- suspension, debarment, or exclusion from eligibility for U.S. government contracts, funding programs and regulatory approvals.

In addition, we could suffer serious reputational harm if allegations of impropriety were made against us, which could jeopardize our other research programs, deter research institutions from engaging with us, and cause our stock price to decrease.

We depend on collaborations with third parties for the development and commercialization of some of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

We have entered into a license and commercialization agreement with Eurofarma pursuant to which we granted Eurofarma rights to commercialize ridinilazole in specified countries in South America, Central America and the Caribbean. We may also enter into additional third-party collaborations for the development and commercialization of ridinilazole in other jurisdictions. Moreover, we may seek third-party collaborators for development and commercialization of any other product candidates.

Our likely future collaborators for any marketing, distribution, development, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. Under our license and commercialization agreement with Eurofarma we have, and under any such arrangements we enter into with any third parties in the future we will likely have, limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities and efforts to successfully perform the functions assigned to them in these arrangements.

Our current collaborations pose, and any future collaboration likely will pose, numerous risks to us, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations and may not perform their obligations as expected;
- collaborators may deemphasize or not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus, including as a result of a sale or disposition of a business unit or development function, or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- 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 products or product candidates 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;
- a collaborator with marketing and distribution rights to multiple products may not commit sufficient resources to the marketing and distribution of our product relative to other products;

- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- disputes may arise between the collaborator and us as to the ownership of intellectual property arising during the collaboration;
- we may grant exclusive rights to our collaborators, which would prevent us from collaborating with others;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our products or product candidates or that result in costly litigation or arbitration that diverts management attention and resources; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

For example, in 2009, we assigned certain technology relating to our DMD program to BioMarin. BioMarin conducted a Phase 1 clinical trial of an early formulation of ezutromid in 48 healthy adult volunteers. In this clinical trial, subjects achieved low systemic exposure of the drug and there was variability of systemic exposure across subjects. Following this clinical trial of an early formulation of ezutromid, BioMarin elected not to continue development of our assigned technology, citing pharmaceutical and pharmacokinetic challenges. In public statements, BioMarin indicated that it had concluded that the likelihood of achieving a therapeutic effect in DMD patients was highly unlikely. In 2010, BioMarin transferred the assets, and all commercialization rights, back to us, and in June 2018, we announced the discontinuation of the development of ezutromid.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

Use of third parties to manufacture our product candidates may increase the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not own or operate manufacturing facilities for the production of clinical or commercial supplies of our product candidates. We have limited personnel with experience in drug manufacturing and lack the resources and the capabilities to manufacture any of our product candidates on a clinical or commercial scale. We currently rely on third parties for supply of the active pharmaceutical ingredients, or API, in our product candidates. Our strategy is to outsource all manufacturing of our product candidates and products to third parties.

We do not currently have any agreements with third-party manufacturers for the long-term clinical or commercial supply of any of our product candidates. We are engaged with a third-party manufacturer to provide clinical material of the API of ridinilazole with a different supplier responsible for fill and finish services to supply the final drug product for use in the Phase 3 clinical trials. We may be unable to conclude agreements for commercial supply with third-party manufacturers, or may be unable to do so on acceptable terms.

Even if we are able to establish and maintain arrangements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Third-party manufacturers may not be able to comply with current good manufacturing practice, or cGMP, regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates.

Our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

In addition, in order to conduct late-stage clinical trials of our product candidates, we will need to have them manufactured in large quantities. Our third-party manufacturers may be unable to successfully increase the manufacturing capacity for any of our product candidates in a timely or cost-effective manner, or at all.

The third-party manufacturer responsible for the fill and finish services to supply the final drug product for our Phase 3 clinical trials of ridinilazole experienced challenges in the fill and finish process used to manufacture test batches of the clinical supply of ridinilazole, specifically the manufacture of ridinilazole in tablet form, which is also the form expected to be used commercially, and which is a change from the capsule form used in our completed clinical trials of ridinilazole. Because of these challenges, we were not able to obtain sufficient quantities of ridinilazole to commence our Phase 3 clinical trials in the first half of 2018 as originally planned and delayed the commencement of those trials until February 2019. If our third-party manufacturer experiences these challenges again or is otherwise unable to manufacture sufficient quantity of the tablet form of ridinilazole, our Phase 3 clinical trials may be further delayed. Moreover, if our third-party manufacturers are unable to successfully scale up the manufacture of our product candidates in sufficient quality and quantity, the development, testing and clinical trials of that product candidate may be delayed or infeasible, and regulatory approval or commercial launch of that product candidate may be delayed or not obtained, which could significantly harm our business.

If the third parties that we engage to manufacture product for our preclinical tests and clinical trials should cease to continue to do so for any reason, we likely would experience delays in advancing these clinical trials while we identify and qualify replacement suppliers, and we may be unable to obtain replacement supplies on terms that are favorable to us. In addition, if we are not able to obtain adequate supplies of our product candidates or the drug substances used to manufacture them, it will be more difficult for us to develop our product candidates and compete effectively. Any inability to obtain adequate supplies of ridinilazole for clinical trials may also impact Eurofarma's ability to commercialize ridinilazole, if marketing approval is obtained, in the jurisdictions where Eurofarma holds commercialization rights. Under our license and commercialization agreement with Eurofarma, we have agreed to use commercially reasonable efforts to supply or cause to be supplied to Eurofarma sufficient commercial supply of ridinilazole.

Our current and anticipated future dependence upon others for the manufacture of our product candidates may adversely affect our future profit margins and our ability, and the ability of Eurofarma and any other future collaborator, to develop product candidates and commercialize any products that receive marketing approval on a timely and competitive basis.

We 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 clinical trials.

We do not independently conduct clinical trials for our product candidates. We rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to perform this function. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities.

Our reliance on these third parties for clinical development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the clinical trial. Moreover, the FDA requires us to comply with standards, commonly referred to as Good Clinical Practice, or GCP, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity of data and confidentiality of clinical trial participants are protected. The EMA imposes similar requirements on us for products that are the subject of clinical trials in European Union, including the United Kingdom.

We also are required to register ongoing clinical trials and post the results of completed clinical trials on a U.S. government-sponsored database, www.ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions. In September 2016, the U.S. Department of Health and Human Services through the U.S. National Institutes of Health issued new regulations that expand the legal requirements for submitting registration and results information for clinical trials involving FDA-regulated drugs, biologics and medical devices. The new rules require sponsors, among other things, to post results of clinical trials for unapproved products, including unfavorable results in clinical trials for unapproved uses of approved products. The EMA has also adopted transparency requirements that apply to clinical trials conducted in the European Union (EMA Policy/0070 on the publication of clinical data for medicinal products for human use, effective as of January 1, 2015). The EMA will implement this policy on the publication of clinical data in two phases. Phase 1 concerns the publication of clinical reports submitted to EMA as part of a marketing authorization application and through the centralized procedure. It entered into force on January 1, 2015. Phase 2 concerns the publication of individual patient data. The EMA will implement this phase at a later stage. This publication requirement for clinical reports may force us to disclose know-how relating to the design of clinical trials for our product candidates, which may harm our interests by disclosing valuable know-how to our competitors, which may be used to develop competing products to our product candidates.

Furthermore, third parties that we rely on for our clinical development activities may also have relationships with other entities, some of which may be our competitors. 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 product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. Our product development costs will increase if we experience delays in testing or obtaining marketing approvals.

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

If we are not able to establish additional collaborations, we may have to alter our development and commercialization plans.

Our product development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate further with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge; and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. We may also be restricted under future license agreements from entering into agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators and changes to the strategies of the combined company.

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 a product candidate, 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 our product candidates or bring them to market and generate product revenue.

If we fail to comply with our obligations in our funding arrangements with third parties, we could be required to repay the grant funding we have received or grant to these third parties rights under certain of our intellectual property.

We have received grant funding for some of our development programs from philanthropic, non-government and not for profit organizations and patient advocacy groups pursuant to agreements that impose development and commercialization diligence obligations on us. If we fail to comply with these obligations, in certain instances the applicable organization could require us to repay the grant funding we have received with interest or grant to the organization rights under certain of our intellectual property, which could materially adversely affect the value to us of product candidates covered by that intellectual property even if we are entitled to a share of any consideration received by such organization in connection with any subsequent development or commercialization of the product candidates.

Risks Related to our Intellectual Property

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

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary technology and products, including our Discuva Platform. We seek to protect our proprietary position by filing patent applications in the United States, in Europe and in certain additional foreign jurisdictions related to our novel technologies and product candidates that are important to our business. This process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, if we license technology or product candidates from third parties in the future, these license agreements may not permit us to control the preparation, filing and prosecution of patent applications, or to maintain or enforce the patents, covering the licensed technology or product candidates. These agreements could also give our licensors the right to enforce the licensed patents without our involvement, or to decide not to enforce the patents at all. Therefore, in these circumstances, these patents and applications may not be prosecuted or enforced in a manner consistent with the best interests of our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents, narrow the scope of our patent protection or make enforcement more difficult or uncertain.

The laws of foreign countries may not protect our patent rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than U.S. law does. In addition, for the foregoing reasons, we may not pursue or obtain patent protection in all major markets or may not obtain protection that enables us to prevent the entry of third parties into the market.

Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent. However, prior to March 16, 2013, in the United States, the first to invent was entitled to the patent. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our U.S. patents or pending U.S. patent applications, or that we were the first to file for patent protection of such inventions outside the United States or, since March 16, 2013, within the United States.

Moreover, we may be subject to a third party preissuance submission of prior art to the U.S. Patent and Trademark Office, or the USPTO, or become involved in opposition, derivation, reexamination, reissue, inter partes review, post grant review, interference proceedings or other patent office proceedings, court litigation or International Trade Commission proceedings, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation concerning our patent rights could reduce the scope of or prevent the enforceability of, or invalidate, our patent rights, allowing third parties to commercialize our technology or products, or equivalent or similar technology or products, and so to compete directly with us, without payment to us, or, where such proceedings involve third-party patents, result in our inability to manufacture or commercialize products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened or narrowed by operation of any of the foregoing, such an event could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with adequate protection to prevent competitors from competing with us or otherwise to provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar, improved or alternative technologies or products in a non-infringing manner.

For example, although ridinilazole is protected by a U.S. composition of matter patent that recites hydrated forms of ridinilazole, and a method of treatment patent for *Clostridium difficile* associated disease, patent protection is not available for composition-of-matter claims that only recite the active pharmaceutical ingredient for ridinilazole without limitation to its use. Because ridinilazole lacks composition-of-matter protection for its active pharmaceutical ingredient, competitors will, subject to obtaining marketing approval, be able to offer and sell products with the same active pharmaceutical ingredient so long as these competitors do not infringe any other issued patents that would otherwise cover the drug's usage, methods of treatment using the drug, drug formulations, drug dosage forms and the like. Moreover, method-of-treatment patent claims are more difficult to enforce than composition-of-matter claims for reasons including off-label sale, potential divided infringement issues and use of the subject compound in non-infringing manners. Physicians are permitted to prescribe an approved product for uses that are not described in the product's labeling. Although off-label prescriptions may infringe our method-of-treatment patents, the practice is common across medical specialties and such infringement is difficult to prevent or prosecute. Off-label sales would limit our ability to generate revenue from the sale of our product candidates, if approved for commercial sale. In addition, if a third party were able to design around our dosage-form and formulation patents and create a different formulation and dosage form that is not covered by our patents or patent applications, we would likely be unable to prevent that third party from manufacturing and marketing its product.

In addition, other companies may attempt to circumvent any regulatory data protection or market exclusivity, such as orphan drug exclusivity in the United States, which we obtain under applicable legislation, which may require us to allocate significant resources to preventing such circumvention. Legal and regulatory developments in the European Union and elsewhere may also result in clinical trial data submitted as part of a marketing authorization application becoming publicly available. Such developments could enable other companies to use our clinical trial data to assist in their own product development and to obtain marketing authorizations in the European Union and in other jurisdictions. Such developments may also require us to allocate significant resources to prevent other companies from circumventing or violating our intellectual property rights. Our attempts to prevent third parties from circumventing our intellectual property and other rights may ultimately be unsuccessful. We may also fail to take the required actions or pay the necessary fees to maintain our patents.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Future changes in U.S. statutory or case law beyond our control could affect some or all of the foregoing possibilities. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. This could be the case even after giving effect to patent term extensions and data exclusivity provisions preventing third parties from relying on clinical trial data filed by us for regulatory approval in support of their own applications for such approval. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

We may become involved in lawsuits or other enforcement proceedings to protect or enforce our patents or other intellectual property, which could be expensive, time-consuming and potentially unsuccessful.

Competitors may infringe our patents, trademarks, copyrights or other intellectual property. To counter infringement or unauthorized use, we may be required to file claims, which can be expensive and time-consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their intellectual property or that our patent and other intellectual property rights are invalid or unenforceable, including for anti-trust reasons. As a result, in a patent infringement proceeding, a court or administrative body may decide that a patent of ours is invalid or unenforceable, in whole or in part, or may construe the patent's claims narrowly and so refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the competitor technology in question. Even if we are successful in a patent infringement action, the unsuccessful party may subsequently raise antitrust issues and bring a follow-on action thereon. Antitrust issues may also provide a bar to settlement or constrain the permissible settlement terms. Further, settlement agreements in the pharmaceutical sector are the subject of ongoing review by the antitrust authorities in the European Union.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies, including our Discuva Platform, without infringing the intellectual property and other proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference, derivation, inter partes review, reexamination, reissue or post-grant review proceedings before the USPTO. The risks of being involved in such litigation and office proceedings may also increase as our product candidates approach commercialization, and as we gain greater visibility as a publicly traded company in the United States. Third parties may assert infringement claims against us based on existing or future intellectual property rights and so restrict our freedom to operate. Third parties may also seek injunctive relief against us, whereby they would attempt to prevent us from practicing our technologies altogether pending outcome of any litigation against us. We may not be aware of all such intellectual property rights potentially relating to our product candidates prior to their assertion against us. For example, we have not conducted an in-depth freedom-to-operate search or analysis for ridinilazole. Any freedom-to-operate search or analysis previously conducted may not have uncovered all relevant patents and pending patent applications, and there may be pending or future patent applications that, if issued, would block us from commercializing ridinilazole. Thus, we do not know with certainty whether ridinilazole or any other product candidate or our commercialization thereof, does not and will not infringe any third party's intellectual property.

If we are found to infringe a third party's intellectual property rights, or in order to avoid or settle litigation, we could be required to obtain a license to enable us to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies as are licensed to us, and could require us to make substantial payments. Absent a license, we could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent or other intellectual property right. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties, or claims that we derived our inventions from another, could have a similar negative impact on our business.

We may be subject to claims by third parties asserting that we or our employees have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary or otherwise confidential information or know-how of others in their work for us, we may be subject to claims that we or these employees have without authorization used or disclosed intellectual property, including trade secrets or other proprietary or confidential information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

In addition, while we typically require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us and agreeing to cooperate and assist us with securing and defending our intellectual property, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

If we fail in prosecuting or 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 prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

Intellectual property litigation could cause us to spend substantial resources and could distract our personnel from their normal responsibilities.

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 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. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of the ADSs and our ordinary shares. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development, sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. 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. Accordingly, costs and lost management time, as well as 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.

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 some of our technology and products, we also rely on trade secrets, including unpatented know-how, technology and other proprietary and confidential information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. However, we cannot guarantee that we have executed these agreements with each party that may have or have had access to our trade secrets or that the agreements we have executed will provide adequate protection. Any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary or confidential 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, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets, particularly unpatented know-how, were to be obtained or independently developed by a competitor, our competitive position would be harmed.

Risks Related to Regulatory Approval and Marketing of our Product Candidates

Even if we complete the necessary clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates, including ridinilazole, and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and by comparable authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us or our collaborators from commercializing the product candidate. We have not received approval to market ridinilazole or any other product candidate from regulatory authorities in any jurisdiction.

We have only limited experience in filing and supporting the applications necessary to obtain marketing approvals for product candidates and expect to rely on third-party contract research organizations to assist us in this process. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Regulatory authorities may determine that ridinilazole or any of our other product candidates are not effective or only moderately effective, or have undesirable or unintended side effects, toxicities, safety profiles or other characteristics that preclude us from obtaining marketing approval or that prevent or limit commercial use.

The process of obtaining marketing approvals is expensive, may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of 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 studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable. If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. On March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, Brexit could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the European Union. Further, the vote for the United Kingdom's withdrawal from the E.U. has resulted in a decision to move the EMA from the United Kingdom to the Netherlands, with operations currently scheduled to begin in the Netherlands by the end of March 2019. This transition may cause disruption in the administrative and medical scientific links between the EMA and the U.K. Medicines and Healthcare products Regulatory Agency, including delays in granting clinical trial authorization or marketing authorization, disruption of importation and export of active substance and other components of new drug formulations, and disruption of the supply chain for clinical trial product and final authorized formulations. The cumulative effects of the disruption to the regulatory framework is unknown and may add considerably to the development lead time to marketing authorization and commercialization of products in the E.U. and/or the United Kingdom.

Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union 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 and/or European Union for our product candidates, which could significantly and materially harm our business.

The United Kingdom has a period of a maximum of two years from the date of its formal notification to negotiate the terms of its withdrawal from, and future relationship with, the European Union. On March 21, 2019, the European Council, in agreement with the United Kingdom, unanimously agreed to extend the deadline to May 22, 2019, if the U.K. Parliament approves in an upcoming vote the withdrawal agreement agreed to between the United Kingdom and the European Union in November 2018, and to April 12, 2019, if the U.K. Parliament does not approve it. If no formal withdrawal agreement is reached between the United Kingdom and the European Union, then it is expected the United Kingdom's membership of the European Union will automatically terminate two years after the submission of the notification of the United Kingdom's intention to withdraw from the European Union. Discussions between the United Kingdom and the European Union focused on finalizing withdrawal issues and transition agreements are ongoing. However, limited progress to date in these negotiations and ongoing uncertainty within the U.K. Government and Parliament sustains the possibility of the United Kingdom leaving the European Union on April 12, 2019, without a withdrawal agreement and associated transition period in place, which is likely to cause significant market and economic disruption.

Our failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed in these other jurisdictions, and any approval we are granted for our product candidates in the United States and Europe would not assure approval of our product candidates in other jurisdictions.

In order to market and sell ridinilazole and our other product candidates in foreign jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements in those jurisdictions. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ from that required to obtain FDA or EMA approval. The regulatory approval process outside the United States and Europe generally includes all of the risks associated with obtaining FDA and EMA approval. In addition, some countries outside the United States and Europe require approval of the sales price of a drug before it can be marketed. In many countries, separate procedures must be followed to obtain reimbursement. We may not obtain marketing, pricing or reimbursement approvals outside the United States and Europe on a timely basis, if at all. Approval by the FDA or the EMA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States and Europe does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA or the EMA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market. Marketing approvals in countries outside the United States and Europe do not ensure pricing approvals in those countries or in any other countries, and marketing approvals and pricing approvals do not ensure that reimbursement will be obtained.

Our ability to obtain and maintain conditional marketing authorizations in the European Union is limited to specific circumstances and subject to several conditions and obligations. A failure to renew any conditional approval that we obtain prior to full approval for the applicable indication would prevent us from continuing to market our products.

Conditional marketing authorizations based on incomplete clinical data may be granted for a limited number of listed medicinal products for human use, including products designated as orphan medicinal products under E.U. law, if (1) the risk-benefit balance of the product is positive, (2) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (3) unmet medical needs will be fulfilled and (4) the benefit to public health of the immediate availability on the market of the medicinal product outweighs the risk inherent in the fact that additional data are still required. Specific obligations, including with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data, may be specified in the conditional marketing authorization. Conditional marketing authorizations are valid for one year and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions. Even if we, or a third-party collaborator, obtain conditional approval for ridinilazole for the treatment of CDI, or any other product candidate, we or they may not be able to renew such conditional approval.

Even if we obtain marketing approvals for our product candidates, the terms of approvals and ongoing regulation of our products may limit how we manufacture and market our products and compliance with such requirements may involve substantial resources, which could materially impair our ability to generate revenue.

Even if marketing approval of a product candidate is granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation, including the requirement to implement a risk evaluation and mitigation strategy or to conduct costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. We and our collaborators must also comply with requirements concerning advertising and promotion for any of our product candidates for which we obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, neither we nor our collaborators will be able to promote any products we develop for indications or uses for which they are not approved. In addition, manufacturers of approved products and those manufacturers' facilities are required to ensure that quality control and manufacturing procedures conform to cGMP, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We and our contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMP.

Accordingly, assuming we receive marketing approval for one or more of our product candidates, we and our contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we are not able to comply with post-approval regulatory requirements, we could have the marketing approvals for our products withdrawn by regulatory authorities and our ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Thus, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Any product candidate for which we obtain marketing approval will be subject to strict enforcement of post-marketing requirements and we could be subject to substantial penalties, including withdrawal of our product from the market, if we fail to comply with all regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include, but are not limited to, restrictions governing promotion of an approved product, submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping.

The FDA and other federal and state agencies, including the Department of Justice, or DOJ, closely regulate compliance with all requirements governing prescription drug products, including requirements pertaining to marketing and promotion of drugs in accordance with the provisions of the approved labeling and manufacturing of products in accordance with cGMP requirements. The FDA and DOJ impose stringent restrictions on manufacturers' communications regarding off-label use, and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing. Violations of such requirements may lead to investigations alleging violations of the Food, Drug and Cosmetic Act and other statutes, including the False Claims Act and other federal and state health care fraud and abuse laws as well as state consumer protection laws. Our failure to comply with all regulatory requirements, and later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, may yield various results, including:

- litigation involving patients taking our products;
- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of our products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Non-compliance by us or any future collaborator with regulatory requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with regulatory requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Non-compliance with E.U. requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the European Union's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Fast track designation by the FDA may not actually lead to a faster development or regulatory review or approval process.

If a drug is intended for the treatment of a serious or life threatening condition and the drug demonstrates the potential to address unmet medical need for this condition, the drug sponsor may apply for FDA fast track designation. The FDA has granted fast track designation for ridinilazole. However, a fast track designation does not ensure that ridinilazole will receive marketing approval or that approval will be granted within any particular timeframe. We may also seek fast track designation for other product candidates. Even if the FDA grants fast track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. In addition, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast track designation alone does not guarantee qualification for the FDA's priority review procedures.

Priority review designation by the FDA may not lead to a faster regulatory review or approval process and, in any event, does not assure FDA approval of our product candidates.

If the FDA determines that a product candidate offers major advances in treatment or provides a treatment where no adequate therapy exists, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. Because the FDA designated ridinilazole as a qualified infectious disease product, or QIDP, ridinilazole also will receive priority review. We may also request priority review for other product candidates. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a priority review designation does not necessarily mean a faster regulatory review process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or thereafter.

The efforts of the Trump Administration to pursue regulatory reform may limit the FDA's ability to engage in oversight and implementation activities in the normal course, and that could negatively impact our business.

The Trump Administration has taken several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. On January 30, 2017, President Trump issued an executive order, applicable to all executive agencies, including the FDA, that requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This executive order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the executive order requires agencies to identify regulations to offset any incremental cost of a new regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within the Office of Management and on February 2, 2017, the administration indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Our relationships with customers, healthcare providers and professionals and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any product candidates, including ridinilazole, for which we obtain marketing approval. Our future arrangements with customers, healthcare providers and professionals and third-party payors may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include, and are not limited to, the following:

- The federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federally funded healthcare programs such as Medicare and Medicaid. This statute has been broadly interpreted to apply to manufacturer arrangements with prescribers, purchasers and formulary managers, among others. Several other countries, including the United Kingdom, have enacted similar anti-kickback, fraud and abuse, and healthcare laws and regulations.

- The federal False Claims Act imposes civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. The government and qui tam relators have brought False Claims Act actions against pharmaceutical companies on the theory that their practices have caused false claims to be submitted to the government. There is also a separate false claims provision imposing criminal penalties.

- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.

- HIPAA also imposes criminal liability for knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services.

- The federal Physician Sunshine Act requirements under the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, referred to together as the Affordable Care Act, require manufacturers of drugs, devices, biologics and medical supplies to report to the Department of Health and Human Services information related to payments and other transfers of value made to or at the request of covered recipients, such as physicians and teaching hospitals, and physician ownership and investment interests in such manufacturers. Payments made to physicians and research institutions for clinical trials are included within the ambit of this law.

- Analogous state laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. Additionally, some state and local laws require the registration of pharmaceutical sales representatives in the jurisdiction.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. Exclusion, suspension and debarment from government funded healthcare programs would significantly impact our ability to commercialize, sell or distribute any drug. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Current and future legislation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been and continue to be a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any future collaborators, to profitably sell any products for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any future collaborators, may receive for any approved products.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA. Among the provisions of the ACA of potential importance to our business and our product candidates are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (and 70% starting January 1, 2019) point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and, due to subsequent legislative amendments to the statute, will stay in effect through 2027 unless additional congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

Since enactment of the ACA, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Act, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Further, each chamber of the Congress has put forth multiple bills designed to repeal or repeal and replace portions of the ACA. Although none of these measures has been enacted by Congress to date, Congress may consider other legislation to repeal and replace elements of the ACA. The Congress will likely consider other legislation to replace elements of the ACA, during the next Congressional session. It is possible that repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. While the timing and scope of any potential future legislation to repeal and replace ACA provisions is highly uncertain in many respects, it is also possible that some of the ACA provisions that generally are not favorable for the research-based pharmaceutical industry could also be repealed along with the ACA coverage expansion provision. We will continue to evaluate the effect that the ACA and its possible repeal and replacement could have on our business.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, or HHS, has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known.

We expect that these healthcare reforms, 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, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

The costs of prescription pharmaceuticals has also been the subject of considerable discussion in the United States, and members of Congress and the Trump Administration have stated that they will address such costs through new legislative and administrative measures. To date, there have been several recent U.S. congressional inquiries and proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, the Trump Administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump Administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

Specifically, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the Trump Administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. For example, on May 11, 2018, the Trump Administration issued a plan to lower drug prices. Under this blueprint for action, the Trump Administration indicated that HHS will: take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies; advance biosimilars and generics to boost price competition; evaluate the inclusion of prices in drug makers' ads to enhance price competition; speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers; avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid; work to give Part D plan sponsors more negotiation power with drug makers; examine which Medicare Part B drugs could be negotiated for a lower price by Part D plans, and improving the design of the Part B Competitive Acquisition Program; update Medicare's drug-pricing dashboard to increase transparency; prohibit Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance; and require that Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases. More recently, on January 31, 2019, the HHS Office of Inspector General proposed modifications to the federal Anti-Kickback Statute discount safe harbor for the purpose of reducing the cost of drug products to consumers which, among other things, if finalized, will affect discounts paid by manufacturers to Medicare Part D plans, Medicaid managed care organizations and pharmacy benefit managers working with these organizations.

At the state level, individual states are increasingly aggressive in 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. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Legislative and regulatory proposals have also been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us and any future collaborators to more stringent product labeling and post-marketing testing and other requirements.

In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our products. In addition to continuing pressure on prices and cost containment measures, legislative developments at the European Union or member state level may result in significant additional requirements or obstacles that may increase our operating costs.

We are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures and legal expenses, which could adversely affect our business, results of operations and financial condition.

Our operations are subject to anti-corruption laws, including the U.K. Bribery Act 2010, or Bribery Act, the U.S. Foreign Corrupt Practices Act, or FCPA, and other anti-corruption laws that apply in countries where we do business and may do business in the future. The Bribery Act, FCPA and these other laws generally prohibit us, our officers, and our employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. We may in the future operate in jurisdictions that pose a high risk of potential Bribery Act or FCPA violations, and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the Bribery Act, FCPA or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United Kingdom and the United States, and authorities in the European Union, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, collectively referred to as the Trade Control laws.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the Bribery Act, the FCPA or other legal requirements, including Trade Control laws. If we are not in compliance with the Bribery Act, the FCPA and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have an adverse impact on our business, financial condition, results of operations and liquidity. Likewise, any investigation of any potential violations of the Bribery Act, the FCPA, other anti-corruption laws or Trade Control laws by U.K., U.S. or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain our chief executive officer and other key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on the principal members of our executive and scientific teams, including Glyn Edwards, our Chief Executive Officer, Dr. David Roblin, our Chief Operating Officer, Chief Medical Officer and President of Research and Development, and Daniel Elger, our Chief Commercial Officer and Senior Vice President, Research and Development. Although we have formal employment agreements with each of our executive officers, these agreements do not prevent our executives from terminating their employment with us at any time. We do not maintain “key person” insurance on any of our executive officers. The unplanned loss of the services of any of these persons could materially impact the achievement of our research, development and commercialization objectives.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel, including in the United States where we plan to continue to expand our physical presence, will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous biotechnology and pharmaceutical companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

We expect to expand our development, regulatory and sales and marketing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs and sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Our employees may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA or Office of Inspector General regulations or similar regulations of comparable non-U.S. regulatory authorities, provide accurate information to the FDA or comparable non-U.S. regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable non-U.S. regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Similar employee fraud or misconduct could occur with respect to reimbursement requests and other reports we are required to submit to BARDA or CARB-X. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation, or a request for the reimbursement of expenses that were not incurred, which could cause BARDA or CARB-X to terminate our contract with them. 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 be in compliance with such laws, standards 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.

Risks Related to Ownership of the American Depositary Shares and our Ordinary Shares

The prices of the ADSs and our ordinary shares may be volatile and fluctuate substantially, which could result in substantial losses for holders of the ADSs and our ordinary shares.

The market prices of the ADSs on the Nasdaq Global Market and of our ordinary shares on the AIM market of the London Stock Exchange may be volatile and fluctuate substantially. The stock market in general and the market for smaller pharmaceutical and biotechnology 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, holders of the ADSs and our ordinary shares may not be able to sell their ADSs or ordinary shares at or above the price at which they were purchased. The market price for the ADSs and ordinary shares may be influenced by many factors, including:

- the success of competitive products or technologies;
- results of clinical trials of ridinilazole and any other product candidate that we develop;
- results of clinical trials of product candidates of our competitors;
- changes or developments in laws or regulations applicable to ridinilazole and any other product candidates that we develop;
- our entry into, and the success of, any collaboration agreements with third parties;
- the operation of our contract with BARDA, and whether BARDA elects to pursue its remaining option work segments beyond the base period;
- the operation of our contract with CARB-X, and whether CARB-X elects to pursue its remaining option work segments beyond the base period;
- 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 product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates, products or technologies;
- 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 biotechnology and pharmaceutical sectors;

- regulatory or legal developments in the United States and other countries;
- general economic, industry and market conditions;
- the trading volume of ADSs on the Nasdaq Global Market and of our ordinary shares on AIM; and
- the other factors described in this "Risk Factors" section.

The dual listing of our ordinary shares and the ADSs may adversely affect the liquidity and value of the ADSs.

The ADSs are traded on the Nasdaq Global Market, and our ordinary shares are listed on AIM. The dual listing of our ordinary shares and the ADSs may dilute the liquidity of these securities in one or both markets and may adversely affect the maintenance of an active trading market for the ADSs in the United States. The price of the ADSs could also be adversely affected by trading in our ordinary shares on AIM. Although our ordinary shares are currently listed on AIM, we may decide at some point in the future to delist our ordinary shares from AIM, and our ordinary shareholders may approve such delisting. We cannot predict the effect such delisting of our ordinary shares on AIM would have on the market price of the ADSs on the Nasdaq Global Market.

Securities traded on AIM may carry a higher risk than shares traded on other exchanges that may impact the value of your investment.

Our ordinary shares are currently traded on AIM. Investment in equities traded on AIM is perceived by some to carry a higher risk than an investment in equities quoted on exchanges with more stringent listing requirements, such as the London Stock Exchange, New York Stock Exchange or the Nasdaq Stock Market. This is because AIM imposes less stringent corporate governance and ongoing reporting requirements than those other exchanges. In addition, AIM requires only semi-annual, rather than quarterly, financial reporting. You should be aware that 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-listed 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 underlying the ADSs may not reflect the underlying value of our company.

Substantial future sales of our ordinary shares or the ADSs in the public market, or the perception that these sales could occur, could cause the price of the ADSs to decline significantly, even if our business is doing well.

Sales of a substantial number of our ordinary shares or ADSs in the public market could occur at any time. These sales, or the perception in the market that these sales could occur, could cause the market price of the ADSs and our ordinary shares to decline. Other than the 2,934,272 ordinary shares we issued in connection with our acquisition of Discuva, which are subject to an orderly sale arrangement limiting the sale of such ordinary shares during the twelve-month period ending September 23, 2019, and the 15,625,000 ADSs, representing an aggregate of 78,125,000 ordinary shares, purchased by Mr. Robert W. Duggan, or the Investor, in January 2019, which are subject to a lock-up restriction expiring on January 9, 2020, the ordinary shares and ADSs held by our major shareholders are available for sale and are not subject to contractual and legal restrictions on resale.

Notwithstanding the lock-up restriction on the ADSs held by the Investor, we have agreed to use commercially reasonable efforts to prepare and file a registration statement covering the resale by the Investor of the ADSs purchased by the Investor in January 2019 promptly following the date that is 180 days after January 9, 2019, but no later than 210 days after January 9, 2019. Furthermore, we have agreed to use commercially reasonable efforts to cause such registration statement to become effective as soon as practicable after its filing and to keep such registration statement continuously effective, subject to certain limited exceptions, until the earliest of the date on which all ADSs covered by such registration statement have been sold or may be resold pursuant to Rule 144 of the Securities Act of 1933 without restriction, or the fifth anniversary of January 9, 2019. The Investor is restricted from selling his ADSs until the lock-up restriction ends on January 9, 2020, or such earlier time as we and the Investor mutually agree in writing to terminate the lock-up restriction. If the Investor, any of our directors, officers or other major shareholders seek to sell substantial amounts of ADSs or ordinary shares, particularly if these sales are in a rapid or disorderly manner, or other investors perceive that these sales could occur, the market price of the ADSs and our ordinary shares could decrease significantly.

Holders of ADSs may not have the same voting rights as the holders of our ordinary shares and may not receive voting materials in time to be able to exercise their right to vote.

Except as provided in the deposit agreement relating to the ADSs, holders of the ADSs will not be able to exercise voting rights attaching to the ordinary shares evidenced by the ADSs. Holders of the ADSs will have the right to instruct the depositary with respect to the voting of the ordinary shares represented by the ADSs. If we tell the depositary to solicit your voting instructions, the depositary is required to endeavor to carry out your instructions. If we do not tell the depositary to solicit your voting instructions (and we are not required to do so), you can still send instructions, and, in that case, the depositary may, but is not required to, carry out those instructions. You may not 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.

As a foreign private issuer, we are exempt from a number of rules under the U.S. securities laws and are permitted to file less information with the Securities and Exchange Commission than U.S. companies. This may limit the information available to holders of the ADSs.

We are a "foreign private issuer," as defined in the rules and regulations of the Securities and Exchange Commission, or the SEC, and, consequently, we are not subject to all of the disclosure requirements applicable to companies organized within the United States. For example, we are exempt from certain rules under the U.S. Securities Exchange Act of 1934, as amended, or 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. 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, we are not required to file periodic reports and financial statements with the SEC as frequently or as promptly as U.S. public companies. Accordingly, there may be less publicly available information concerning our company than there is for public companies organized in the United States.

As a foreign private issuer, we will continue to file an annual report on Form 20-F within four months of the close of each fiscal year ending January 31 and reports on Form 6-K relating to certain material events promptly after we publicly announce these events. However, because of the above exemptions for foreign private issuers, our shareholders will not be afforded the same protections or information generally available to investors holding shares in public companies organized in the United States.

As a foreign private issuer, we are not subject to certain Nasdaq corporate governance rules applicable to public companies organized in the United States.

We rely on a provision in the Nasdaq Stock Market's Listed Company Manual that allows us to follow English company law in general and the U.K. Companies Act 2006 in particular with regard to certain aspects of corporate governance. This allows us to follow certain corporate governance practices that differ in significant respects from the corporate governance requirements applicable to U.S. companies listed on the Nasdaq Stock Market.

For example, we are exempt from regulations of the Nasdaq Stock Market that require listed companies organized in the United States to:

- have a majority of the board of directors consist of independent directors;
- require non-management directors to meet on a regular basis without management present;
- adopt a code of conduct and promptly disclose any waivers of the code for directors or executive officers that should address certain specified items;
- have an independent compensation committee;
- have an independent nominating committee
- solicit proxies and provide proxy statements for all shareholder meetings;
- review related party transactions; and
- seek shareholder approval for the implementation of certain equity compensation plans and issuances of ordinary shares.

As a foreign private issuer, we are permitted to follow home country practice in lieu of the above requirements. Accordingly, holders of the ADSs and our ordinary shares may not have the same protections afforded to shareholders of companies that are subject to these Nasdaq Stock Market requirements.

In accordance with our Nasdaq Stock Market listing, our Audit Committee is required to comply with the provisions of Section 301 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and Rule 10A-3 of the Exchange Act, both of which are also applicable to U.S. companies listed on the Nasdaq Stock Market. Because we are a foreign private issuer, however, our Audit Committee is not subject to additional requirements of the Nasdaq Stock Market applicable to listed U.S. companies, including a determination that all members of the Audit Committee are "independent," using more stringent criteria than those applicable to us as a foreign private issuer.

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

As a "foreign private issuer" we are not required to comply with all the periodic disclosure and current reporting requirements of the Exchange Act and related rules and regulations. Under SEC rules, 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 July 31, 2019.

In the future, we would lose our foreign private issuer status if a majority of our ordinary shares (including those represented by ADSs) are owned by U.S. shareholders and 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. The regulatory and compliance costs to us under applicable U.S. securities laws as a U.S. domestic issuer may be significantly higher than our current regulatory and compliance costs. 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, 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 will also have to report our results under U.S. Generally Accepted Accounting Principles, rather than under International Financial Reporting Standards, as a domestic registrant. We will 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 corporate governance practices required for 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 of the Nasdaq Stock Market that are available to foreign private issuers.

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

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company until January 31, 2021, or such earlier time that we are no longer an emerging growth company. 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:

- 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.

We expect to continue to take advantage of some or all of the available exemptions. We cannot predict whether investors will find the ADSs less attractive if we rely on these exemptions. If some investors find the ADSs less attractive as a result, there may be a less active trading market for the ADSs and the market price of the ADSs may be more volatile.

In addition, the JOBS Act also 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 certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

We incur increased costs as a result of operating as a company with ADSs that are publicly traded in the United States, and our management is required to devote substantial time to compliance initiatives.

As a company with ADSs that are publicly traded in the United States, and particularly after we are no longer an "emerging growth company," we have incurred and will continue to incur significant legal, accounting and other expenses that we did not previously incur. In addition, the Sarbanes-Oxley Act, the Dodd-Frank Act, the listing requirements of the Nasdaq Stock Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly.

However, for as long as we remain an emerging growth company, we may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies as described in the preceding risk factor. We may remain an emerging growth company until January 31, 2021, although if the market value of our share capital held by non-affiliates exceeds $700 million as of any July 31 before that time or if we have annual gross revenues of $1.07 billion or more in any fiscal year, we would cease to be an emerging growth company as of January 31 of the applicable year. We also would cease to be an emerging growth company if we issue more than $1.0 billion of non-convertible debt over a three-year period.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, shareholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of the ADSs.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404 of the Sarbanes-Oxley Act, or Section 404, or any subsequent testing by our independent registered public accounting firm, as and when required, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of the ADSs.

Pursuant to Section 404, we are required to furnish a report by our management on our internal control over financial reporting. However, as an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm until we are no longer an emerging growth company. To achieve compliance with Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

We cannot assure you that we will not be classified as a passive foreign investment company for any taxable year, which may result in adverse U.S. federal income tax consequences to U.S. holders.

Based on our estimated gross income, the average value of our gross assets and the nature of our business, taking into account the market price of the ADSs, we do not believe that we were a "passive foreign investment company," or PFIC, for U.S. federal income tax purposes for our tax year ended January 31, 2019, and do not expect to be a PFIC during our tax year ending January 31, 2020. A corporation organized outside the United States generally will be classified as a PFIC for U.S. federal income tax purposes (1) in any taxable year in which at least 75% of its gross income is passive income or on average at least 50% of the gross value of its assets is attributable to assets that produce passive income or are held for the production of passive income and (2) as to a given holder who was a holder in such year and regardless of such corporation's income or asset composition in any subsequent taxable year unless, as to that holder, certain elections are made that can entail substantial tax costs to that holder. Passive income for this purpose generally includes dividends, interest, royalties, rents and gains from commodities and securities transactions. Our status in any taxable year will depend on our assets and activities in each year, and because this is a factual determination made annually after the end of each taxable year, there can be no assurance that we will not be considered a PFIC for the current taxable year or any future taxable year. The market value of our assets may be determined in large part by reference to the market price of the ADSs and our ordinary shares, which fluctuate and which may fluctuate considerably given that market prices of biotechnology companies have been especially volatile. If we were to be treated as a PFIC for any taxable year during which a U.S. holder held the ADSs, however, certain adverse U.S. federal income tax consequences could apply to the U.S. holder. See "Item 10.E Taxation."

U.S. investors may have difficulty enforcing civil liabilities against us, certain of our directors or members of senior management and the experts named in this Annual Report.

Certain of our directors, members of our senior management and some of the experts named in this Annual Report are non-residents of the United States, and all or a substantial portion of the assets of such persons are located outside the United States. As a result, it may not be possible to serve process on such persons or us in the United States or to enforce judgments obtained in U.S. courts against them or us based on civil liability provisions of the securities laws of the United States. Further, there is doubt as to whether English courts would enforce certain civil liabilities under U.S. securities laws pursuant to judgments of U.S. courts based upon these civil liability provisions. In addition, awards of punitive damages in actions brought in the United States or elsewhere may be unenforceable in the United Kingdom. An award for monetary damages under the U.S. securities laws would be considered punitive if it does not seek to compensate the claimant for loss or damage suffered and is intended to punish the defendant. The enforceability of any judgment in the United Kingdom will depend on the particular facts of the case as well as the laws and treaties in effect at the time. The United States and the United Kingdom do not currently have a treaty providing for recognition and enforcement of judgments (other than arbitration awards) in civil and commercial matters.

The rights of our shareholders may differ from the rights typically offered to shareholders of a U.S. corporation.

We are incorporated under U.K. law. The rights of holders of ordinary shares and, therefore, certain of the rights of holders of ADSs, are governed by U.K. law, including the provisions of the Companies Act 2006, and by our Articles of Association. These rights differ in certain respects from the rights of shareholders in typical U.S. corporations.

Holders of ordinary shares and ADSs may not receive a return on their ordinary shares or ADSs other than through the sale of their ordinary shares or ADSs.

Under current U.K. 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 not paid dividends in the past on our ordinary shares. We intend to retain earnings, if any, for use in our business and do not anticipate paying any cash dividends in the foreseeable future. Accordingly, other than through the sale of the ADSs or our ordinary shares, holders of such securities are unlikely to receive a return in the foreseeable future.

Holders of ADSs 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 such holders.

The depositary for the ADSs has agreed to pay to holders of the ADSs or distribute 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. Holders of ADSs will receive these distributions in proportion to the number of our ordinary shares such 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 the ADSs. We have no obligation to take any other action to permit the distribution of the ADSs, ordinary shares, rights or anything else to holders of the ADSs. This means that holders of the ADSs 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 such holders. These restrictions may have a material adverse effect on the value of the ADSs.

Our executive officers, directors and principal shareholders maintain the ability to control or significantly influence all matters submitted to stockholders for approval.

As of March 1, 2019, our executive officers, directors and principal shareholders beneficially owned, in the aggregate, ordinary shares and ADSs representing approximately 65.82% of our outstanding share capital. In particular, as of March 1, 2019, the Investor beneficially owned 48.81% of our outstanding share capital following his subscription of ADSs in January 2019. We entered into a relationship agreement, or the relationship agreement, with the Investor and Cairn Financial Advisers LLP, as our nominated adviser, on December 14, 2018, to regulate our relationship with the Investor and to limit the Investor's influence over our corporate actions and activities and the outcome of general matters pertaining to us. Specifically, the Investor agreed to, among other things, exercise his voting rights to ensure that we are capable of carrying on our business and making decisions independently of the Investor and his affiliates and abstain from voting on any resolution containing any transaction, agreement or arrangement involving us or our subsidiaries to which the Investor or any of his affiliates is a party. For more information about the relationship agreement, see "Item 7.B Related Party Transactions." However, we cannot assure you that we will be able to operate completely independently of the Investor, despite the relationship agreement. If the Investor and the other shareholders mentioned above were to choose to act together, they would be able to control or significantly influence all matters submitted to our shareholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control or significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. In addition, the Investor would be able to unilaterally prevent the passing of any special resolution proposed at a general meeting of company, as the passing of any special resolution requires a three-quarters majority of votes cast. This concentration of voting power could delay or prevent an acquisition of our company on terms that other holders of ADSs and ordinary shares may desire.

In addition, and in accordance with the terms of our articles of association, our board maintains a classified board structure such that not all members of the board are elected at one time. All of our directors are subject to election by our shareholders at the first annual general meeting after their appointment to our board and to re-election by our shareholders at least once every three years thereafter. Because our board of directors is responsible for appointing the members of our management team, this structure may frustrate or prevent any attempts by our shareholders to replace or remove our current management by making it more difficult for shareholders to replace members of our board of directors.

If equity research analysts stop publishing research or reports about our business or if they issue unfavorable commentary or downgrade the ADSs or our ordinary shares, the prices of the ADSs or our ordinary shares could decline.

The trading market for the ADSs and our ordinary shares relies in part on the research and reports that equity research analysts publish about us and our business. We do not control these analysts. The price of the ADSs or our ordinary shares could decline if one or more equity research analysts downgrades such securities or if analysts issue other unfavorable commentary about us or our business. In addition, if one or more of these analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause the trading prices and trading volumes of the ADSs and our ordinary shares to decline.

We are exposed to risks related to currency exchange rates.

We conduct a significant portion of our operations outside of the United Kingdom. Because our financial statements are presented in pounds sterling, changes in currency exchange rates have had and could have a significant effect on our operating results when our operating results are translated into U.S. dollars. Exchange rate fluctuations between local currencies and the pound sterling create risk in several ways, including the following: weakening of the pound sterling may increase the pound sterling cost of overseas research and development expenses and the cost of sourced product components outside the United Kingdom; strengthening of the pound sterling may decrease the value of our revenues denominated in other currencies; the exchange rates on non-sterling transactions and cash deposits can distort our financial results; and commercial pricing and profit margins are affected by currency fluctuations.

We have broad discretion in the use of our cash and cash equivalents and may not use them effectively.

Our management has broad discretion in the use of our cash and cash equivalents and could spend our cash in ways that do not improve our results of operations or enhance the value of the ADSs and ordinary shares. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the market price of the ADSs and ordinary shares to decline and delay the development of our product candidates.

Item 4: Information on the Company

A. History and Development of the Company

We were founded in 2003 and are a public limited company incorporated under the laws of England and Wales with the Registrar of Companies of England and Wales, United Kingdom. Our principal office is located at 136a Eastern Avenue, Milton Park, Abingdon, Oxfordshire, OX14 4SB, and our telephone number is +(44) 1235 443 939. Our U.S. operations are conducted by our wholly owned subsidiary Summit Therapeutics Inc., a Delaware corporation. Our ordinary shares have traded on AIM, which is a sub-market of the London Stock Exchange, since October, 2004, under the symbol "SUMM" and our American Depositary Shares have traded on the Nasdaq Global Market since March 2015, under the symbol "SMMT."

Our website address is www.summitplc.com. The information contained on, or that can be accessed from, our website does not form part of this Annual Report. Our agent for service of process in the United States is C T Corporation System, 111 Eighth Avenue, New York, New York 10011.

In the three-year period ended January 31, 2019, we have invested a total of £0.7 million in equipment and facilities.

The U.S. Securities and Exchange Commission, or SEC, maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of the SEC's Internet site is http://www.sec.gov.

For additional information relating to the development of our company, see "Item 4 B. Information on the Company – Business." For additional information relating to our capital expenditures, see "Item 5 A. Operating Results."

B. Business

Overview

We are a biopharmaceutical company focused on the discovery, development and commercialization of novel antibiotics for serious infectious diseases. We are conducting a Phase 3 clinical program focused on the infectious disease *Clostridium difficile* infection, or CDI. We are also seeking to expand our product candidate portfolio through the development of new mechanism antibiotics using our proprietary Discuva Platform.

Ridinilazole for Clostridium difficile Infection

Our lead CDI product candidate is ridinilazole (formerly SMT19969), an orally administered small molecule antibiotic. We dosed the first patient in our Phase 3 clinical trials of ridinilazole for CDI in February 2019. The Phase 3 clinical program consists of two Phase 3 clinical trials that are each designed to assess, as their primary endpoint, the superiority of ridinilazole compared to vancomycin in sustained clinical response, or SCR, which is defined as clinical cure based on the resolution of diarrhea at the assessment of cure, or AOC, visit on day 12 and no recurrence of CDI within 30 days after the end of treatment. We have also included other endpoints as well as health economic outcome measures. We expect to report top-line results from both Phase 3 clinical trials of ridinilazole in the second half of 2021.

Ridinilazole is designed to selectively target *Clostridium difficile*, or *C. difficile*, bacteria without causing collateral damage to the gut flora and thereby reduce CDI recurrence rates, which is the key clinical issue in the disease. The FDA has designated ridinilazole as a qualified infectious disease product, or QIDP, and the FDA granted ridinilazole fast track designation. In 2013, the Centers for Disease Control and Prevention of the U.S. Department of Health and Human Services, or CDC, highlighted CDI as one of three pathogens that pose an immediate public health threat and require urgent and aggressive action.

CDI is a bacterial infection of the colon that produces toxins causing inflammation of the colon and severe diarrhea. CDI can also result in more serious disease complications, including pseudomembranous colitis, bowel perforation, toxic megacolon and sepsis. CDI typically develops following the use of broad-spectrum antibiotics that can cause widespread damage to the natural gut flora and allow overgrowth of *C. difficile* bacteria. CDI represents a serious healthcare issue in hospitals, long-term care homes and, increasingly, in the wider community.

In November 2015, we reported top-line results from our double blind, randomized, active controlled Phase 2 clinical trial that evaluated ridinilazole compared to the current standard of care, vancomycin, for the treatment of CDI. The Phase 2 clinical trial exceeded its primary endpoint of non-inferiority, with ridinilazole achieving statistical superiority over vancomycin in SCR. The statistical superiority was driven by a large numerical reduction in recurrent disease compared with vancomycin. We subsequently reported that data from our Phase 2 clinical trial of ridinilazole showed ridinilazole to be highly preserving of the gut microbiome compared to patients who received vancomycin and experienced substantial damage to their gut microbiome that for many patients persisted during the 30-day post-treatment period. Ridinilazole was well tolerated at all doses tested in the Phase 2 clinical trial.

We have been awarded a contract from Biomedical Advanced Research and Development Authority, or BARDA, an agency of the U.S. government's Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response worth up to $62 million that will, in part, fund our ongoing Phase 3 clinical trials and potential regulatory applications for marketing approval for ridinilazole in the United States. We have also entered into a license and commercialization agreement with Eurofarma Laboratórios S.A., or Eurofarma, pursuant to which we granted to Eurofarma exclusive rights to commercialize ridinilazole in specified countries in South America, Central America and the Caribbean. We have retained commercial rights to ridinilazole for the treatment of CDI in the rest of the world.

Infectious Disease Pipeline

Our goal is to build a franchise in the field of infectious diseases through the discovery and development of new antibiotics focused on treating patients with serious bacterial infections where there is a substantial unmet need and where we believe we have the ability to show meaningful advantages over current treatments. Our focus is on pathogens that represent serious healthcare threats.

Discuva Platform

In December 2017, we expanded our activities in the field of infectious diseases with the acquisition of Discuva Limited, a privately held U.K.-based company. Through this acquisition, we obtained a bacterial genetics-based technology which we call our Discuva Platform, and which facilitates the discovery and development of new mechanism antibiotics. Our Discuva Platform can be used to help elucidate new bacterial targets for drug discovery, understand the mechanism of action of antibiotics and optimize preclinical antibiotic candidates against the propensity to develop bacterial resistance. We are using our Discuva Platform to support our plan to expand our antibiotic product candidate portfolio.

Neisseria gonorrhoeae program

We are currently developing a preclinical program targeting infections caused by the bacteria *Neisseria gonorrhoeae*, or *N. gonorrhoeae*. We have used our Discuva Platform to identify two new bacterial targets for the potential treatment of gonorrhea. There is a pressing need for novel antibiotics targeting gonorrhea due to increasing antibiotic resistance and a lack of new treatments. Gonorrhea has been identified as one of three urgent threats by the CDC and is classified as a high priority pathogen by the World Health Organization, or WHO. In September 2018, we nominated SMT-571 as a preclinical candidate to advance into investigational new drug, or IND, -enabling studies. We expect to commence a Phase 1 clinical trial of SMT-571 in the second half of 2019. In July 2018, we were granted a sub-award of up to $4.5 million from the Trustees of Boston University under the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator program, or CARB-X.

ESKAPE program

We announced in September 2018 the initiation of a discovery stage program against the group of pathogens that are commonly referred to as ESKAPE pathogens. The ESKAPE pathogens collectively comprise the leading cause of hospital acquired infections globally and are subject to increasing rates of resistance to existing antibiotic classes. We have used our Discuva Platform to discover multiple new mechanism antibiotic compounds with activity against different ESKAPE pathogens. We continue to use our Discuva Platform to support our research activities aimed at identifying potential preclinical candidates.

Our Product Development Pipeline

The following table summarizes our product development pipeline. We are also developing an earlier stage pipeline of antibiotic compounds for serious bacterial infections.

Program	Preclinical	Phase 1	Phase 2	Phase 3	Remarks
***Clostridium difficile* Infection**					
Ridinilazole* (formerly SMT19969)	*Qualified Infectious Disease Product Designation (FDA)* *Fast Track Designation (FDA)*				Expect to report top-line data from two ongoing Phase 3 clinical trials in the second half of 2021.
***Neisseria gonorrhoeae* Infections**					
SMT-571					Expect to commence Phase 1 clinical trial in the second half of 2019.

* We have granted Eurofarma an exclusive license to the commercial rights for ridinilazole in specified countries in South America, Central America and the Caribbean. We retain commercialization rights in the rest of the world.

Our Strategy

Our goal is to become a fully integrated biopharmaceutical company focused on the discovery, development and commercialization of novel antibiotics for the treatment of serious infectious diseases. Our most advanced program targets *C. difficile* infection, and we have an emerging pipeline of new mechanism antibiotics. The key elements of our strategy to achieve this goal are:

Rapidly advance the development of our lead product candidate ridinilazole for the treatment of CDI.

We are focusing our resources and business efforts primarily on rapidly advancing the development of ridinilazole for the treatment of CDI. We are currently conducting two global Phase 3 clinical trials that are evaluating the benefits of ridinilazole compared to the current standard of care antibiotic vancomycin by testing for superiority in the endpoint of sustained clinical response. We expect to report top-line results from our Phase 3 clinical trials in the second half of 2021.

Commercialize ridinilazole for CDI in the United States with our own sales team.

We hold exclusive commercialization rights for ridinilazole for all indications in the United States. If ridinilazole receives marketing approval, we intend to commercialize it initially in the United States with our own focused, specialized sales force that we plan to establish. We will evaluate our options to maximize the commercial opportunity for ridinilazole in other key territories where we retain exclusive commercialization rights, including Europe and Asia. We have granted the exclusive right to commercialize ridinilazole in certain countries in South America, Central America and the Caribbean to Eurofarma in exchange for an upfront payment and specified development, commercial and sales milestones, as well as specified product supply transfer payments.

Expand our product portfolio of new mechanism antibiotics using our Discuva Platform.

We are focused on expanding our product portfolio through the identification of new mechanism antibiotics that target pathogens that are classified as posing serious or urgent healthcare threats by organizations such as the CDC and WHO. We are using our proprietary Discuva Platform that includes libraries of a wide range of bacteria to facilitate the discovery and development of our new mechanism antibiotic compounds. For example, we are developing SMT-571 as a new mechanism antibiotic for the treatment of infections caused by the bacteria *N. gonorrhoeae*. We nominated SMT-571 as a preclinical candidate to progress into IND-enabling studies in September 2018, and we are planning to commence a Phase 1 clinical trial in the second half of 2019. We are also developing potential new mechanism antibiotics against different bacteria that as a group are collectively referred to as the ESKAPE pathogens.

Maintain and expand our leadership in the field of antibiotic research and development.

We are seeking to apply our existing knowledge and experience to position ourselves as a leader in antibiotic research and development and generate a pipeline of new mechanism antibiotics. We aim to design new mechanism antibiotics that are targeted for the pathogen or infection. We may expand our development capabilities or product pipeline through opportunistically in-licensing or acquiring the rights to complementary products, product candidates or technologies that we believe will enhance our leadership in the field of antibiotic innovation. We believe our strategy will allow us to develop new antibiotics that are able to show meaningful advantages over existing standards of care, which will promote their use in patients and not have them held in reserve. We believe our strategy is aligned with the principals of good antibiotic stewardship.

Seek additional governmental and other third-party grants and support.

We have obtained development funding and other assistance from government entities, philanthropic, non-government and not for profit organizations for our product candidates. For example, the Wellcome Trust Limited provided funding for ridinilazole up until the completion of our Phase 2 proof of concept clinical trial, and BARDA is providing funding, that in part, supports our ongoing Phase 3 clinical trials and regulatory development of ridinilazole. We have also received funding from CARB-X and Innovate UK to support the development of our preclinical programs. We plan to continue to encourage these types of organizations to provide additional funding and support for our development programs.

Antimicrobial Resistance

In 2016, healthcare providers in the United States prescribed 270.2 million antibiotics, a number equivalent to 836 prescriptions per 1,000 persons. The CDC estimates that 50% of these antibiotics are used inappropriately in the outpatient setting, including 30% which are unnecessary for treating the illness.

Overuse and misuse of antibiotics contribute to two serious public health issues: antimicrobial resistance, or AMR, and *C. difficile* infection.

AMR is a natural process that has allowed microbes (bacteria, viruses, fungi and parasites) to survive in their environments for millions of years. As microbes are challenged with antimicrobial substances, some microbes will be able to survive and can pass their AMR genes to the next generation. The overuse and inappropriate use of antimicrobial medicines has increased the rate at which microbes are acquiring AMR.

Approximately 700,000 people die every year from antimicrobial resistant infections. According to the 2016 report, *Tackling Drug-Resistant Infections Globally*, chaired by Jim O'Neill, the number of deaths due to antimicrobial resistant infections is projected to rise to 10 million by 2050, a number that surpasses deaths due to cancer. The rise of AMR could render once easily treated infections untreatable and undermine physicians' abilities to perform surgeries and other medical procedures.

From the 1920s through the 1980s, new classes of antibiotics were discovered and approved for use in patients at a pace where AMR was not considered a clinical issue. However, since the 1990s, there has been a reduction in the number of antibiotics developed. Consequently, AMR has emerged as a serious clinical issue.

Recently approved antibiotics have generally been broad-spectrum analogues of older antibiotics already in use. These antibiotics are not necessarily the most appropriate drug for a given infection and resistance has generally developed quickly after their introduction to the clinic. The Pew Trust regularly publishes a pipeline of antibiotics currently in global clinical development, and in March 2019, this report showed that of the 42 antibiotics in clinical development, 13 antibiotics are in Phase 3 clinical trials, of which only two are new mechanism antibiotics.

Antimicrobial Stewardship

The CDC defines antimicrobial stewardship as ensuring patients receive the right antibiotic at the right dose, at the right time and for the right duration with the goal of improving patient care, more effectively combating AMR and ultimately saving lives. Our strategy for the development of new antibiotics is closely aligned with good antibiotic stewardship. We believe we can design antibiotics for a specific pathogen or infection, allowing physicians to reserve broad-spectrum antibiotics for idiopathic infections. We believe this approach will serve to improve patient outcomes and reduce resistance development.

***Clostridium difficile* Infection Overview**

Clostridium difficile infection is a bacterial infection of the colon that produces toxins causing inflammation of the colon and severe diarrhea. CDI can also result in more serious disease complications, including pseudomembranous colitis, bowel perforation, toxic megacolon and sepsis. CDI represents a serious healthcare issue in hospitals, long-term care homes and, increasingly, in the wider community. We estimate there are over one million cases of CDI each year in the United States and Europe, based on an epidemiology report on CDI that was published in 2015 by Decision Resources, a healthcare research and consulting company. In addition, CDI is associated with approximately 29,000 deaths per year in the United States, according to a study published in the *New England Journal of Medicine* in 2015. A separate study published in 2012 in *Clinical Microbiology and Infection*, a peer reviewed journal published by the European Society of Clinical Microbiology and Infectious Diseases, indicated that CDI may be underdiagnosed in approximately 25% of cases. A study published in *The Journal of Hospital Infection*, a peer reviewed journal published by the Healthcare Infection Society, reported that CDI is two to four times more common than hospital associated infections caused by methicillin-resistant *Staphylococcus aureus*, a bacterium frequently associated with such infections. The Healthcare Cost and Utilization Project, a family of databases developed through a federal-state-industry partnership sponsored by the Agency for Healthcare Research and Quality of the U.S. Department of Health and Human Services, reported an approximate 3.5 fold increase in hospital stays associated with CDI between 2000 and 2008. The economic impact of CDI is significant. A study published in 2016 in *BMC Infectious Diseases* estimated that the total costs attributable to the management of CDI were approximately $6.3 billion per year in the United States based on a review of 42 cost studies of CDI case management that were published between 2005 to 2015.

CDI originates from a bacterium known as *Clostridium difficile*, *Clostridioides difficile* or *C. difficile*. *C. difficile* sometimes can be a harmless resident of the gastrointestinal tract. The complex community of microorganisms that make up the natural gut flora usually moderates levels of *C. difficile*. The natural gut flora are an essential part of the normal function of the gastrointestinal tract and also have wide implications in human health, such as the proper function of the immune system. CDI typically develops following the use of broad spectrum antibiotic agents that can cause widespread damage to the natural gut flora and allow overgrowth of *C. difficile*. Hypervirulent *C. difficile* strains have also emerged and are frequently associated with more severe disease. A paper published in 2018 in the peer-reviewed journal, *American Journal of Infection Control*, reported that in the United States, the hypervirulent strain, ribotype 027, accounts for approximately one-fifth of all CDI cases.

The primary clinical issue with CDI is disease recurrence. This is in contrast to other bacterial threats for which drug resistance is the principal concern. According to an article published in 2012 in the peer reviewed journal *Clinical Microbiology and Infection*, up to 25% of patients with CDI suffer a second episode of the infection. The risk of further recurrence rises to 65% after a patient suffers a third episode of CDI. In addition, each episode of recurrent disease is associated with greater disease severity and higher mortality rates. Recurrent disease is associated with an increased burden on the healthcare system.

In 2013, the CDC highlighted CDI as one of three pathogens that pose an immediate public health threat and require urgent and aggressive action. In 2012, the Generating Antibiotics Incentives Now Act provisions of the FDA Safety and Innovation Act, or GAIN, became law. The goal of GAIN is to encourage the development of new antibiotics that treat specific pathogens, including *C. difficile*, which cause serious and life threatening infections.

Current CDI Treatments

Existing treatment options for CDI are limited. Currently the mostly commonly used treatments for CDI are vancomycin or off label use of metronidazole, both of which are broad-spectrum antibiotics. Broad-spectrum antibiotics may not be the most appropriate treatment for CDI because although the antibiotics reduce levels of *C. difficile*, they also cause significant collateral damage to the gut flora as a result of their broad spectrum of activity. This collateral damage to the gut flora leaves patients vulnerable to recurrent CDI. A review published in 2012 in the peer reviewed journal *International Journal of Antimicrobial Agents* reported recurrence rates of 24.0% for vancomycin and 27.1% for metronidazole. Metronidazole is frequently used in mild or moderate cases of CDI and has been associated with a number of side effects. A narrower spectrum antibiotic fidaxomicin was approved in the United States and the European Union, but it has not been shown to be superior to vancomycin in the treatment of patients with the hypervirulent strain ribotype 027. In October 2016, the FDA approved bezolotoxumab, a monoclonal antibody for use in conjunction with an antibiotic in patients who have a high risk of disease recurrence. Bezolotoxumab binds to toxin B, one of the toxins produced by the *C. difficile* bacteria, to neutralize its effects. In February 2018, updated guidelines on the treatment of CDI in adults and children were published in *Clinical Infectious Diseases* by the Infectious Diseases Society of America and Society for Healthcare Epidemiology of America. These revised guidelines recommend the use of vancomycin or fidaxomicin in preference to metronidazole in the treatment of an initial episode of CDI. Use of metronidazole is only recommended when it is not possible to access vancomycin or fidaxomicin. We believe that the current use of the broad-spectrum antibiotics vancomycin and metronidazole to treat CDI is not aligned with good antibiotic stewardship.

Ridinilazole for the Treatment of CDI

We are developing ridinilazole as an orally administered small molecule antibiotic for the treatment of CDI. Ridinilazole is designed to selectively target *C. difficile* bacteria without causing collateral damage to the gut flora and thereby treat the initial infection and reduce CDI recurrence rates. Ridinilazole promotes good stewardship through its targeted, narrow-spectrum activity and potential to improve patient outcomes. The active ingredient in ridinilazole is a bis-benzimidazole tetrahydrate. We believe, based on preclinical studies conducted to date, that ridinilazole is part of a novel structural class of antibiotics that is distinct from the major classes of marketed antibiotics.

We are conducting a Phase 3 clinical program that is evaluating the benefits of ridinilazole compared to the current standard of care antibiotic, vancomycin, in patients with CDI. Our Phase 3 clinical program comprises two randomized, double blind, active controlled, multicenter Phase 3 clinical trials with the primary endpoint in both trials testing for superiority in sustained clinical response, or SCR, which is defined as clinical cure based on the resolution of diarrhea at the assessment of cure, or AOC, visit on day 12 and no recurrence of CDI within 30 days after the end of treatment. We dosed the first patient in our Phase 3 clinical trials in February 2019. We expect to report top-line results from both Phase 3 clinical trials in the second half of 2021.

In November 2015, we reported top-line results from our double blind, randomized, active controlled Phase 2 clinical trial that evaluated ridinilazole compared to the current standard of care, vancomycin, for the treatment of CDI. The Phase 2 clinical trial exceeded its primary endpoint of non-inferiority, with ridinilazole achieving statistical superiority over vancomycin in SCR. The statistical superiority was driven by a large numerical reduction in recurrent disease compared with vancomycin. We subsequently reported that data from our Phase 2 clinical trial also showed ridinilazole to be highly preserving of the gut microbiome compared to patients who received vancomycin and experienced substantial damage to the gut microbiome which for many patients persisted during the 30-day post-treatment period. In September 2017, we reported top-line data from our exploratory, open label, active controlled Phase 2 clinical trial evaluating ridinilazole compared to fidaxomicin for the treatment of CDI. In the trial, ridinilazole preserved the gut microbiome of CDI patients to a greater extent than fidaxomicin, achieving a key secondary endpoint. Ridinilazole was well tolerated at all doses tested in our completed Phase 1 and Phase 2 clinical trials.

We have been awarded a contract from BARDA worth up to $62 million that will, in part, fund our ongoing Phase 3 clinical trials of ridinilazole. We have also received $2.5 million upfront as part of our license and commercialization agreement with Eurofarma Laboratórios S.A., or Eurofarma, pursuant to which we granted to Eurofarma exclusive rights to commercialize ridinilazole in specified countries in South America, Central America and the Caribbean and are eligible to receive an additional $3.75 million in development milestones upon the achievement of staged patient enrollment targets in our ongoing Phase 3 clinical trials of ridinilazole. Under our license and commercialization agreement with Eurofarma, we are also eligible to receive up to an additional $21.4 million through other development milestones, commercial milestones, and one-time sales milestones based on cumulative net sales up to $100 million in the licensed territory, as well as specified product supply transfer payments. We have retained commercial rights to ridinilazole for the treatment of CDI in the rest of the world.

The FDA has designated ridinilazole as a qualified infectious disease product, or QIDP. The QIDP incentives are provided through GAIN. The QIDP designation provides for priority review by the FDA, eligibility for “fast track” designation and extension of statutory exclusivity periods in the United States for an additional five years upon FDA approval of the product for the treatment of CDI. The FDA granted fast track designation to ridinilazole in July 2015.

Ridinilazole Clinical Development

Phase 3 Clinical Trial Program

We are currently evaluating ridinilazole in two randomized, double blind, active controlled, multicenter Phase 3 clinical trials in patients with CDI. We refer to these two Phase 3 clinical trials as "Ri-CoDIFy 1" and "Ri-CoDIFy 2." We plan to conduct the Phase 3 clinical trials at approximately 300 sites located in United States, Europe, South America, Central America, Australia, South Korea and Israel. We expect to enroll up to 680 patients into each of the Phase 3 clinical trials, and we enrolled the first patient in February 2019. We expect to report top-line results from the two Phase 3 clinical trials of ridinilazole during the second half of 2021.

In the trials, we are randomizing patients in a one to one ratio to receive either a 200 mg dose of ridinilazole administered twice per day for ten days or a 125 mg dose of vancomycin administered four times per day for ten days. Due to the different treatment regimens, we have also developed dummy placebos that will be administered to the patients in the Phase 3 clinical trials according to a schedule designed to maintain the blind within each trial. Enrolled patients must be 18 years of age or older, have a confirmed diagnosis of CDI as measured by the presence of toxin A and/or toxin B of *C. difficile* in the stool as confirmed by a positive free toxin test, and must not have had more than one prior episode of CDI in the previous three months, or more than three episodes in the prior 12 months.

The primary objective of each of the clinical trials is to measure the efficacy of ten days of dosing with ridinilazole compared to treatment with vancomycin. The primary efficacy endpoint will test for superiority in sustained clinical response, or SCR, which is defined as clinical cure based on the resolution of diarrhea at the assessment of cure, or AOC, visit on day 12 and no recurrence of CDI within 30 days after the end of treatment, or EOT. Secondary endpoints of these clinical trials assess clinical cure at the AOC visit, SCR over 60 days post the EOT and SCR over 90 days post EOT. We will also assess the safety and tolerability of ten days of dosing of ridinilazole compared to vancomycin. We are also evaluating a number of exploratory endpoints including assessing the impact of ridinilazole on the gut flora of patients in the clinical trial. We are also including health economics and outcomes research, or HEOR, measures in the Phase 3 clinical trials. We are including these HEOR measures, as we believe they will help to support the commercial positioning of ridinilazole, if approved.

Phase 2 Clinical Trial in Patients with CDI

In November 2015, we reported top-line results from our randomized, double blind, active controlled, multicenter, Phase 2 clinical trial of ridinilazole in patients with CDI, and we subsequently presented additional data. We have referred to this as our Phase 2 proof of concept clinical trial and as “CoDIFy.”

We conducted this clinical trial at approximately 35 sites in the United States and Canada. The trial was conducted under an Investigational New Drug Application, or IND, that we submitted to the FDA in January 2014. We enrolled a total of 100 patients between 18 to 90 years of age. The trial randomized patients in a one-to-one ratio to receive either a 200 mg dose of ridinilazole administered twice per day for ten days or a 125 mg dose of vancomycin administered four times per day for ten days. Patients who received ridinilazole were also administered a placebo twice a day for ten days to ensure the trial remained blinded.

The primary objective of this clinical trial was to evaluate the efficacy of ten days of dosing with ridinilazole compared to treatment with vancomycin. The primary efficacy endpoint was non-inferiority on sustained clinical response, or SCR, which is defined as clinical cure based on the resolution of diarrhea at the test of cure, or TOC, visit on day 12 and no recurrence of CDI within 30 days after the end of treatment. The secondary efficacy endpoints were investigator assessed clinical response at the TOC visit and rate of recurrence of CDI within 30 days after the end of treatment. Secondary objectives of this clinical trial were the assessment of the safety and tolerability of ten days of dosing of ridinilazole compared to vancomycin, the plasma and fecal concentrations of ridinilazole in patients with CDI who received ridinilazole and the health status of CDI patients who received ten days of treatment of ridinilazole compared to patients who received ten days of treatment of vancomycin. We also assessed the impact of ridinilazole on the gut flora of patients in the clinical trial as one of a number of exploratory objectives.

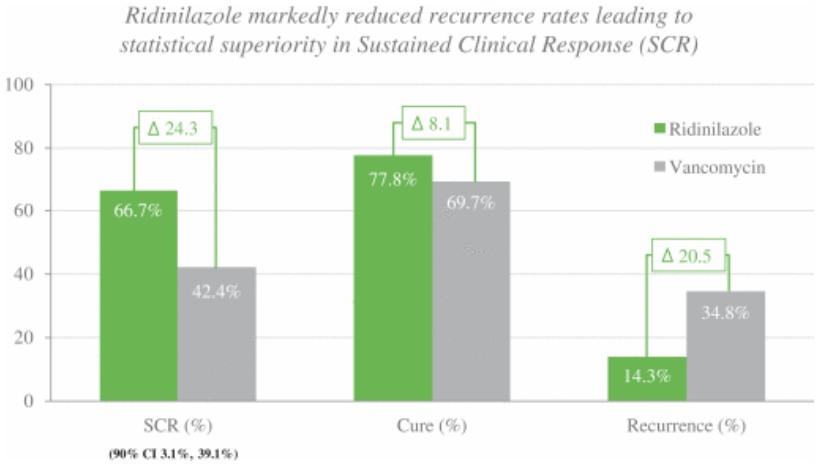
Analysis of Results

We observed the following results in our Phase 2 proof of concept trial:

- ***Ridinilazole Demonstrated Statistical Superiority Over Vancomycin.*** Our Phase 2 proof of concept trial met its primary endpoint with ridinilazole achieving a SCR rate of 66.7% compared to 42.4% for vancomycin (non-inferiority margin of 15%, p=0.0004). This represented statistical superiority of ridinilazole over vancomycin using the pre-specified 90% confidence interval. The primary analysis was conducted on the modified intent-to-treat, or mITT, population (36 patients dosed with ridinilazole, 33 patients dosed with vancomycin) that comprised patients

with CDI confirmed by the presence of free toxin in feces. The results of the mITT population were consistent with the intent-to-treat, or ITT, population (50 patients dosed with ridinilazole, 50 patients dosed with vancomycin) and the per protocol, or PP, population (31 patients dosed with ridinilazole, 25 patients dosed with vancomycin). We also observed a generally consistent trend to improved SCR with ridinilazole across subgroups at higher risk of recurrence, including the elderly, patients who were on concomitant antibiotics at the start of treatment and patients with a prior history of CDI.

- ***Ridinilazole Demonstrated a Large Reduction in Rates of Recurrence Compared to Vancomycin.*** We observed that the statistical superiority in SCR with ridinilazole compared to vancomycin was driven by a large numerical reduction in rates of disease recurrence. Clinical cure rates at the end of ten days of treatment were similar, with ridinilazole achieving a rate of 77.8% compared to 69.7% for vancomycin, but ridinilazole achieved a recurrence rate of 14.3% compared to 34.8% for vancomycin during the 30-day post-treatment period.



- ***Ridinilazole Preserved the Gut Microbiome.*** Stool samples were obtained from 82 patients enrolled in the Phase 2 clinical trial to evaluate the efficacy of ridinilazole compared to vancomycin. These samples were analyzed on study entry, day five and day ten of treatment, day 25 and day 40 post-entry and at the time of any recurrence for five specific bacterial groups associated with a healthy gut microbiome (*Bacteroides*, *Prevotella*, *Enterbactericeae*, *C. coccoides* and *C. leptum*) and also for total bacteria present. We observed that patients treated with vancomycin had a significant decrease ($p<0.001$) in four of the five bacterial groups (*Bacteroides*, *Prevotella*, *C. coccoides* and *C. leptum*) at day five and day ten, and a significant decrease in total bacteria. Patients treated with ridinilazole did not have a significant decrease in these specific bacterial groups nor the total bacteria. Moreover, we observed the initial evidence of recovery of these key bacterial groups in some patients treated with ridinilazole. We believe that these data provide evidence that ridinilazole is able to preserve a healthy gut microbiome during treatment for CDI and that the recovery of the key bacterial groups contributed to the large numerical reduction in disease recurrence we observed in the trial results.
- ***Ridinilazole was Retained in the Gastrointestinal Tract.*** Ridinilazole was targeted to the gastrointestinal tract, which is the site where CDI occurs in the body. Systemic exposure was close to or below the level of detection in patients with CDI, with plasma concentrations very similar to those observed in our Phase 1 clinical trial in healthy volunteers.
- ***Ridinilazole Reduced Biomarkers of Inflammation.*** We measured levels of two key markers of inflammation, calprotectin and lactoferrin, in feces collected from the 69 patients who comprised the mITT group. The samples analyzed were collected at the time of randomization (prior to initiation of treatment), at day five and at day ten. We observed that ridinilazole and vancomycin reduced concentrations of calprotectin and lactoferrin by similar levels when analyzing the results for all patients. We also observed that a subset of patients with severe CDI had a greater reduction in levels of calprotectin and lactoferrin when treated with ridinilazole compared to vancomycin. We believe these data indicate that ridinilazole is associated with a greater reduction in inflammatory markers compared to vancomycin in patients with severe CDI.
- ***Ridinilazole was Well Tolerated.*** Ridinilazole was generally well tolerated. The overall rate of adverse events and serious adverse events reported in the ridinilazole and vancomycin treatment arms were comparable.

Phase 2 Exploratory Clinical Trial of Ridinilazole Compared to Fidaxomicin

In September 2017, we reported top-line data from our randomized, open label, active controlled, multicenter Phase 2 clinical trial evaluating ridinilazole compared to fidaxomicin for the treatment of CDI. This exploratory clinical trial was designed to generate data comparing ridinilazole to fidaxomicin, a CDI antibiotic launched in 2011, and the results of this clinical trial are expected to help to inform the commercial positioning of ridinilazole. We conducted this clinical trial at sites in the United Kingdom, Europe and the United States, enrolling 27 patients between 18 and 90 years of age. We randomized patients in a one-to-one ratio to receive either a 200 mg dose of ridinilazole administered twice per day for ten days or a 200 mg dose of fidaxomicin administered twice per day for ten days. The trial population was unbalanced with more patients randomized to ridinilazole having predisposing factors for recurrent CDI, and at a higher risk of poorer clinical outcomes as measured by ATLAS score, a tool for evaluating CDI in patients by age, temperature, leukocytes and albumin levels, and use of systemic antibiotics.

The primary efficacy objective of this clinical trial was to determine the safety and tolerability of ten days of dosing with 200 mg of ridinilazole compared to dosing with 200 mg of fidaxomicin. The secondary objectives of the clinical trial were to assess the following:

- the plasma pharmacokinetics of ridinilazole in patients with CDI;
- the qualitative and quantitative effect of ridinilazole and fidaxomicin on gut flora;
- the plasma, urine and fecal concentrations of ridinilazole and its metabolites; and
- the efficacy of ten days of dosing with ridinilazole compared to fidaxomicin for the treatment of CDI.

The measurement of efficacy was based on investigator assessed clinical response at the test of cure, or TOC, visit, with clinical cure defined as resolution of diarrhea while on treatment and maintained at the TOC visit, and sustained clinical response, defined as clinical cure at the TOC visit and no recurrence of CDI within 30 days after the end of treatment.

We reported the following findings:

- ***Ridinilazole Preserved the Microbiome to a Greater Extent than Fidaxomicin.*** We observed that following ten days of treatment, ridinilazole had markedly less of an impact on the gut microbiome of trial patients by measures of overall diversity and changes in key bacterial families when compared to those trial patients dosed with fidaxomicin. We observed that while ridinilazole and fidaxomicin both reduced the abundance of *C. difficile*, fidaxomicin treated patients had reduced abundance of other bacterial families, including Firmicutes phylum, that are thought to have direct functional roles in protecting against CDI. We observed that for a number of these bacterial families, the difference between the two treatments reached statistical significance. We also reported alpha diversity, as measured by the Simpson's Diversity Index, as another measure of microbiome health. We observed a greater reduction in alpha-diversity during fidaxomicin treatment compared with ridinilazole treatment. These measures were a key secondary endpoint of the trial. We believe that these measures provide further evidence of ridinilazole's precision in killing *C. difficile* while preserving the gut microbiome.
- ***Ridinilazole was Well Tolerated.*** The primary endpoint of the trial was safety, as measured by the number of treatment emergent adverse events and serious adverse events. During the trial, no new or unexpected safety signals were identified and ridinilazole was well tolerated.
- ***Comparable Rates of Sustained Clinical Response.*** We observed that seven of the 14 ridinilazole treated patients and six of the 13 fidaxomicin treatment patients were cured at the end of treatment and did not have a recurrence of CDI within the following 30 days to achieve a sustained clinical response. The trial was however not designed for efficacy comparisons due to the small number of patients enrolled, and so we believe no conclusions on efficacy should be made based solely on these data.

Phase 1 Clinical Trial in Healthy Volunteers

In 2013, we completed a randomized, partially blind, placebo controlled Phase 1 clinical trial of ridinilazole in healthy volunteers. We conducted this clinical trial at a single site in the United Kingdom under approval from the U.K. Medicines and Healthcare products Regulatory Agency, or MHRA, and the Ethics Review Committee. We enrolled 56 healthy male subjects in the clinical trial who were between 18 and 55 years of age. The primary objective of the clinical trial was to determine the safety and tolerability of single and multiple ascending oral doses of ridinilazole. The secondary objectives included determining the single and multiple oral dose pharmacokinetics of ridinilazole, assessing the effect of food on systemic exposure of ridinilazole and assessing the effect of multiple oral doses of ridinilazole on gut flora.

We conducted the clinical trial in two parts. Part 1 consisted of an ascending single dose study and a food effect evaluation study. In Part 1, we evaluated a total of 40 subjects, divided into the following six cohorts:

- four fasted subjects, randomized for three subjects to receive a single 2 mg dose of ridinilazole and one subject to receive placebo;
- four fasted subjects, randomized for three subjects to receive a single 20 mg dose of ridinilazole and one subject to receive placebo;
- eight fasted subjects, randomized for six subjects to receive a single 100 mg dose of ridinilazole and two subjects to receive placebo;
- eight fasted subjects, randomized for six subjects to receive a single 400 mg dose of ridinilazole and two subjects to receive placebo;
- eight fasted subjects, randomized for six subjects to receive a single 2,000 mg dose of ridinilazole and two subjects to receive placebo; and
- eight subjects, randomized for six subjects to receive a single 1,000 mg dose of ridinilazole under fasted conditions and a single 1,000 mg dose under fed conditions, and two subjects to receive two single doses of placebo on the same dosing schedule. The doses under fed and fasted conditions were separated by a minimum of six days.

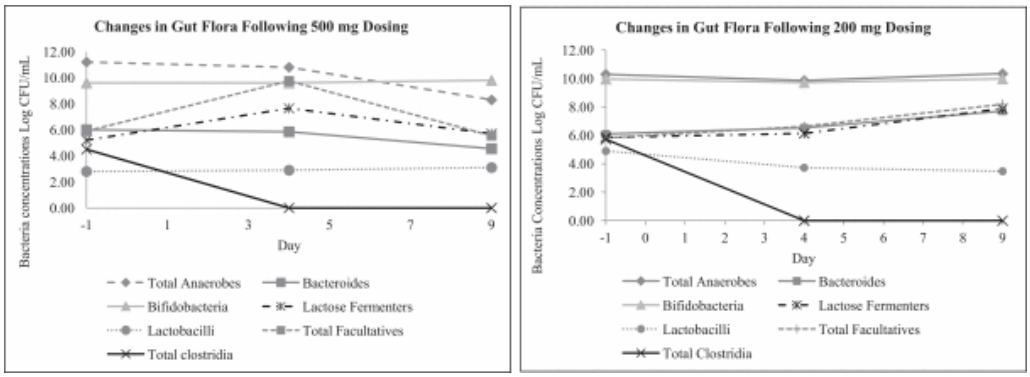
Part 2 of the clinical trial consisted of a multiple dose study. In Part 2, we evaluated a total of 16 subjects, who were divided into the following two cohorts:

- eight subjects randomized for six subjects to receive 200 mg doses of ridinilazole twice per day for nine days with a single final dose on day ten and two subjects to receive placebo on the same dosing schedule; and
- eight subjects randomized for six subjects to receive 500 mg doses of ridinilazole twice per day for nine days with a single final dose on day ten and two subjects to receive placebo on the same dosing schedule.

Analysis of Trial Results

We observed the following results in this clinical trial:

- ***Ridinilazole was Well Tolerated.*** Ridinilazole was well tolerated at all doses tested in the clinical trial. The incidence of adverse events in the clinical trial was low for patients treated with ridinilazole and comparable to the incidence of adverse events for patients receiving placebo. The majority of the adverse events that were considered to be possibly related to ridinilazole were classified as gastrointestinal disorders and were mild in severity and resolved without intervention. One patient withdrew from the clinical trial after suffering from appendicitis on day one. The trial investigator determined this serious adverse event was unlikely to be related to treatment with ridinilazole.
- ***Ridinilazole was Retained in the Gastrointestinal Tract.*** Ridinilazole was targeted to the gastrointestinal tract, which is the site where CDI occurs in the body. Systemic exposure was close to or below the level of detection in both fed and fasted subjects.
- ***Ridinilazole was Highly Selective for Total Clostridia Bacteria with Minimal Impact on Other Natural Gut Flora.*** We measured levels of bacteria in fecal samples from Part 2 of the clinical trial for gut flora composition on the day prior to commencement of dosing and on days four and nine of drug administration during the clinical trial. As illustrated in the figure below, in both the 200 mg and 500 mg dose cohorts, median levels of key bacteria groups that comprise the natural gut flora remained relatively constant during this period and did not fluctuate substantially from baseline. The one exception was the total clostridia bacterial group. The counts of total clostridia decreased from the baseline level to zero by day four of dosing and remained at zero on day nine of dosing. *C. difficile* is a member of the total clostridia group. We did not detect any *C. difficile* viable cells or spores in the fecal samples of any of the healthy volunteer subjects at any point during the clinical trial. Bacteria levels are shown in the figure below on a logarithmic scale, which condenses the wide range of values to a format showing the relative differences in values. We believe these data, which are consistent with the data from our preclinical studies, support the highly selective antibiotic effect of ridinilazole.



CDI Preclinical Data

In a range of preclinical studies, ridinilazole demonstrated an encouraging profile as a potential antibiotic for the treatment of initial CDI and reduction of CDI recurrence. The following is a summary of key observations from these studies:

- ***Potency Against C. difficile***. We screened ridinilazole *in vitro* against panels of *C. difficile* clinical isolates from the United States and the United Kingdom. In these studies, ridinilazole displayed a potent bactericidal effect against all clinical isolates of *C. difficile*, including hypervirulent strains, such as ribotype 027. Ridinilazole was more potent than both vancomycin and metronidazole, and was either equally potent to, or more potent than, fidaxomicin. We have also tested ridinilazole against a panel of *C. difficile* clinical isolates that maximize the diversity of resistance to key classes of commonly used antibiotics. Ridinilazole did not display evidence of cross resistance with other classes of key antibiotics in common use.
- ***Targeted Spectrum of Activity***. We conducted *in vitro* testing of ridinilazole, vancomycin, metronidazole and fidaxomicin against a wide panel of bacteria that are commonly found in the gut flora and are necessary for normal function of the gastrointestinal tract and also have wide implications on human health, such as the proper function of the immune system. As illustrated in the figure below, in this study ridinilazole had a minimal antibiotic effect against these beneficial bacterial groups. Ridinilazole also displayed higher selectivity for *C. difficile* in this study as compared to vancomycin, metronidazole and fidaxomicin. *In vitro* potency is measured by determining the concentration of a drug (in micrograms per liter) needed to inhibit the growth of 90% of the bacterial strains being tested, referred to as a MIC90 measurement. A high number, typically higher than 256, indicates a weak antimicrobial effect, and a low number, typically less than eight, indicates a potent antimicrobial effect. We believe that the targeted spectrum of activity for ridinilazole seen in this study compared to the relatively broad spectrum of activity of other antibiotics indicates the potential for ridinilazole to selectively target *C. difficile* bacteria without causing collateral damage to the gut flora and thereby reduce CDI recurrence rates.

Profile of Selectivity of Ridinilazole vs. Other CDI Antibiotics

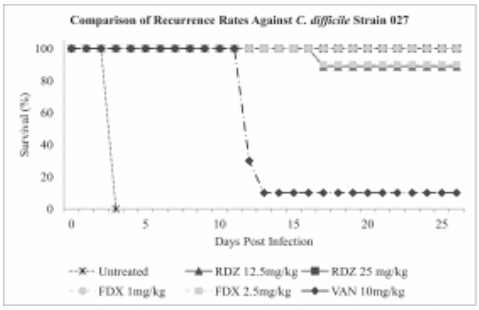
Key Bacterial Groups	Spectrum of Activity – MIC_{90} (µg/mL)			
	RDZ	MTZ	VAN	FDX
Bacteroides spp.	>512	2	128	>512
Bifidobacterium spp.	>512	128	1	0.125
Lactobacillus spp.	>512	>512	>512	>512
Eggerthella lenta	>512	0.5	4	≤0.03
Peptostreptococcus spp.	64	1	0.5	≤0.03
Staphylococcus aureus	>512	>512	1	16

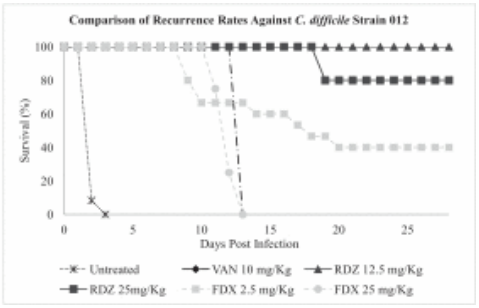
Antibiotic effect: Weak; Medium; Potent

RDZ: Ridinilazole VAN: Vancomycin
MTZ: Metronidazole FDX: Fidaxomicin

- ***Protection Against CDI Recurrence***. In a hamster model, we infected one group of hamsters with the hypervirulent CDI strain ribotype 027 and a second group of hamsters with a second CDI strain ribotype 012. In the United States, the hypervirulent CDI strain ribotype 027 accounts for approximately one-fifth of all CDI cases. We then treated hamsters from each of the two infected groups with different doses of ridinilazole, vancomycin and fidaxomicin for five days. We evaluated disease recurrence over the 21 days following treatment. In this hamster model, a hamster fatality within the first five days is a result of initial *C. difficile* infection, while a fatality from day six to day 25 is a result of recurrent disease. As illustrated in the figure below, the hamsters from both infected

groups that were treated with two different doses of ridinilazole had survival rates of 90% to 100% against strain ribotype 027 and 80% to 100% against strain ribotype 012. These survival rates were higher than hamsters treated with vancomycin (0% to 10% survival rates) for both CDI strains, comparable to hamsters treated with two different doses of fidaxomicin against strain ribotype 027 (90% to 100% survival rates) and higher than hamsters treated with two different doses of fidaxomicin against strain ribotype 012 (0% to 40% survival rates). All infection control hamsters received placebo and died by the second day following infection.





- ***Inhibition of Sporulation***. In the *in vitro* testing of ridinilazole described above, we treated *C. difficile* cells with different concentrations of ridinilazole and measured the percentage of spores formed 96 hours after treatment. Untreated cells had a 100% conversion rate into *C. difficile* spores, which are the dormant protected form of the bacteria, after 96 hours. In this study, treatment with ridinilazole resulted in a meaningful reduction in spore count compared with untreated cells against all strains of *C. difficile* tested. We believe the reduction in sporulation may benefit rates of recurrent disease as the spores are highly resistant to standard cleaning practices and lead to increased risks of environmental persistence and disease transmission.
- ***Reduction in Toxin and Inflammation Levels***. In an *in vitro* study, Caco-2 cells, a type of cell found in the colon of humans commonly used in studies of intestinal function, were exposed to *C. difficile* and then treated with ridinilazole, metronidazole and vancomycin or were untreated to act as a control. Following treatment with ridinilazole, toxin A levels were reduced by 91%, toxin B was not detected and IL-8 levels were reduced by 74%. Metronidazole and vancomycin had minimal effect on toxin A or B concentrations, and IL-8 concentrations were similar to control. Toxins A and B are produced by *C. difficile* to elicit an inflammatory response, including IL-8 release, which results in the symptoms of the disease including severe diarrhea. We believe that these data indicate that ridinilazole has the potential to reduce the severity of disease symptoms and that it has the potential to be more effective than current treatment options.
- ***Concomitant Antibiotic Use***. In an *in vitro* bacterial culture study, we administered ridinilazole in combination with selected other antibiotics. In this study, concomitant use of antibiotics had neither a synergistic nor an antagonistic effect on the MIC90 values of ridinilazole against the *C. difficile* strains tested. We believe these results indicate that concomitant use of other antibiotics will not diminish the potency of ridinilazole. We believe this is an important finding because a significant portion of CDI patients receive antibiotic treatment for persistent or new infections.
- ***Low Propensity for Resistance***. In an *in vitro* study, we treated *C. difficile* bacteria with ridinilazole and assessed the number of resistant bacteria at the end of treatment. We repeated this process multiple times, with each cycle referred to as a serial passage. We observed that use of ridinilazole resulted in a low frequency of spontaneous mutation and no resistance after 14 serial passages of treatment. We have also evaluated ridinilazole mutant prevention concentration, or MPC, a measure evaluating the ability of an antibiotic to minimize the development of resistant organisms, against *C. difficile* clinical isolates. *In vitro* results show that ridinilazole has low MPC values against these isolates, providing further evidence supporting ridinilazole's profile for low resistance development.
- ***Ridinilazole Arrests Cell Division***. In an *in vitro* study, we treated *C. difficile* bacteria with ridinilazole and assessed its effects on killing the bacteria. The study revealed that ridinilazole halts *C. difficile* cell division, characterized by a significant increase in the length of *C. difficile* cells and an absence of division septum formation.

Infectious Diseases Pipeline

We are seeking to build a pipeline of new antibiotics focused on treating patients with serious bacterial infections where there is a substantial unmet need and where we believe we have the ability to show meaningful advantages over current treatments. In December 2017, we expanded our activities in this field when we acquired Discuva Limited, a privately held U.K.-based company. Through this acquisition, we obtained our bacterial genetics-based Discuva Platform that facilitates the discovery and development of new mechanism antibiotics. With this acquisition, we believe we are better placed to advance additional potential drug treatments for patients with serious bacterial infections. We are currently developing a preclinical program targeting infections caused by *Neisseria gonorrhoeae* and a discovery stage program against a group of bacteria that collectively are known as the ESKAPE pathogens.

Discuva Platform

Our Discuva Platform is a genetics-based technology that can be used throughout the stages of drug discovery from hit to lead through to candidate selection. Our Discuva Platform aligns modified bacterial transposon mutagenesis with next generation sequencing and a proprietary end user interface.

The Discuva Platform uses pathogen specific transposons. Transposons are small segments of DNA that are capable of replicating and inserting copies of DNA at random sites in the same or a different chromosome. Our pathogen specific transposons have three different activating promoters to drive bacterial gene up-regulation, to cause gene disruption, or cause the down-regulation of bacterial gene expression. There is normally a single transposon insertion per genome. The density of transposon insertion at the different genomic loci is determined in the whole library with insertion rates potentially being as high as every two to three base pairs.

We currently have multiple pathogen libraries across a wide range of bacteria including *Neisseria gonorrhoeae* and five of the six ESKAPE pathogens *(Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii,* and *Pseudomonas aeruginosa)*. With our Discuva Platform, we also have the ability to create additional bacteria libraries to expand our discovery research and development capabilities in bacterial infectious diseases.

We believe that our Discuva Platform has three principle uses:

i) Identifying essential genes in bacteria. We are able to use our Discuva Platform to identify genes within bacteria that are essential for their survival and which we believe will allow us to identify new bacterial targets against which to develop new antibiotic drugs.

ii) Elucidating mechanism of action. We are able to use our Discuva Platform to elucidate the mechanism of action of a compound to be inferred by the genes that are upregulated during experiments when in the presence of a drug. We are able to rapidly identify the mechanism of action of a potential drug and this represents an important capability of our Discuva Platform. We have been able to validate the ability of our Discuva Platform to elucidate mechanisms of action by testing antibiotic compounds whose mechanisms of action are known.

iii) Understanding emergent mechanisms of resistance. We are able to use our Discuva Platform to test a compound's susceptibility towards known mechanisms of antibiotic resistance to allow us to select potential drug candidates with what we believe will be much better resistance profiles. We believe the importance of understanding emergent mechanisms of resistance is that it will allow us to discover new antibiotics that have potential for longer use in patients prior to the development of widespread resistance.

SMT-571 for the treatment of gonorrhea

We are developing SMT-571 as a new mechanism antibiotic for the potential treatment of infection caused by the bacteria *Neisseria gonorrhoeae*, or *N. gonorrhoeae*. We identified SMT-571 using our Discuva Platform. There is an urgent unmet need for the development of new antibiotics against *N. gonorrhoeae*. It is estimated by the WHO that there are approximately 78 million new cases of gonorrhea globally per year. *N gonorrhoeae* has consistently developed resistance to each class of antibiotics recommended for the treatment of gonorrhea infections, and there is now only one treatment that is recommended by the CDC, a combination of the cephalosporin antibiotic ceftriaxone and the macrolide antibiotic azithromycin. The WHO ranks gonorrhea as a "high" priority for research and development investment into the search for antibiotics that are effective against *N. gonorrhoeae*, while the CDC states that due to the increased problems with resistance, additional treatment options are urgently needed.

SMT-571 is our lead preclinical development candidate for the treatment of gonorrhea. SMT-571 has demonstrated an encouraging profile as a potential antibiotic for the treatment of *N. gonorrhoeae*. SMT-571 has a new mechanism of action that targets cell division, and it has shown high potency for a range of *N. gonorrhoeae* strains in *in vitro* studies, including those that are multi-drug resistant and extensively-drug resistant. The following is a summary of key observations from some of our preclinical studies on SMT-571:

- ***Potency Against N. gonorrhoeae***. We have screened SMT-571 *in vitro* against panels of *N. gonorrhoeae* clinical isolates that represented a large geographical, temporal and genetically diverse selection. The panels included international reference strains of *N. gonorrhoeae*, including the 2016 WHO strains and gonorrhea clinical isolates that have *in vitro* or clinical resistance to current antibiotics used to treat gonorrhea infections. In these studies, SMT-571 demonstrated a potent and rapid bactericidal effect against all clinical isolates of *N. gonorrhoeae*, including multi-drug resistant strains and extensively-drug resistant strains.
- ***Low Potential for Resistance Development***. We have used our Discuva Platform to test SMT-571 for its likelihood to develop resistance towards *N. gonorrhoeae*. SMT-571 shows a very low potential for development of resistance with no spontaneous *N. gonorrhoeae* resistant mutants isolated from *in vitro* microbiology studies.

In September 2018, we nominated SMT-571 as our preclinical candidate for progression into IND enabling studies. We expect to initiate a Phase 1 clinical trial of SMT-571 in the second half of 2019.

In July 2018, we were granted a sub-award of up to $4.5 million from the Trustees of Boston University under the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator program, or CARB-X. CARB-X is a public private partnership dedicated to accelerating antibacterial research and development to address the rising global threat of drug resistant bacteria. Our award from CARB-X, if funded in full, could support the advancement of a lead clinical candidate in our gonorrhea program through the end of a Phase 1 clinical trial.

In June 2018, we announced the identification of a second novel target to kill *N. gonorrhoeae* that is distinct from the one targeted by SMT-571, along with the discovery of a promising new series of compounds that may have activity against this target. The development of this second series of early-stage compounds has been supported, in part, by a grant from Innovate UK. We have currently put on hold our research on this second novel target in order to focus our resources on the development of SMT-571.

ESKAPE Program

We have an early-stage research and development program targeting a group of bacteria called the ESKAPE pathogens. The ESKAPE pathogens are the bacteria *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa* and *Enterobacter spp*., and collectively, they represent the leading cause of hospital acquired infections around the world. They are subject to increasing rates of resistance to existing antibiotic classes, creating a major unmet medical need. We are using our Discuva Platform to identify novel bacterial targets against the ESKAPE pathogens and support the identification and development of new mechanism antibiotics against these bacteria. We expect to provide an update on our ESKAPE research and development program during 2019.

Roche Collaboration

Prior to our acquisition of Discuva Limited, Roche and Discuva entered into a collaboration using the Discuva Platform for the discovery and development of new antibiotic compounds in 2014. The joint research element of the collaboration concluded in early 2018, and Roche is solely responsible for continuing development of any compound that was identified under the collaboration. We are eligible to receive from Roche milestones and royalty payments based on the successful development and commercialization of any such compound.

Duchenne Muscular Dystrophy Program

In June 2018, we discontinued the development of ezutromid, our lead utrophin modulator for the treatment of the neuromuscular disease Duchenne muscular dystrophy, or DMD. We took this decision following the announcement of the results of our Phase 2 clinical trial of ezutromid in patients with DMD, which we have referred to as PhaseOut DMD. PhaseOut DMD did not meet its primary or secondary endpoints.

PhaseOut DMD was a 48-week, open label clinical trial conducted at trial sites in the United Kingdom and the United States. PhaseOut DMD enrolled a total of 40 ambulatory boys between their fifth and tenth birthday, inclusive, and who had a genetically confirmed diagnosis of DMD. The primary objective of our PhaseOut DMD clinical trial was to investigate changes in magnetic resonance parameters from baseline in leg muscle health. The secondary objectives of our PhaseOut DMD trial investigated changes in utrophin expression in muscle and muscle fiber regeneration through the examination of muscle fiber biopsies taken from patients at baseline and after 24 weeks or 48 weeks of treatment with ezutromid.

In June 2018, we reported top-line 48-week data that showed that PhaseOut DMD had missed its primary and secondary endpoints. We had reported interim 24-week data from PhaseOut DMD in January 2018, with further findings reported in February 2018, and while these showed positive changes in some of the primary and secondary endpoint measurements after 24 weeks of treatment, we did not see these effects after 48 weeks of treatment. Ezutromid was shown to be well tolerated after 48 weeks of dosing in PhaseOut DMD. We announced the discontinuation of the development of ezutromid in June 2018, and we have now substantially completed the activities related to the close-out of the PhaseOut DMD clinical trial.

We had also been developing future generation utrophin modulators in collaboration with the University of Oxford. We have now discontinued development of these future generation utrophin modulators as part of our strategy to focus on advancing our pipeline of new mechanism antibiotics. Our collaboration with the University of Oxford was terminated by mutual consent in March 2019.

Our Collaborations and Funding Arrangements

BARDA

In September 2017, we were awarded a contract from the Biomedical Advanced Research and Development Authority, or BARDA, to fund, in part, the clinical and regulatory development of ridinilazole for the treatment of infections caused by *C. difficile*. The contract includes a base period with federal government funding of approximately $32 million. In addition, there are three option work segments that, if exercised in full by BARDA, would increase the total federal government funding under the contract to approximately $62 million. In August 2018, BARDA exercised one of the option work segments worth $12 million to bring the total amount of committed BARDA funding to $44 million.

The contract provides for a cost-sharing arrangement under which BARDA funds a specified portion of estimated costs for the continued clinical and regulatory development of ridinilazole for CDI. Under this cost sharing arrangement, we are responsible for a portion of the costs associated with each segment of work, including any costs in excess of the estimated amounts.

During the base period of the contract, BARDA has agreed to fund, in part, activities for our two Phase 3 clinical trials of ridinilazole, which included obtaining requisite regulatory approvals for the opening of trial sites, arranging for the manufacture of clinical supply of ridinilazole and engaging third-party contract research organizations to conduct the clinical trials including initial patient enrollment and treatment. The three option work segments, if exercised in full, would provide for up to an additional $30 million of funding from BARDA and would support the development of ridinilazole through to potential submission of applications for marketing approval. In August 2018, one of these three option work segments was exercised by BARDA with the $12 million in funding to be drawn down to specifically support drug manufacturing activities required for the submission of marketing approval applications and other regulatory activities. Activities to be covered by the two remaining option work segments include the completion of patient enrollment and treatment in our two Phase 3 clinical trials and the delivery of final reports related to both trials; and the preparation, submission and review of applications for marketing approvals of ridinilazole for CDI in the United States.

Each of the two remaining option work segments is an independent, discrete work segment that is eligible to be exercised, in BARDA's sole discretion, upon the completion of agreed-upon milestones and deliverables. If all option work segments are exercised by BARDA, the contract would run into 2022, unless extended by us and BARDA.

The contract specifies the plan of activities to be conducted under the contract. In addition to our obligations to conduct the activities provided for by the plan, we are obligated to satisfy various federal reporting requirements, addressing clinical progress, technical issues, and intellectual property and financial matters. Payments to us under the contract are expected to be made monthly after we invoice BARDA for allowable costs that have been incurred.

BARDA may terminate this agreement upon our uncured default in our performance of the agreement or at any time if the contracting officer determines that it is in the U.S. government's interest to terminate the agreement.

Under standard U.S. government contracting terms, the U.S. government receives only limited rights for government use of certain of our pre-existing data and certain data produced with non-federal funding, to the extent such data are required for delivery to BARDA under the contract. The U.S. government receives unlimited rights to use and disclose new data first produced under the contract with BARDA. Except for commercialization rights to ridinilazole in South America, Central America and the Caribbean, we currently have exclusive worldwide commercialization rights to ridinilazole and retain these rights under the BARDA contract. However, the U.S. government is entitled to a nonexclusive, nontransferable, worldwide, royalty-free license to practice or have practiced any patent on an invention that is conceived or first reduced to practice under the contract, which is referred to as a subject invention.

In addition, the U.S. government may obtain additional rights if we do not elect to retain ownership of a subject invention or if we do not satisfy certain disclosure and patent prosecution obligations with respect to a subject invention. Furthermore, the government is entitled to march-in rights under our contract with BARDA. March-in rights permit the U.S. government to require that we grant a license to a subject invention to a third party if we have not taken effective steps to achieve practical application of the invention within a reasonable time; if such action is necessary to meet health and safety needs and/or requirements for public use that we are not meeting; or if we have not obtained from any exclusive licensee the required agreement for manufacturing such invention substantially in the United States or a waiver of this requirement.

Wellcome Trust

In October 2012, we entered into a translation award funding agreement with the Wellcome Trust Limited, as trustee of the Wellcome Trust, in order to support a Phase 1 and a Phase 2 clinical trial of ridinilazole for the treatment of CDI. We refer to the translation award funding agreement as the translation award agreement. Under the translation award agreement, we were eligible to receive up to £4.0 million from the Wellcome Trust, of which we received the entire £4.0 million. The

translation award agreement followed a funding agreement we and the Wellcome Trust entered in October 2009, which we refer to as the discovery award agreement, under which we received £2.3 million for preclinical development of CDI antibiotics. We refer to any compound or product that is covered by intellectual property rights created under the discovery award agreement or the translation award agreement, or that is covered by intellectual property rights that we created or to which we had rights prior to October 2009 and that relate to the activities under the discovery award agreement or the translation award agreement, as the award products. We agreed to use commercially reasonable efforts to achieve certain development milestones by specified dates.

We would be required to make a full or partial repayment to the Wellcome Trust of the funding we received under the translation award agreement, plus accrued interest, under specified conditions, including our unauthorized use of the award amount, our fraudulent or willful misconduct, our knowingly withholding material information from the Wellcome Trust, or an acquisition by certain third parties of all or a material part of our business or assets or of a majority of our equity. Upon such a full repayment, our obligation to share a portion of net revenue with the Wellcome Trust would terminate.

Termination

Unless earlier terminated by the Wellcome Trust, the translation award agreement will terminate on the earlier of our full repayment of the award amount, plus accrued interest, to the Wellcome Trust following its request for repayment, or the expiration of all payment obligations under the translation award agreement and the revenue sharing agreement. The Wellcome Trust may terminate the translation award agreement for specified reasons, including our material breach or insolvency related events or the Wellcome Trust's determination that the clinical trials should be terminated due to a serious failure in the progress, management or conduct of the clinical trials, if we do not remedy such condition within a specified period after receiving notice.

Assignment

We may not, without the Wellcome Trust's prior consent, assign, transfer or declare a trust over the translation award agreement or otherwise dispose of any of our rights or obligations under the translation award agreement, with such consent not being unreasonably withheld, delayed or conditioned, other than an assignment to our affiliates.

Revenue Sharing Agreement

The terms of the translation award agreement required us to enter into a revenue sharing agreement with the Wellcome Trust prior to the further development (beyond the Phase 2 trial supported by the 2012 translational award agreement) and commercialization, which together we refer to as the "Exploitation" of any compound or product that is covered by the intellectual property rights created under the translational award agreement or the discovery award agreement, or that is covered by background intellectual property rights. Under such revenue sharing agreement, the Wellcome Trust would be entitled to a share of the net revenue that we, our affiliates, licensees or third-party collaborators receive under the Exploitation of the award products or any intellectual property associated with such Exploitation.

In October 2017, we entered into a revenue sharing agreement with the Wellcome Trust. Under the terms of the revenue sharing agreement: (i) if we commercialize ridinilazole, the Wellcome Trust is eligible to receive a low-single digit percentage of net revenue (as defined in the translation award agreement), and a one-time milestone payment of a specified amount if cumulative net revenues exceed a specified amount; (ii) if a third party commercializes ridinilazole, the Wellcome Trust is eligible to receive a mid-single digit percentage of the net revenues we receive from commercial sales by such third party, and a one-time milestone payment of a specified amount if cumulative net revenues we receive exceed a specified amount. In addition, following the first commercial sale by such third party, the Wellcome Trust is eligible to receive a one-time milestone payment equal to a low-single digit percentage of the aggregate amount of any pre-commercial payments we receive from third-party licensees prior to such commercial sale; and (iii) in the event of an assignment or sale of the assets or intellectual property pertaining to ridinilazole, the net proceeds we receive from such assignment or sale would be treated as net revenue under the revenue sharing agreement.

Under the revenue sharing agreement, it was agreed that any development funding or grant funding we receive from BARDA or other third parties, including licensees, would not be classified as net revenue or as a pre-commercial payment. In addition, under the revenue sharing agreement, the Wellcome Trust agreed to terminate all of its rights under the translation award agreement to develop or commercialize the award products or the related intellectual property in specified markets and in specified indications, in the event that we were not developing or commercializing the award products or such intellectual property for such markets or in such indications.

Unless earlier terminated, the revenue sharing agreement will expire upon later of the expiration of the last patent or patent application covering ridinilazole; the expiration of any agreement or payment obligations entered into by ourselves with a third party relating to the Exploitation of ridinilazole; and the expiration of any payment obligations owed to the Wellcome Trust relating to the Exploitation of ridinilazole. In addition, each party has the right to terminate the revenue sharing agreement if the other party materially breaches the agreement, and the breach remains uncured for a specified period or the breach is uncurable, or if the other party experiences specified insolvency related events.

Discuva Limited Acquisition

Share Purchase Agreement

In December 2017, we entered into a share purchase agreement with the shareholders of Discuva, a private limited company organized under the laws of England and Wales pursuant to which we acquired all of the outstanding share capital of Discuva. Discuva was a discovery stage company with a bacterial genetics-based platform that facilitates the discovery and development of new mechanism antibiotics.

Under the terms of the share purchase agreement, we paid the Discuva shareholders a total upfront consideration comprised of (A) £5.0 million in cash plus an amount equal to the cash and cash equivalents of Discuva minus (i) indebtedness, (ii) any other liabilities of Discuva at the closing of the transaction that had arisen outside of the ordinary course of business and (iii) funds to be held in escrow and (B) £5.0 million of our ordinary shares, satisfied by the issue of 2,934,272 of our fully-paid, new ordinary shares at a price per share of £1.704. We made payment of the amount held in escrow, and an additional balancing amount in respect of the closing cash position was made to the Discuva shareholders in December 2018.

In addition, the Discuva shareholders will be entitled to receive contingent payments from us based on (i) the receipt of potential research and development tax credits to which Discuva may be entitled for the period from April 1, 2015, to the date of the share purchase agreement and (ii) approximately one-half of the economic benefit from any amounts received in connection with certain payments made to us under an existing collaboration agreement between Discuva and F. Hoffman - La Roche Limited, or Roche. We made an initial payment in respect of a research and development tax credit for the period from April 1, 2015, to March 31, 2016, to the Discuva shareholders in December 2018. Separately, certain employees, former employees and former directors of Discuva are eligible for further payments from Discuva of up to £7.9 million based on specified development and clinical milestones related to proprietary product candidates developed under the platform.

Under the terms of the share purchase agreement, the Discuva shareholders agreed, subject to certain limited exceptions, to a lock-up period during which they will not sell, transfer or otherwise dispose of, or create any encumbrance over any of, the ordinary shares received as consideration; this lock-up period expired in September 2018. Following the lock-up period, each of the Discuva shareholders has agreed for a period of twelve months to only dispose of their ordinary shares in accordance with certain orderly market undertaking provisions specified in the share purchase agreement, which, among other things, limit the number of ordinary shares each seller may dispose of during such twelve-month period.

The share purchase agreement also prohibits the selling Discuva shareholders from engaging in certain business activities which are competitive with the business of Discuva at the time of the transaction and from soliciting customers or hiring employees of Discuva, subject to certain limited exceptions as set forth in the agreement, for a period of two years following the date of the agreement.

The share purchase agreement contained customary representations and warranties that ourselves and the selling Discuva shareholders made to each other as of specific dates. The assertions embodied in those representations and warranties were made solely for purposes of the share purchase agreement and may be subject to important qualifications and limitations agreed to by us and the Discuva shareholders in connection with negotiating its terms. Moreover, the representations and warranties may be subject to a contractual standard of materiality that may be different from what may be viewed as material to shareholders or may have been used for the purpose of allocating risk between us and the Discuva shareholders rather than establishing matters as facts. For the foregoing reasons, no person should rely on such representations and warranties as statements of factual information at the time they were made or otherwise.

Eurofarma Laboratórios S.A.

In December 2017, we entered into an exclusive license and commercialization agreement with Eurofarma, pursuant to which we granted Eurofarma the exclusive right to commercialize ridinilazole in Argentina, Belize, Bolivia, Brazil, Chile, Colombia, Costa Rica, Ecuador, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Suriname, Dominican Republic, Uruguay and Venezuela, which we refer to as the licensed territory. We have retained commercialization rights in the rest of the world.

Financial terms

Under the terms of the license agreement, we received an upfront payment of $2.5 million and are entitled to receive an additional $3.75 million in development milestones upon the achievement of staged patient enrollment targets in the licensed territory in one of our two ongoing Phase 3 clinical trials of ridinilazole. We are eligible to receive up to $21.4 million in development, commercial and sales milestones when cumulative net sales equal or exceed $100.0 million in the licensed territory. Each subsequent achievement of an additional $100.0 million in cumulative net sales will result in us receiving additional milestone payments, which, when combined with anticipated product supply transfer payments from Eurofarma paid to us in connection with a commercial supply agreement to be entered into between the two parties, will provide payments estimated to range from a mid- to high-teens percentage of cumulative net sales in the licensed territory. We estimate such product supply transfer payments from Eurofarma will range from a high single-digit to low double-digit percentage of cumulative net sales in the licensed territory.

Regulatory and Commercial

Under the license agreement, Eurofarma is responsible for all costs related to obtaining regulatory approval of ridinilazole in the licensed territory and is obligated to use commercially reasonable efforts to file applications for regulatory approval in specified countries in the licensed territory within a specified time period after we have filed an application for regulatory approval, or obtained regulatory approval, for ridinilazole in a jurisdiction where we retain commercial rights. To assist Eurofarma in obtaining regulatory approvals in the licensed territory, we are responsible, at our expense, to conduct such additional chemistry, manufacturing and control studies as may be required by regulatory authorities in countries within the licensed territory. We retain sole responsibility for the clinical development of ridinilazole in all countries and are responsible for all costs related to obtaining regulatory approval for ridinilazole outside of the licensed territory.

We are obligated to use commercially reasonable efforts to supply or cause to be supplied to Eurofarma sufficient commercial supply of ridinilazole, and Eurofarma has agreed to purchase its supply of ridinilazole exclusively from us. If we are unable to supply Eurofarma with commercial supply of ridinilazole during the term of the agreement, we are obligated to transfer to Eurofarma or its third-party suppliers' know-how that would be needed for Eurofarma or its third-party suppliers to manufacture the product for commercial sale in the licensed territory.

Termination

Unless earlier terminated, the license and commercialization agreement will expire upon the latest of (i) the earliest date on which there are no longer any valid patent claims covering ridinilazole in the licensed territory, (ii) the earliest date on which there is no longer regulatory exclusivity for ridinilazole in the licensed territory or (iii) ten years from the date of the first commercial sale of ridinilazole in the licensed territory. The license agreement may be terminated by Eurofarma in its entirety upon six months' prior written notice any time after Eurofarma has paid to us the specified development milestones related to our ongoing Phase 3 clinical trials of ridinilazole. Either party may, subject to a cure period, terminate the license agreement in the event of the other party's uncured material breach. Eurofarma may also terminate the license agreement under specified circumstances relating to the safety, efficacy or regulatory approvability of ridinilazole or under specified circumstances if Eurofarma determines certain commercialization plans are no longer economically viable.

Each of the parties has granted to the other a right of reference to copy and use all information included in any regulatory filing in connection with such other party's development, manufacture and commercialization, as applicable, of ridinilazole in the territories where such other party retains such rights. In addition, during the term of the license agreement, except in certain limited circumstances, Eurofarma has agreed not to commercialize any competing antibiotic treatments actively marketed for the treatment of CDI in the licensed territory or our territory without our prior written consent. Similarly, we have agreed not to commercialize any antibiotic treatments competing with the licensed products which would be actively marketed for the treatment of CDI in the licensed territory.

CARB-X

In July 2018, we were granted a sub-award of up to $4.5 million from the Trustees of Boston University under the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator program, or CARB-X. Under our CARB-X award, we received an initial $2.0 million in funding from CARB-X in July 2018 which, in part, helped fund the selection of a preclinical candidate from our lead gonorrhea series of clinical candidates. The remaining $2.5 million is split into two option segments, which may be exercised by CARB-X upon the achievement of certain development milestones. If exercised in full, this funding could support the development of the selected gonorrhea candidate through the end of a Phase 1 clinical trial.

Sarepta Therapeutics, Inc.

In October 2016, we entered into an exclusive license and collaboration agreement with Sarepta, pursuant to which we granted Sarepta the exclusive right to commercialize products in our utrophin modulator pipeline in the European Union, Switzerland, Norway, Iceland, Turkey and the Commonwealth of Independent States, which we refer to as the licensed territory. Such products include ezutromid and our future generation of small molecule utrophin modulators, which we refer to as licensed products. We also granted Sarepta an option to expand the licensed territory to include certain specified countries in Central and South America. We retained commercialization rights in the rest of the world.

Under the terms of the license and collaboration agreement, we received an aggregate of $62.0 million in payments from Sarepta that were comprised of an upfront payment of $40.0 million and a development milestone payment of $22.0 million that we received following the first dosing of the last patient enrolled in our PhaseOut DMD clinical trial. In addition, we were eligible to receive additional payments from Sarepta upon the achievement of specified development, regulatory and sales milestones. With the discontinuation of our development of ezutromid and our other utrophin modulators, we do not expect to receive any milestone payments from Sarepta.

Under the license and collaboration agreement, Sarepta is responsible for 45.0% of the budgeted research and development costs related to the licensed products in the licensed territory, and Sarepta is obligated to reimburse us for a portion of the wind-down costs of PhaseOut DMD.

The license and collaboration agreement may be terminated by Sarepta upon six months' prior written notice in its entirety. Either party may, subject to a cure period, terminate the license and collaboration agreement in the event of the other party's uncured material breach. Sarepta may also terminate the license and collaboration agreement under specified circumstances relating to the safety or regulatory approvability of ezutromid.

The license and collaboration agreement also contains a standstill provision pursuant to which, among other things, each party has agreed that, for a period from the execution of the license and collaboration agreement until the date that regulatory approval is first received for a licensed product, subject to certain exceptions, or unless invited in writing by the other party to do so, neither party nor its respective affiliates will, directly or indirectly: (i) effect or seek, offer or propose to effect, or cause or participate in any acquisition of securities or assets of the other party; any tender or exchange offer, merger, consolidation or other business combination involving the other party; any recapitalization, restructuring, liquidation, dissolution or other extraordinary transaction with respect to the other party; or any "solicitation" of "proxies" or consents to vote any voting securities of the other party, or in any way advise or, assist any other person in doing so; (ii) form, join or in any way participate in a "group" with respect to any securities of the other party; (iii) act in concert with any person in relation to voting securities of the other party; (iv) otherwise act to seek to control or influence the management, board of directors or policies of the other party; (v) take any action reasonably expected to force the other party to make a public announcement regarding any such matters; or (iv) enter into any agreements, discussions or arrangements with any third party with respect to any of the foregoing.

University of Oxford

In November 2013, we acquired all of the outstanding equity of MuOx Limited, or MuOx, a spin out of the University of Oxford. MuOx is our wholly owned subsidiary. In connection with that acquisition, we and MuOx entered into a set of agreements with the University of Oxford and its technology transfer division, Isis Innovation Limited, which is now known as Oxford University Innovation Limited, or OUI, regarding the development of small molecule utrophin modulators. In November 2015, this set of agreements was extended through November 2019. In March 2019, the set of agreements with the University of Oxford and OUI was terminated by mutual consent, as we no longer plan to exploit any intellectual property related to utrophin modulation. Under the termination provisions, we were obligated to make a final payment of £0.13 million to the University of Oxford. Following the termination, the University of Oxford will own any intellectual property that arises from the utrophin modulator research we previously sponsored pursuant to our now-terminated research agreement with OUI, as well as a number of the compounds (other than ezutromid) in our utrophin modulator program that were developed prior to our entry into the research sponsorship agreement. We will not retain any rights to this intellectual property.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technologies, knowledge, experience and scientific resources provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, government agencies and private and public research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Many of our competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, 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 marketing approvals for their products more rapidly than we obtain approval for ours. In addition, our ability to compete may be affected because in some cases insurers or other third-party payors seek to encourage the use of generic products. This may have the effect of making branded products less attractive, from a cost perspective, to buyers.

The key competitive factors affecting the success of our product candidates are likely to be their efficacy, safety, convenience, price and the availability of coverage and reimbursement from government and other third-party payors.

The competition for ridinilazole includes the following:

Several pharmaceutical and biotechnology companies have established themselves in the market for the treatment of CDI, and several additional companies are developing products for the treatment of CDI. We expect that these products will compete with ridinilazole.

Antibiotics. Currently the mostly commonly used treatments for CDI are the broad-spectrum antibiotics vancomycin and metronidazole, both of which are available in generic form in the United States. Generic antibiotic therapies typically are sold at lower prices than branded antibiotics and generally are preferred by managed care providers of health services. The antibiotic fidaxomicin (Dificid™ in the United States, Dificlir™ in Europe) is approved for the treatment of CDI in the United States and the European Union. Fidaxomicin was originally developed by Optimer Pharmaceuticals, Inc., which was later acquired by Cubist Pharmaceuticals, Inc., or Cubist. Cubist was subsequently acquired by Merck & Co., Inc., or Merck.

Other CDI approaches. A number of other approaches for the treatment of CDI are in development. Merck received FDA approval for the monoclonal antibody bezlotoxumab (Zinplava™) in October 2016 and EMA approval in January 2017. Bezlotoxumab is an antibody that neutralizes certain toxins that are produced by *C. difficile* bacteria and indicated to reduce recurrence for CDI in patients who are receiving antibacterial drug treatment and are at high risk of disease recurrence. Sanofi Pasteur SA is developing the vaccine ACAM-CDIFF for primary prevention of CDI. ACAM-CDIFF is likely to be used only in high-risk patients given the difficulty of administering a vaccine to a broad population. In December 2017, Sanofi announced it was ending development stating there was a low probability of the trial meeting its primary endpoint following a review of interim data. Pfizer is developing the vaccine PF-06425090 that aims to induce a functional antibody response to neutralize the *C. difficile* bacterial toxins. Pfizer reported top-line Phase 2 results in January 2017 and commenced enrollment into a Phase 3 trial in March 2017.

Fecal biotherapy aims to recolonize the bacteria that comprise the natural gut flora and would also be adjunctive therapy to antibiotics. Fecal biotherapy approaches in development include SER-109 and SER-262, which are being developed by Seres Therapeutics Inc., formerly Seres Health, Inc., and RBX2660, which was originally being developed by Rebiotix Inc., prior to Rebiotix being acquired by Ferring Pharmaceuticals in April 2018. Seres reported interim results from a Phase 2 trial in 2016 in which SER-109 missed its primary efficacy endpoint; a Phase 3 clinical trial of SER-109 was commenced in June 2017. Seres reported results from a Phase 1b clinical trial of SER-262 in CDI patients in August 2018 and indicated these findings will inform the future development of SER-262. In April 2017, Rebiotix reported positive top-line data from an open-label Phase 2 clinical trial of RBX2660 and in August 2017, enrolled the first patient into a Phase 3 clinical trial. Finch Therapeutics Group Inc is developing the fecal biotherapy CP101, which is being evaluated in a Phase 2 clinical trial in patients with CDI. Synthetic Biologics, Inc., is developing ribaxamase, an oral enzyme designed to degrade certain IV beta-lactam antibiotics within the GI tract to preserve the natural balance of the microbiome and reduce the risk of colonization by bacteria, including *C. difficile*. In January 2017, it was reported that ribaxamase met its primary endpoint in a Phase 2b clinical trial; Phase 3 clinical trials are currently planned to be initiated in 2019.

Manufacturing

We do not own or operate, and currently have no plans to establish, manufacturing facilities for the production of clinical or commercial quantities of ridinilazole or for the other compounds that we are evaluating in our infectious diseases programs. We currently rely, and expect to continue to rely, on third parties for the manufacture of our product candidates and any products that we may develop.

We currently engage a third-party manufacturer to provide clinical material of the API of ridinilazole with the same supplier responsible for fill and finish services to supply the final drug product for use in the ongoing Phase 3 clinical trials. We believe these suppliers are suitable for commercial manufacture. We are using a different third-party supplier for clinical packaging, labeling and distribution of the finalized ridinilazole drug product. We obtain the supplies of our API and drug products from these manufacturers pursuant to agreements that include specific supply timelines and volume expectations.

We obtain the supplies of our product candidates from these manufacturers under master services contracts and specific work orders. However, we do not have long-term supply arrangements in place. We do not currently have arrangements in place for redundant supply or a second source for API for ridinilazole. If any of our current manufacturers should become unavailable to us for any reason, we believe that there are a number of potential replacements, although we might incur some delay in identifying and qualifying such replacements.

All of our product candidates are organic compounds of low molecular weight and are referred to as small molecules. We have selected these compounds based on their potential efficacy and safety, although they are also associated with reasonable cost of goods, ready availability of starting materials and ease of synthesis. We believe that the chemistry for ridinilazole is amenable to scale-up and does not currently require unusual equipment in the manufacturing process. We expect to continue to develop product candidates that can be produced cost-effectively at contract manufacturing facilities.

Intellectual Property

Our success depends in large part on our ability to obtain and maintain proprietary protection for our product candidates, technology and know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. We strive to protect the proprietary technology that we believe is important to our business by, among other methods, seeking and maintaining patents, where available, that are intended to cover our product candidates, compositions and formulations, their methods of use and processes for their manufacture and any other inventions that are commercially important to the development of our business. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary and competitive position.

As of March 15, 2019, we owned or exclusively licensed a total of six U.S. patents, one U.S. patent application, four European patents and one European patent application, including original filings, continuations and divisional applications, as well as numerous other foreign counterparts to these U.S. and European patents and patent applications.

Our CDI patent portfolio includes the following granted patents and patent applications that we own or exclusively license:

- a granted U.S. patent covering the use of ridinilazole in the treatment of CDI, which is scheduled to expire in 2029;
- a corresponding granted European patent covering the use of ridinilazole in the treatment of CDI, which is scheduled to expire in 2029;
- a granted U.S. patent covering hydrates of ridinilazole, which is scheduled to expire in 2029;
- a granted European divisional patent covering hydrates of ridinilazole and pharmaceutical compositions comprising ridinilazole;
- a further granted U.S. patent covering the use of ridinilazole in the treatment of CDI, which is scheduled to expire in 2029; and
- two granted U.S. patents, a granted European patent and a pending European divisional application covering second generation agents for the treatment of CDI, which are scheduled to expire in 2031.

While patent protection is not available for composition of matter claims that only recite the API for ridinilazole, protection may be available for the pharmaceutical compositions comprising ridinilazole as well as other forms thereof such as hydrates (and indeed claims have been secured for the latter in both Europe and the United States).

As of March 15, 2019, we owned a total of one U.S. patent and one European patent and a number of pending patent applications, including original filings and continuations, as well as numerous other foreign counterparts to these U.S. and European patents and patent applications, covering the genetics-based technology platform acquired in connection with the Discuva acquisition. We also have two families of pending patent applications covering potential antibiotic compounds that are being identified using our Discuva Platform. One of these patent families contains a single pending international patent cooperation treaty, or PCT, application. The other patent family has recently entered national/regional phase, and contains multiple pending national/regional applications in territories including the United States and Europe.

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the filing date of a non-provisional patent application. In the United States, a patent's term may, in certain cases, be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office, or the USPTO, in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier filed patent.

The term of a U.S. patent that covers a drug, biological product or medical device approved pursuant to a pre-market approval, or PMA, may also be eligible for patent term extension when FDA approval is granted, provided that certain statutory and regulatory requirements are met. The length of the patent term extension is related to the length of time the drug is under regulatory review while the patent is in force. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration date set for the patent. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be granted an extension and only those claims reading on the approved drug may be extended. Similar provisions are available in Europe such as a supplementary protection certificate, or SPC, an additional form of protection linked to the patent and coming into force after the patent's expiry. Certain other foreign jurisdictions including Australia, Israel, Japan, Korea, Singapore and Taiwan also have provisions to extend the term of a patent that covers an approved drug, provided that statutory and regulatory requirements are met. Thus, in the future, if and when our product candidates receive approval by the FDA or foreign regulatory authorities, we expect to apply for patent term extensions on issued patents covering those products, depending upon the length of the clinical trials for each drug and other factors. The expiration dates of our patents and patent applications referred to above are without regard to potential patent term extension or other market exclusivity that may be available to us.

In addition to patents, we may rely, in some circumstances, on trade secrets to protect our technology and maintain our competitive position. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements with our employees, corporate and scientific collaborators, consultants, scientific advisors, contractors and other third parties. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems.

Sales and Marketing

In light of our stage of development, we have not yet established a sales and marketing organization or distribution capabilities.

We expect to commercialize ridinilazole in the United States with our own focused, specialty sales force that we plan to establish. Under the terms of our exclusive license and commercialization agreement with Eurofarma, we have granted Eurofarma the exclusive right to commercialize ridinilazole in certain countries in South America, Central America and the Caribbean. We have retained commercialization rights in all other territories, including in the United States and Europe.

We will continue to evaluate our options for maximizing the commercial opportunity for ridinilazole in other key territories where we retain exclusive commercialization rights, including Europe and Asia. We intend to evaluate the relative merits of retaining commercialization rights for ourselves or entering into collaboration arrangements with third parties depending on factors such as the anticipated development costs required to achieve marketing approval, the sales and marketing resources required in each territory in which we receive approval, the relative size of the market opportunity in such territory, the particular expertise of the third party and the proposed financial terms of the arrangement.

We are also in the process of building key capabilities, such as marketing, market access, sales management and medical affairs, to implement marketing and medical strategies for any products that we market through our own sales organization and to oversee and support our sales force. The responsibilities of the marketing organization would include developing educational initiatives with respect to approved products and expanding relationships with thought leaders in relevant fields of medicine.

Government Regulation

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

Review and Approval of Drugs in the United States

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The failure to comply with the FDCA and applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice, or DOJ, or other federal and state governmental entities.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with current good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each indication;

- preparation and submission to the FDA of a new drug application, or NDA;
- review of the product candidate by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of user fees and securing FDA approval of the NDA; and
- compliance with any post-approval requirements, including Risk Evaluation and Mitigation Strategies, or REMS, where applicable, and any post-approval studies required by the FDA.

Preclinical Studies

Before an applicant begins testing a compound with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of the purity and stability of the active pharmaceutical ingredient, or API, and the formulated drug or drug product, as well as *in vitro* and animal studies to assess the safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted.

Companies usually must complete some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and must also develop additional information about the chemistry and physical characteristics of the investigational product 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 candidate product and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the candidate product does not undergo unacceptable deterioration over its shelf life.

The IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved drug to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer an investigational drug to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug that is not the subject of an approved NDA. In support of a request for an IND, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. Clinical holds are imposed by the FDA whenever there is concern for patient safety and may be a result of new data, findings, or developments in clinical, nonclinical, and/or chemistry, manufacturing, and controls, or CMC. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all FDA IND requirements must be met unless waived. When the foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA

in order to use the study as support for an IND or application for marketing approval. Specifically, on April 28, 2008, the FDA amended its regulations governing the acceptance of foreign clinical studies not conducted under an investigational new drug application as support for an IND or a new drug application. The final rule provides that such studies must be conducted in accordance with good clinical practice, or GCP, including review and approval by an independent ethics committee, or IEC, and informed consent from subjects. The GCP requirements in the final rule encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

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

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

Information about clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on its ClinicalTrials.gov website.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational drugs for patients who may benefit from investigational therapies. FDA regulations allow access to investigational drugs under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the drug under a treatment protocol or Treatment IND Application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere with initiation, conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product.

On December 13, 2016, the 21st Century Cures Act established (and the 2017 Food and Drug Administration Reauthorization Act later amended) a requirement that sponsors of one or more investigational drugs for the treatment of a serious disease(s) or condition(s) make publicly available their policy for evaluating and responding to requests for expanded access for individual patients. Although these requirements were rolled out over time, they have now come into full effect. This provision requires drug and biologic companies to make publicly available their policies for expanded access for individual patient access to products intended for serious diseases. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 study; or 15 days after the drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

In addition, on May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

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

Phase 1. The investigational drug is initially introduced into healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.

Phase 2. The investigational drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

Phase 3. The investigational drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product. These clinical trials are commonly referred to as "pivotal" studies, which denotes a study that presents the data that the FDA or other relevant regulatory agency will use to determine whether or not to approve a product candidate.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Concurrent with clinical trials, companies often complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must develop methods for testing the identity, strength, quality, purity, and potency of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

Under the Pediatric Research Equity Act of 2003, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of the Food and Drug Administration Safety and Innovation Act, or FDASIA, in 2012, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

For drugs intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of an applicant, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, FDA will meet early in the development process to discuss pediatric study plans with sponsors and FDA must meet with sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than ninety (90) days after FDA's receipt of the study plan.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

The FDA Reauthorization Act of 2017 established new requirements to govern certain molecularly targeted cancer indications. Any company that submits an NDA three years after the date of enactment of that statute must submit pediatric assessments with the NDA if the drug is intended for the treatment of an adult cancer and is directed at a molecular target that FDA determines to be substantially relevant to the growth or progression of a pediatric cancer. The investigation must be designed to yield clinically meaningful pediatric study data regarding the dosing, safety and preliminary efficacy to inform pediatric labeling for the product.

Submission of an NDA to the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most applications is subject to an application user fee, which for federal fiscal year 2019 is $2,588,478 for an application requiring clinical data. The sponsor of an approved application is also subject to an annual program fee, which for fiscal year 2019 is $309,915. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses.

Following submission of an application, the FDA conducts a preliminary review of an NDA within 60 calendar days of its receipt and strives to inform the sponsor by the 74th day after the FDA's receipt of the submission whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review.

The FDA has agreed to certain performance goals in the review process of NDAs. Under that agreement, 90% of applications seeking approval of new molecular entities, or NMEs, are meant to be reviewed within ten months from the date on which FDA accepts the NDA for filing, and 90% of applications for NMEs that have been designated for "priority review" are meant to be reviewed within six months of the filing date. For applications seeking approval of drugs that are not NMEs, the ten-month and six-month review periods run from the date that FDA receives the application. The review process may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections cover all facilities associated with an NDA submission, including drug component manufacturing (such as active pharmaceutical ingredients), finished drug product manufacturing, and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Under the FDA Reauthorization Act of 2017, the FDA must implement a protocol to expedite review of responses to inspection reports pertaining to certain applications, including applications for products in shortage or those for which approval is dependent on remediation of conditions identified in the inspection report.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity. REMS can include medication guides, physician communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The FDA may require a REMS before approval or post-approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS can materially affect the potential market and profitability of a product.

The FDA may refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Fast Track, Breakthrough Therapy, Priority Review and Regenerative Advanced Therapy Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast track designation, breakthrough therapy designation, priority review designation and regenerative advanced therapy designation.

Specifically, the FDA may designate a product for fast track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For fast track products, sponsors may have greater interactions with the FDA, and the FDA may initiate review of sections of a fast track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a fast track application does not begin until the last section of the application is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, a product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case- by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

Finally, with passage of the 21st Century Cures Act, or Cures Act, in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a drug for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a drug when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and 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. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a drug.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. For example, accelerated approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large clinical trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. As a result, a drug candidate

approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

Limited Population Antibacterial Drug Pathway

With passage of the Cures Act, Congress authorized the FDA to approve an antibacterial or antifungal drug, alone or in combination with one or more other drugs, as a "limited population drug." To qualify for this approval pathway, the drug must be intended to treat a serious or life-threatening infection in a limited population of patients with unmet needs; the standards for approval of drugs and biologics under the FDCA and the Public Health Service Act, or PHSA, must be satisfied; and the FDA must receive a written request from the sponsor to approve the drug as a limited population drug pursuant to this provision. The FDA's determination of safety and effectiveness for such a product must reflect the benefit-risk profile of such drug in the intended limited population, taking into account the severity, rarity, or prevalence of the infection the drug is intended to treat and the availability or lack of alternative treatment in such a limited population.

Any drug or biologic approved under this pathway must be labeled with the statement "Limited Population" in a prominent manner and adjacent to the proprietary name of the drug or biological product. The prescribing information must also state that the drug is indicated for use in a limited and specific population of patients and copies of all promotional materials relating to the drug must be submitted to the FDA at least 30 days prior to dissemination of the materials. If the FDA subsequently approves the drug for a broader indication, the agency may remove any post-marketing conditions, including requirements with respect to labeling and review of promotional materials applicable to the product. Nothing in this pathway to approval of a limited population drug prevents sponsors of such products from seeking designation or approval under other provisions of the FDCA, such as accelerated approval.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record keeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with 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 program fee requirements for any marketed products, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the 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 safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, suspension of the approval, 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 NDAs or supplements to approved NDAs, 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 strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. Regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA, as reflected in the product's prescribing information. In the United States, health care professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information.

If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion, and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, and its implementing regulations, as well as the Drug Supply Chain Security Act, or DSCA, which regulate the distribution and tracing of prescription drug samples at the federal level, and set minimum standards for the regulation of distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples, and the DSCA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

Section 505(b)(2) NDAs

NDAs for most new drug products are based on two full clinical studies which must contain substantial evidence of the safety and efficacy of the proposed new product for the proposed use. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the applicant to rely, in part, on the FDA's previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the applicant for approval of the application "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Thus, Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the applicant. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the statute. To obtain

approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. In support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, and the strength of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug." Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity. A new chemical entity is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

The FDA must establish a priority review track for certain generic drugs, requiring the FDA to review a drug application within eight (8) months for a drug that has three (3) or fewer approved drugs listed in the Orange Book and is no longer protected by any patent or regulatory exclusivities, or is on the FDA's drug shortage list. The new legislation also authorizes FDA to expedite review of ''competitor generic therapies'' or drugs with inadequate generic competition, including holding meetings with or providing advice to the drug sponsor prior to submission of the application.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a "Paragraph IV certification." If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the ANDA applicant is not seeking approval).

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV

certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent or a decision in the infringement case that is favorable to the ANDA applicant.

To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. As a result, approval of a Section 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

Pediatric Exclusivity

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

GAIN Exclusivity for Antibiotics

The FDA has designated ridinilazole as a qualified infectious disease product, or QIDP, under the Generating Antibiotic Incentives Now Act, or GAIN Act. Congress passed this legislation to encourage the development of antibacterial and antifungal drug products that treat pathogens that cause serious and life-threatening infections. To that end, the GAIN Act grants an additional five years of exclusivity upon the approval of an NDA for a drug product designated by the FDA as a QIDP. Thus, for a QIDP, the periods of five-year new chemical entity exclusivity, three-year new clinical investigation exclusivity and seven-year orphan drug exclusivity, would become ten years, eight years and 12 years, respectively.

A QIDP is defined in the GAIN Act to mean "an antibacterial or antifungal drug for human use intended to treat serious or life-threatening infections, including those caused by: (1) an antibacterial or antifungal resistant pathogen, including novel or emerging infectious pathogens;" or (2) certain "qualifying pathogens." A "qualifying pathogen" is a pathogen that has the potential to pose a serious threat to public health (such as resistant gram-positive pathogens, multi-drug resistant gram-negative bacteria, multi-drug resistant tuberculosis and *Clostridium difficile*) and that is included in a list established and maintained by the FDA. A drug sponsor may request the FDA to designate its product as a QIDP any time before the submission of an NDA. The FDA must make a QIDP determination within 60 days of the designation request. A product designated as a QIDP will be granted priority review by FDA and can qualify for "fast track" status.

The additional five years of exclusivity under the GAIN Act for drug products designated by the FDA as QIDPs applies only to a drug that is first approved on or after July 9, 2012. Additionally, the five year exclusivity extension does not apply to: a supplement to an application under FDCA Section 505(b) for any QIDP for which an extension is in effect or has expired; a subsequent application filed with respect to a product approved by the FDA for a change that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength; or a product that does not meet the definition of a QIDP under Section 505(g) based upon its approved uses.

Patent Term Restoration and Extension

The term of a U.S. patent that covers a drug, biological product or medical device approved pursuant to a PMA may also be eligible for patent term extension when FDA approval is granted, provided that certain statutory and regulatory requirements are met. The length of the patent term extension is related to the length of time the drug is under regulatory review while the patent is in force. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration date set for the patent. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be granted an extension and only those claims reading on the approved drug may be extended. Similar provisions are available in Europe and certain other foreign jurisdictions to extend the term of a patent that covers an approved drug, provided that statutory and regulatory requirements are met. The USPTO reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Regulation Outside the United States

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of drug products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Regulation and Marketing Authorization in the European Union

Clinical Trial Approval

The Clinical Trials Directive 2001/20/EC, the Directive 2005/28/EC on Good Clinical Practice, or GCP, and the related national implementing provisions of the individual E.U. Member States govern the system for the approval of clinical trials in the E.U. Under this system, an applicant must obtain prior approval from the competent national authority of the E.U. Member States in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. The clinical trial application must be accompanied by, among other documents, an investigational medicinal product dossier (the Common Technical Document) with supporting information prescribed by Directive 2001/20/EC, Directive 2005/28/EC, where relevant the implementing national provisions of the individual E.U. Member States and further detailed in applicable guidance documents.

In April 2014, the new Clinical Trials Regulation, (E.U.) No 536/2014 (Clinical Trials Regulation) was adopted. The Regulation was published on June 16, 2014, but is not expected to apply until later in 2019. The Clinical Trials Regulation will be directly applicable in all the E.U. Member States, repealing the current Clinical Trials Directive 2001/20/EC and replacing any national legislation that was put in place to implement the Directive. Conduct of all clinical trials performed in the E.U. will continue to be bound by currently applicable provisions until the new Clinical Trials Regulation becomes applicable. The extent to which ongoing clinical trials will be governed by the Clinical Trials Regulation will depend on when the Clinical Trials Regulation becomes applicable and on the duration of the individual clinical trial. If a clinical trial continues for more than three years from the day on which the Clinical Trials Regulation becomes applicable the Clinical Trials Regulation will at that time begin to apply to the clinical trial.

The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the E.U. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the “E.U. Portal and Database”; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the appointed reporting Member State, whose assessment report is submitted for review by the sponsor and all other competent authorities of all E.U. Member States in which an application for authorization of a clinical trial has been submitted (Concerned Member States). Part II is assessed separately by each Concerned Member State. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the Concerned Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

As in the United States, similar requirements for posting clinical trial information are present in the European Union (EudraCT) website: https://eudract.ema.europa.eu/ and other countries.

PRIME Designation in the E.U.

In March 2016, the European Medicines Agency, or EMA, launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority MEdicines, or PRIME, scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises, or SMEs, may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, a dedicated Agency contact and rapporteur from the Committee for Human Medicinal Products ('CHMP') or Committee for Advanced Therapies ('CAT') are appointed early in PRIME scheme facilitating increased understanding of the product at EMA’s Committee level. A kick-off meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Marketing Authorization

To obtain a marketing authorization for a product under E.U. regulatory systems, an applicant must submit an MAA either under a centralized procedure administered by the EMA, or one of the procedures administered by competent authorities in the E.U. Member States (decentralized procedure, national procedure or mutual recognition procedure). A marketing authorization may be granted only to an applicant established in the E.U. Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the E.U., applicants have to demonstrate compliance with all measures included in an EMA-approved Paediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver or (3) a deferral for one or more of the measures included in the PIP.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid across the European Economic Area (i.e. the E.U. as well as Iceland, Liechtenstein and Norway). Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, ATMPs and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of cancer. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional. The centralized procedure may at the request of the applicant also be used in certain other cases. We anticipate that the centralized procedure will be mandatory for the product candidates we are developing.

Under the centralized procedure, the CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the E.U., the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. If the CHMP accepts such request, the time limit of 210 days will be reduced to 150 days, but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment. At the end of this period, the CHMP provides a scientific opinion on whether or not a marketing authorization should be granted in relation to a medicinal product. Within 15 calendar days of receipt of a final opinion from the CHMP, the European Commission must prepare a draft decision concerning an application for marketing authorization. This draft decision must take the opinion and any relevant provisions of E.U. law into account. Before arriving at a final decision on an application for centralized authorization of a medicinal product the European Commission must consult the Standing Committee on Medicinal Products for Human Use. The Standing Committee is composed of representatives of the E.U. Member States and chaired by a non-voting European Commission representative. The European Parliament also has a related “droit de regard.” The European Parliament's role is to ensure that the European Commission has not exceeded its powers in deciding to grant or refuse to grant a marketing authorization.

The European Commission may grant a so-called “marketing authorization under exceptional circumstances.” Such authorization is intended for products for which the applicant can demonstrate that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use, because the indications for which the product in question is intended are encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence, or in the present state of scientific knowledge, comprehensive information cannot be provided, or it would be contrary to generally accepted principles of medical ethics to collect such information. Consequently, marketing authorization under exceptional circumstances may be granted subject to certain specific obligations, which may include the following:

- the applicant must complete an identified program of studies within a time period specified by the competent authority, the results of which form the basis of a reassessment of the benefit/risk profile;
- the medicinal product in question may be supplied on medical prescription only and may in certain cases be administered only under strict medical supervision, possibly in a hospital and in the case of a radiopharmaceutical, by an authorized person; and
- the package leaflet and any medical information must draw the attention of the medical practitioner to the fact that the particulars available concerning the medicinal product in question are as yet inadequate in certain specified respects.

A marketing authorization under exceptional circumstances is subject to annual review to reassess the risk-benefit balance in an annual reassessment procedure. Continuation of the authorization is linked to the annual reassessment and a negative assessment could potentially result in the marketing authorization being suspended or revoked. The renewal of a marketing authorization of a medicinal product under exceptional circumstances, however, follows the same rules as a “normal” marketing authorization. Thus, a marketing authorization under exceptional circumstances is granted for an initial five years, after which the authorization will become valid indefinitely, unless the EMA decides that safety grounds merit one additional five-year renewal.

The European Commission may also grant a so-called "conditional marketing authorization" prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional marketing authorizations may be granted for product candidates (including medicines designated as orphan medicinal products), if (i) the risk-benefit balance of the product candidate is positive, (ii) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (iii) the product fulfills an unmet medical need and (iv) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions and/or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization.

The E.U. medicines rules expressly permit the E.U. Member States to adopt national legislation prohibiting or restricting the sale, supply or use of any medicinal product containing, consisting of or derived from a specific type of human or animal cell, such as embryonic stem cells. While the products we have in development do not make use of embryonic stem cells, it is possible that the national laws in certain E.U. Member States may prohibit or restrict us from commercializing our products, even if they have been granted an E.U. marketing authorization.

Unlike the centralized authorization procedure, the decentralized marketing authorization procedure requires a separate application to, and leads to separate approval by, the competent authorities of each E.U. Member State in which the product is to be marketed. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference E.U. Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned E.U. Member States who, within 90 days of receipt, must decide whether to approve the assessment report and related materials. If a concerned E.U. Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the European Commission, whose decision is binding on all E.U. Member States.

The mutual recognition procedure similarly is based on the acceptance by the competent authorities of the E.U. Member States of the marketing authorization of a medicinal product by the competent authorities of other E.U. Member States. The holder of a national marketing authorization may submit an application to the competent authority of an E.U. Member State requesting that this authority recognize the marketing authorization delivered by the competent authority of another E.U. Member State.

Regulatory Data Protection in the E.U.

In the E.U., innovative medicinal products approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Directive 2001/83/EC. Regulation (EC) No 726/2004 repeats this entitlement for medicinal products authorized in accordance to the centralized authorization procedure. Data exclusivity prevents applicants for authorization of generics of these innovative products from referencing the innovator's data to assess a generic (abridged) application for a period of eight years. During an additional two-year period of market exclusivity, a generic marketing authorization application can be submitted and authorized, and the innovator's data may be referenced, but no generic medicinal product can be placed on the E.U. market until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Periods of Authorization and Renewals

A marketing authorization has an initial validity for five years in principle. The marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the E.U. Member State. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. The European Commission or the competent authorities of the E.U. Member States may decide, on justified grounds relating to pharmacovigilance, to proceed with one further five-year period of marketing authorization. Once subsequently definitively renewed, the marketing authorization shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the E.U. market (in case of centralized procedure) or on the market of the authorizing E.U. Member State within three years after authorization ceases to be valid (the so-called sunset clause).

Pediatric Studies

Prior to obtaining a marketing authorization in the European Union, applicants have to demonstrate compliance with all measures included in an EMA-approved Paediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. The respective requirements for all marketing authorization procedures are set forth in Regulation (EC) No 1901/2006, which is referred to as the Paediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The Paediatric Committee of the EMA, or PDCO, may grant deferrals for some medicines, allowing a company to delay development of the medicine in children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine in children is not needed or is not appropriate, such as for diseases that only affect the elderly population.

Before a marketing authorization application can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP.

Regulatory Requirements after a Marketing Authorization has been Obtained

In case an authorization for a medicinal product in the E.U. is obtained, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include:

- Compliance with the E.U.'s stringent pharmacovigilance or safety reporting rules must be ensured. These rules can impose post-authorization studies and additional monitoring obligations.
- The manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable E.U. laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with E.U. cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the E.U. with the intention to import the active pharmaceutical ingredients into the E.U.
- The marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the E.U. notably under Directive 2001/83EC, as amended, and E.U. Member State laws. Direct-to-consumer advertising of prescription medicines is prohibited across the EU..

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the EU (commonly referred to as "Brexit"). Thereafter, on March 29, 2017, the country formally notified the E.U. of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The withdrawal of the United Kingdom from the E.U. will take effect either on the effective date of the withdrawal agreement or, in the absence of agreement, two years after the United Kingdom provides a notice of withdrawal pursuant to the E.U. Treaty. Since the regulatory framework for pharmaceutical products in the United Kingdom. covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from E.U. directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the United Kingdom.

The United Kingdom has a period of a maximum of two years from the date of its formal notification to negotiate the terms of its withdrawal from, and future relationship with, the European Union. If no formal withdrawal agreement is reached between the United Kingdom and the European Union, then it is expected the United Kingdom's membership of the European Union will automatically terminate two years after the submission of the notification of the United Kingdom's intention to withdraw from the European Union. On March 21, 2019, the European Council, in agreement with the United Kingdom, unanimously agreed to extend the deadline to May 22, 2019, if the U.K. Parliament approves in an upcoming vote the withdrawal agreement agreed to between the United Kingdom and the European Union in November 2018, and to April 12, 2019, if the U.K. Parliament does not approve it. Discussions between the United Kingdom and the European Union focused on finalizing withdrawal issues and transition agreements are ongoing. However, limited progress to date in these negotiations and ongoing uncertainty within the U.K. Government and Parliament sustains the possibility of the United Kingdom leaving the European Union on April 12, 2019, without a withdrawal agreement and associated transition period in place, which is likely to cause significant market and economic disruption.

General Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the E.U., including personal health data, is subject to the E.U. General Data Protection Regulation (GDPR), which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the E.U., including the U.S., and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

Pricing Decisions for Approved Products

In the E.U., pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the E.U. provides options for its Member States to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. Member States may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other Member States allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the E.U. have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage health care expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the E.U. The downward pressure on health care costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various Member States, and parallel trade, i.e., arbitrage between low-priced and high-priced Member States, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Patent Term Extension

In order to compensate the patentee for delays in obtaining a marketing authorization for a patented product, a supplementary certificate, or SPC, may be granted extending the exclusivity period for that specific product by up to five years. Applications for SPCs must be made to the relevant patent office in each E.U. member state and the granted certificates are valid only in the member state of grant. An application has to be made by the patent owner within six months of the first marketing authorization being granted in the European Union (assuming the patent in question has not expired, lapsed or been revoked) or within six months of the grant of the patent (if the marketing authorization is granted first). In the context of SPCs, the term “product” means the active ingredient or combination of active ingredients for a medicinal product and the term “patent” means a patent protecting such a product or a new manufacturing process or application for it. The duration of an SPC is calculated as the difference between the patent’s filing date and the date of the first marketing authorization, minus five years, subject to a maximum term of five years.

A six month pediatric extension of an SPC may be obtained where the patentee has carried out an agreed pediatric investigation plan, the authorized product information includes information on the results of the studies and the product is authorized in all member states of the European Union.

Healthcare Law and Regulation

Health care providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, patient privacy laws and regulations and other health care laws and regulations that may constrain business and/or financial arrangements. Restrictions under applicable federal and state health care laws and regulations, include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or

recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;

- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to health care matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- Foreign Corrupt Practices Act, or FCPA, which prohibits companies and their intermediaries from making, or offering or promising to make improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment;
- the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for health care benefits, items or services;
- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or the Affordable Care Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-government third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. State and foreign laws also govern 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.

Pharmaceutical Insurance Coverage and Health Care Reform

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated health care costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage and establish adequate reimbursement levels for, the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, results

of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

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

There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States. In March 2010, the United States Congress enacted the Affordable Care Act, or ACA, which, among other things, includes changes to the coverage and payment for drug products under government health care programs. Among the provisions of the ACA of importance to our potential product candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% (and 70% starting January 1, 2019) point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

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 up to 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments, will remain in effect through 2027 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Since enactment of the ACA, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by the President on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, among other things, amends the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D

and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." The Congress will likely consider other legislation to replace elements of the ACA during the next Congressional session.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known.

Further, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. For example, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

For example, on May 11, 2018, the Administration issued a plan to lower drug prices. Under this blueprint for action, the Administration indicated that the Department of Health and Human Services (HHS) will: take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies; advance biosimilars and generics to boost price competition; evaluate the inclusion of prices in drug makers' ads to enhance price competition; speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers; avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid; work to give Part D plan sponsors more negotiation power with drug makers; examine which Medicare Part B drugs could be negotiated for a lower price by Part D plans, and improving the design of the Part B Competitive Acquisition Program; update Medicare's drug-pricing dashboard to increase transparency; prohibit Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance; and require that Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases. More recently, on January 31, 2019, the HHS Office of Inspector General proposed modifications to the federal Anti-Kickback Statute discount safe harbor for the purpose of reducing the cost of drug products to consumers which, among other things, if finalized, will affect discounts paid by manufacturers to Medicare Part D plans, Medicaid managed care organizations and pharmacy benefit managers working with these organizations.

At the state level, individual states are increasingly aggressive in 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. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

C. Organizational Structure

The following is a list of our subsidiaries:

Name of subsidiary	Country of registration	Activity	% holding
Summit (Oxford) Limited	England and Wales	Research and Development	100%
Discuva Limited	England and Wales	Research and Development	100%
Summit Therapeutics Inc.	USA	Research and Development Services	100%
Summit Corporation Limited	England and Wales	Dormant	100%
Summit (Wales) Limited	England and Wales	Dormant	100%
Summit (Cambridge) Limited	England and Wales	Dormant	100%
Summit Discovery 1 Limited	England and Wales	Dormant	100%
Summit Corporation Employee Benefit Trust Company Limited	England and Wales	Dormant	100%
MuOx Limited	England and Wales	Dormant	100%
Summit Infectious Diseases Limited	England and Wales	Dormant	100%

D. Property, Plants and Equipment

We maintain the following leased properties:

Type/Uses	Location	Size	Lease Expiry
Executive office	Oxfordshire, United Kingdom	6,781 square feet	February 2027
Executive office	Cambridge, Massachusetts	570 square feet	Rolling
Laboratory and office	Cambridge, United Kingdom	8,834 square feet	December 2021

For information about environmental issues that may affect our utilization of our facilities, please see the section of this Annual Report titled “Item 3.D. Risk Factors - Risks Related to Development and Commercialization of our Product Candidates - 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.”

Item 4A: Unresolved Staff Comments

Not applicable.

Item 5: Operating and Financial Review and Prospects

You should read the following discussion and analysis of our financial condition and results of operations together with "Selected Consolidated Financial Data" and our consolidated financial statements and the related notes thereto appearing at the end of this Annual Report. We present our consolidated financial statements in pounds sterling and in accordance with International Financial Reporting Standards, or IFRS, as issued by the International Accounting Standards Board, or IASB.

Some information included in this discussion and analysis, including statements regarding industry outlook, our expectations regarding our future performance, liquidity and capital resources and other statements regarding our plans and strategy for our business and related financing, are forward-looking statements. These forward-looking statements are subject to numerous risks and uncertainties. You should read the "Risk Factors" section of this Annual Report for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Solely for the convenience of the reader, unless otherwise indicated, all pound sterling amounts as of and for the year ended January 31, 2019 have been translated into U.S. dollars at the noon buying rate of the Federal Reserve Bank of New York on January 31, 2019, of £1.00 to $1.3135. All pound sterling amounts as of and for the years ended January 31, 2018 and January 31, 2017 were translated into U.S. dollars at the rate of £1.00 to $1.4190 and $1.2585, respectively. These translations should not be considered representations that any such amounts have been, could have been or could be converted into U.S. dollars at that or any other exchange rate as of that or any other date.

Overview

We were founded in 2003 and are incorporated under the laws of England and Wales with the Registrar of Companies of England and Wales, United Kingdom. Our principal offices are located in the United Kingdom. Our ordinary shares have traded on AIM, which is a sub-market of the London Stock Exchange, since October 2004 and our American Depositary Shares, or ADSs, have traded on the Nasdaq Global Market since March 2015. Our historic business activities have included the research and development of drug candidates across a number of disease areas. We have also in the past provided drug discovery services to other pharmaceutical and biotechnology companies. However, we sold these drug discovery services businesses in 2009 as part of a broader restructuring initiative to focus on identifying and developing medicines in a range of major therapy areas. In 2012, we made a strategic decision to further refine our business focus and concentrate on the development of our clinical stage programs for Duchenne muscular dystrophy, or DMD, and *Clostridium difficile* infection, or CDI, in order to more efficiently capitalize on the scientific and commercial potential of these programs. We expanded our future generation utrophin modulator pipeline effort in November 2013 through the formation of a strategic alliance with the University of Oxford. In 2014, we opened an office in Cambridge, Massachusetts, in order to strengthen our presence in the United States. We expect to undertake a significant proportion of our future development efforts for our clinical programs in the United States. In 2017, we acquired Discuva Limited, a U.K.-based company, providing us with access to a bacterial genetics-based technology we refer to as our Discuva Platform. In 2018, we discontinued the development of our DMD program after our lead utrophin modulator, ezutromid, did not meet its primary or secondary endpoints in a Phase 2 proof of concept clinical trial. We refocused our strategy on the discovery, development and commercialization of antibiotics for the treatment of serious infectious diseases. We are currently conducting Phase 3 clinical trials of ridinilazole, our product candidate for the treatment of CDI. We are also seeking to expand our product candidate portfolio through the development of new antibiotics using our proprietary Discuva Platform.

To date, we have financed our operations primarily through issuances of our ordinary shares and American Depositary Shares, or ADSs, payments to us under our license and collaboration agreement with Sarepta Therapeutics, Inc., or Sarepta, and our license and commercialization agreement with Eurofarma Laboratórios SA, or Eurofarma, and development funding and other assistance from government entities, philanthropic, non-government and not for profit organizations and patient advocacy groups for our product candidates. In particular, we have received funding from the Biomedical Advanced Research and Development Authority, or BARDA, the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator program, or CARB-X, the Wellcome Trust, Innovate UK, and a number of not for profit organizations.

We have generated losses since inception. Our net profit was approximately £7.5 million for the year ended January 31, 2019. Our net loss was approximately £20.2 million for the year ended January 31, 2018 and £21.4 million for the year ended January 31, 2017. As of January 31, 2019, we had an accumulated deficit of £76.1 million. The profit recorded for the year ended January 31, 2019 was due to the recognition of all remaining deferred revenue related to the Sarepta agreement following our decision to discontinue the development of ezutromid in June 2018. This recognition of deferred revenues did not impact our cash flows. We expect to incur significant expenses and increasing operating losses for at least the next several years in connection with conducting clinical trials for our lead product candidate, ridinilazole (formerly SMT19969) for the treatment of CDI, conducting preclinical research and development activities and seeking marketing approval for ridinilazole in the United States as well as other geographies where we retain commercialization rights. In addition, subject to obtaining regulatory approval for ridinilazole or any of our future product candidates, we expect to incur significant commercialization expenses for product sales, marketing, distribution and outsourced manufacturing. We also incur additional costs associated with operating as a public company in the United States in addition to in the United Kingdom. Accordingly, we will need additional financing to support our continuing operations. Adequate additional financing may not

be available to us on acceptable terms, or at all. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

A. Operating Results

Important Financial and Operating Terms and Concepts

Revenue

Revenue currently consists of amounts received under an exclusive license and collaboration agreement with Sarepta, entered into in October 2016, amounts received under an exclusive license and commercialization agreement with Eurofarma, entered into in December 2017, and amounts received from a research collaboration agreement between our subsidiary, Discuva Limited, and F. Hoffmann-La Roche Ltd, or Roche. The terms of the agreements with Sarepta and Eurofarma have been assessed, and we believe the development services to be indistinguishable from the initial license and as a result the upfront payments have been initially reported as deferred revenue on the Consolidated Statement of Financial Position and are being recognized as revenue over the development period. The terms of the research collaboration agreement with Roche have been assessed, and amounts received are recognized as revenue over the research services period.

Under the terms of the agreement with Sarepta, we received an upfront payment of $40.0 million (£32.8 million) and a development milestone payment of $22.0 million (£17.2 million), which was payable after the first dosing of the last patient in PhaseOut DMD, our Phase 2 clinical trial of ezutromid. We also agreed to collaborate with Sarepta on the research and development of our utrophin modulators, or the licensed products, pursuant to a joint development plan. We were solely responsible for all research and development costs for the licensed products until December 31, 2017. From January 1, 2018, we are responsible for 55.0% of the budgeted research and development costs related to the licensed products in the licensed territory, and Sarepta is responsible for 45.0% of such costs.

In June 2018, we announced the discontinuation of the development of ezutromid after the Phase 2 proof of concept clinical trial did not meet its primary or secondary endpoints. As a result, we have updated the development period over which the revenues are recognized and deemed it to have concluded in June 2018 in line with when the development of ezutromid was discontinued. This resulted in all revenues relating to the Sarepta license and collaboration agreement that were previously deferred in the Statement of Financial Position being recognized in full. We continue to receive cost share income for wind-down activities in relation to PhaseOut DMD and our earlier-stage utrophin modulation development activities. We do not expect to receive any further milestone payments from Sarepta.

Under the terms of the agreement with Eurofarma, we received an upfront payment of $2.5 million (£1.9 million) from Eurofarma in December 2017. We also will be eligible for future ridinilazole-related development, regulatory and sales milestone payments totaling up to $32.7 million. This includes $3.75 million in development milestones upon the achievement of staged patient enrollment targets in the Phase 3 clinical trials of ridinilazole and up to an additional $21.4 million through other development milestones, commercial milestones, and one-time sales milestones based on cumulative net sales up to $100.0 million in the territory where Eurofarma has commercialization rights. Further, the agreement provides for product supply transfer payments expected to provide a return equivalent to a high single digit to low double-digit percentage of net sales. For each incremental $100.0 million in cumulative net sales achieved, we are entitled to a further milestone payment which, when combined with the aforementioned product supply transfer payments, is expected to provide a return equivalent to a mid- to high-teens percentage of net sales in the territories where we have granted Eurofarma commercialization rights.

Other Operating Income

Other operating income includes income received and recognized from grants and clinical trial support from government entities, philanthropic, non-government and not for profit organizations and patient advocacy groups which are accounted for in accordance with IAS 20, "*Accounting for Government Grants and Disclosure of Government Assistance*." Amounts received through these sources are held either as deferred revenue or recognized as accrued income, as appropriate, in the Consolidated Statement of Financial Position. Income is recognized in the Consolidated Statement of Comprehensive Income as the underlying expenditure is incurred and to the extent the conditions of the grant are met.

The BARDA contract provides for a cost-sharing arrangement under which BARDA funds a specified portion of estimated costs for specified activities related to the continued clinical and regulatory development of ridinilazole for the treatment of CDI. We also receive grant income from funding arrangements with CARB-X and Innovate UK for our antibiotic pipeline development activities. Income is recognized in respect of the BARDA, CARB-X and Innovate UK funding arrangements as the underlying research and development expenditure is incurred.

Operating Expenses

The majority of our operating expenses since inception have consisted of research and development activities and general and administrative costs.

Research and Development Expenses

Research and development expenses consist of all costs associated with our research and development activities.

These include:

- costs incurred in conducting our preclinical studies and clinical trials through contract research organizations, including preclinical toxicology, pharmacology, formulation and manufacturing work;
- employee related expenses, which include salary and benefits, for our research and development staff;
- costs associated with our former strategic alliance with the University of Oxford; and
- facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies.

We utilize our employee and infrastructure resources across multiple research projects. We track expenses related to our clinical programs and certain preclinical programs on a per project basis. We expect our research and development expenses to continue to increase as compared to prior periods as we continue to enroll our Phase 3 clinical trials of ridinilazole for the treatment of CDI, initiate a Phase 1 clinical trial of SMT-571 and continue our research activities and initiate preclinical programs for future product candidates, including under our Discuva Platform. The timing and amount of these expenses will depend upon the outcome of our clinical trials and the associated costs. The timing and amount of these expenses will also depend on the costs associated with potential future clinical trials of our product candidates and the related expansion of our research and development organization, regulatory requirements, advancement of our preclinical programs and product candidate manufacturing costs. Following the discontinuation of our utrophin modulator development program, we do not expect to incur significant future expenses for our DMD program.

The table below summarizes our research and development expenses by category. Our CDI program expenses, antibiotic pipeline development activities and DMD program expenses include costs paid to contract research organizations, manufacturing costs for our clinical trials, laboratory testing costs and research related expenses incurred in connection with our former strategic alliance with the University of Oxford. Other research and development costs include staff and travel costs (including those of our internal CDI, antibiotic development and DMD teams), research and development related legal costs, ongoing patent maintenance fees, an allocation of facility-related costs and historically non-core program related expenses.

	Year ended January 31,			
	2019	2019	2018	2017
			(Adjusted*)	
	(in thousands)			
CDI program	$ 23,538	£ 17,920	£ 5,635	£ 4,088
DMD program	12,501	9,517	15,959	9,480
Antibiotic pipeline research and development costs	2,519	1,918	—	—
Other research and development costs	12,897	9,819	7,376	5,384
Total	$ 51,455	£ 39,175	£ 28,970	£ 18,952

* See Note 3 - 'Changes to accounting policies - Adoption of IFRS 15 *Revenue from contracts with customers*' within the financial statements filed as part of this Annual Report.

From inception to January 31, 2019, our total CDI program expenses were £41.3 million, our total antibiotic pipeline research and development expenses were £1.9 million and our total DMD program expenses were £53.2 million. We no longer expect to incur significant future costs related to the DMD program with the close-out activities related to ezutromid substantially completed and the research collaboration with Oxford University having been terminated.

The successful development and commercialization of our product candidates is highly uncertain. At this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the remainder of the development of ridinilazole or any of our future product candidates. This is due to the numerous risks and uncertainties associated with product development and commercialization, including the uncertainty of:

- the progress, costs and results of clinical trials of ridinilazole for CDI;
- the scope, rate of progress, costs and results of preclinical development, laboratory testing and clinical trials for our future product candidates;
- the costs, timing and outcome of regulatory review of our product candidates;

- the efficacy and potential advantages of our product candidates compared to alternative treatments, including any standard of care, and our ability to achieve market acceptance for any of our product candidates that receive marketing approval;
- the costs and timing of commercialization activities, including product sales, marketing, distribution and manufacturing, for any of our product candidates that receive marketing approval and the rate we expand our physical presence; and
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining, enforcing and protecting our intellectual property rights and defending against any intellectual property-related claims.

A change in the outcome of any of these variables with respect to the development of ridinilazole or any other product candidate that we may develop could result in a significant change in the costs and timing associated with the development of that product candidate. For example, if the European Medicines Agency, or EMA, the U.S. Food and Drug Administration, or the FDA, or another regulatory authority were to require us to conduct clinical trials or other testing beyond those that we currently contemplate will be required for the completion of clinical development of ridinilazole or any other product candidate, or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional resources and time on the completion of clinical development of that product candidate.

General and Administration Expenses

General and administration expenses consist primarily of salaries and benefits related to our executive, finance, business development, human resources and support functions. Other general and administration expenses include share-based compensation expenses, facility-related costs, consulting costs and expenses associated with the requirements of being a listed public company in the United Kingdom and the United States, including insurance, legal, professional, audit and taxation services fees.

We anticipate that our general and administration expenses will continue to increase in the future as we increase our headcount to support our continued research and development and potential commercialization of our product candidates. We also anticipate continued increased accounting, audit, regulatory, compliance, insurance and investor and public relations expenses associated with being a publicly traded company in the United Kingdom and the United States. Our ADSs have traded on the Nasdaq Global Market since March 5, 2015.

Taxation

As a U.K. resident trading entity, we are subject to U.K. corporate taxation. Due to the nature of our business, we have generated losses since inception. To date, we have not recognized a deferred tax asset with respect to these tax losses because we do not consider it probable that there will be suitable taxable profits in the foreseeable future based on the evidence available. As a company that carries out extensive research and development activities, we benefit from the U.K. research and development tax credit regime and are able to surrender some of our trading losses that arise from our research and development activities for a cash rebate ranging from 9.72% to 33.35% of eligible research and development expenditure. In the event we generate revenues in the future, we may benefit from the "patent box" initiative that allows profits attributable to revenues from patents or patented products to be taxed at a lower rate than other revenue. This relief applies to profits earned from April 1, 2013, and following the transitional arrangements that will phase in the relief, the rate of tax for relevant streams of revenue for companies receiving this relief will be 10%.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with IFRS as issued by the IASB. In the preparation of these financial statements, we are required to make judgments, estimates and assumptions about the carrying amounts of assets and liabilities that are not readily apparent from other sources. The estimates and associated assumptions are based on historical experience and other factors that are considered to be relevant. Actual results may differ from these estimates under different assumptions or conditions. Our estimates and assumptions are reviewed on an ongoing basis. Revisions to accounting estimates are recognized in the period in which the estimate is revised if the revision affects only that period or in the period of the revisions and future periods if the revision affects both current and future periods.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing at the end of this Annual Report, we believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our financial statements.

Revenue Recognition

We recognize revenue from licensing fees, collaboration fees, development, regulatory and approval milestone fees, sales milestones and sales-based royalties. Agreements generally include a non-refundable upfront fee, milestone payments, the receipt of which is dependent upon the achievement of certain clinical, regulatory or commercial milestones, as well as royalties on product sales of licensed products, if and when such product sales occur. For these agreements, we are required to apply judgment as follows: the identification of the number of performance obligations within a contract, the allocation of the transaction price to those performance obligations and the timing of when milestone payments are included in the transaction price.

In relation to the license and collaboration agreement with Sarepta and the license and commercialization agreement with Eurofarma, we have assessed that the license to commercialize our intellectual property is not distinct in the context of the contract and that there is a transformational relationship between the license and the research and development activities delivered as they are highly interrelated elements of the contract. We have therefore determined that there is one single performance obligation under IFRS 15 in relation to the license granted and research and development activities which is the transfer of a license for which the associated research and development activities are completed over time. In the case of the Sarepta agreement, following our entry into the agreement, we assessed that there were a number of further performance obligations which were the research and clinical development activities relating to the future generation small molecule utrophin modulators, the license granted to commercialize in Latin America, which was at the option of Sarepta, and the cost-share arrangement. Following the discontinuation of our development of ezutromid, we are still entitled to reimbursement of a portion of the costs related to wind-down activities of terminated clinical trials, which we continue to view as a performance obligation. These performance obligations are separate and distinct from the transfer of a license for which the associated research and development activities are completed over time.

The allocation of the transaction price is based on the relative stand-alone selling price of those services provided and the performance obligation activities to which the terms of the payments specifically relate. Milestone payments and other variable consideration are only included in the transaction price allocated to a performance obligation when it becomes highly probable that a significant reversal in the amount of cumulative revenue recognized will not occur. The allocated transaction price is recognized over the respective performance period of each performance obligation.

As a result, the upfront payments, development milestones and development cost-share income allocated to the license granted and research and development activities, which is the transfer of a license for which the associated research and development activities are completed over time, are initially reported as deferred revenue in the Consolidated Statement of Financial Position and are recognized as revenue over the development period.

Recognition of Research and Development Expenses

We recognize expenses incurred in carrying out our research and development activities in line with our best estimation of the stage of completion of each separately contracted study or activity. This includes the calculation of research and development accruals at each period to account for expenditure that has been incurred. This requires estimations of the costs to complete each study or activity and also estimation of the current stage of completion. There have been no material adjustments to estimates based on the actual costs incurred for the periods presented. In all cases, we expense the full cost of each study or activity by the time the final study report or, where applicable, product, has been received.

We will recognize an internally generated intangible asset arising from our development activities only when an asset is created that can be identified, it is probable that the asset created will generate future economic benefits and the development cost of the asset can be measured reliably. We have determined that regulatory approval is the earliest point at which the probable threshold for the creation of an internally generated intangible asset can be achieved. We therefore expense all research and development expenditure incurred prior to achieving regulatory approval as it is incurred. None of our product candidates have yet received regulatory approval.

Financial Liabilities on Funding Arrangements

When entering into funding agreements with charitable and not for profit organizations, we are required to assess whether, based on the terms of the agreement, we can avoid a transfer of cash only by settling a non-financial obligation. An example of this would be the obligation to transfer the rights to the research to a funding provider. In the circumstances where we cannot avoid the obligation, all or part of the funding agreement should be accounted for as a financial liability rather than as a charitable grant. In calculating the financial liabilities, both at inception and when it is subsequently remeasured, a number of assumptions need to be made by management, which include significant estimates. Assumptions used in the model include the following: reported disease prevalence; expected market share based on management's estimates; drug reimbursement pricing in different territories, potential licensing terms which may be offered to us (for relevant products); expected patent life; and the timing and probabilities of achieving clinical development milestones which are based on industry standards and adjusted for therapy area. Discount factors in the range of 16% to 18% have been used in the model which has been calculated using appropriate measures and rates which could have been obtained in the period that the funding agreement was entered into. Sensitivity analysis is included in the notes to the financial statements and has been calculated based on a range of discount factors, estimated level of revenue and development probabilities of success. The financial liabilities are remeasured, and we are required to apply judgment, when there is a specific significant event that

provides evidence of a significant change in the probability of successful development such as the completion of a phase of research or changes in use or market for a product.

Share-based Compensation

We measure share options at fair value at their grant date in accordance with IFRS 2, "*Share-based Payment*." We calculate the fair value of the share option using either the Black-Scholes model, or for options with performance conditions, a simulation model. We charge the fair value to the Consolidated Statement of Comprehensive Income over the expected vesting period. In the case of options that are issued below market value, the fair value will be higher than an option granted at market value, and we recognize a larger charge for such options.

Acquired Intangible Assets and Assumed Contingent Liabilities Valuations

When we execute an acquisition resulting in a business combination as accounted under IFRS 3 "*Business Combinations,*" identifiable intangible assets and assumed contingent liabilities are required to be recognized in the Consolidated Financial Statements at fair value. In determining the fair value of such assets and liabilities, a number of assumptions need to be made by management which include significant estimates, which are described in more detail in the notes to our consolidated financial statements.

Jumpstart Our Business Startups Act of 2012

As a company with less than $1.07 billion in revenue during our last fiscal year, we qualify as an "emerging growth company" as defined in the Jumpstart our Business Startups Act of 2012, or the JOBS Act. An emerging growth company may take advantage of specified reduced reporting and other burdens that are otherwise applicable generally to public companies. These provisions include:

- an exemption from compliance with the auditor attestation requirement on the effectiveness of our internal controls over financial reporting;
- an exemption from compliance with any requirement that the Public Company Accounting Oversight Board may adopt 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 about our executive compensation arrangements; and
- exemptions from the requirements to obtain a non-binding advisory vote on executive compensation or a shareholder approval of any golden parachute arrangements.

We may take advantage of these provisions until January 31, 2021, or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company if we have more than $1.07 billion in annual revenues, have more than $700 million in market value of our share capital held by non-affiliates or issue more than $1 billion of non-convertible debt over a three-year period. We may choose to take advantage of some, but not all, of the available benefits under the JOBS Act. We have taken advantage of some reduced reporting burdens in this Annual Report. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

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 provision allows an emerging growth company to delay the adoption of some accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of delayed adoption of new or revised accounting standards and, therefore, we will be subject to the same requirements to adopt new or revised accounting standards as other public companies that are not emerging growth companies.

Results of Operations

Comparison of Years Ended January 31, 2019, and 2018

The following table summarizes the results of our operations for the years ended January 31, 2019, and 2018, together with the changes to those items:

	Year ended January 31,		Change 2019 vs. 2018	
	2019	2018 (Adjusted*)	Increase/(Decrease)	
	(in thousands, except percentages)			
Revenue	£ 43,012	£ 12,360	£ 30,652	248.0 %
Other operating income	15,156	2,725	12,431	456.2
Operating expenses				
Research and development	(39,174)	(28,970)	10,204	35.2
General and administration	(12,342)	(11,999)	343	2.9
Impairment of goodwill and intangible assets	(3,985)	—	3,985	100.0
Operating profit / (loss)	2,667	(25,884)	(28,551)	(110.3)
Finance income	2,788	3,096	(308)	(9.9)
Finance cost	(424)	(1,164)	(740)	(63.6)
Profit / (loss) before income tax	5,031	(23,952)	(28,983)	(121.0)
Income tax credit	2,496	3,762	(1,266)	(33.7)
Profit / (loss) for the year	£ 7,527	£ (20,190)	£ (27,717)	(137.3)%

* See Note 3 - 'Changes to accounting policies - Adoption of IFRS 15 *Revenue from contracts with customers*' within the financial statements filed as part of this Annual Report.

Revenue

Revenue was £43.0 million for the year ended January 31, 2019, compared to £12.4 million for the year ended January 31, 2018. See Note 3 'Changes to accounting policies - Adoption of IFRS 15 *Revenue from contracts with customers*' for details of the impact of the initial adoption of IFRS 15.

Revenues in each of these periods relates primarily to the Group's license and collaboration agreement with Sarepta. The increase in revenues was driven by the recognition of all remaining deferred revenue related to the Sarepta agreement following the Group's decision to discontinue development of ezutromid in June 2018. This recognition of deferred revenues did not impact the Group's cash flows. Revenue recognized during the year ended January 31, 2019, relating to the Sarepta agreement amounted to £42.3 million. This included £6.3 million of cost-share income which the Group continues to receive.

The Group also recognized £0.5 million of revenue during the year ended January 31, 2019, relating to the receipt of a $2.5 million (£1.9 million) upfront payment in respect of the license and commercialization agreement signed with Eurofarma in December 2017 and £0.2 million of revenue pursuant to a research collaboration agreement between the Group's subsidiary Discuva Limited and Roche. The research services period under the Roche agreement ended in February 2018.

Other Operating Income

Other operating income was £15.2 million for the year ended January 31, 2019, as compared to £2.7 million for the year ended January 31, 2018. This increase resulted primarily from the recognition of £13.1 million during the year ended January 31, 2019, as compared to £1.8 million during the year ended January 31, 2018, from the Group's funding contract with BARDA for the development of ridinilazole for the treatment of CDI.

The Group also recognized other operating income of £1.2 million during the year ended January 31, 2019, related to the Group's funding arrangements with CARB-X and Innovate UK awards for its antibiotic pipeline activities. In addition, £0.3 million was recognized in respect of UK Research and Development Expenditure Credits.

During the year ended January 31, 2019, the Group also recognized £0.5 million of other operating income resulting from the release of the Group's financial liabilities on funding arrangements relating to DMD-related US not for profit organizations because of the discontinuation of ezutromid's development.

Operating Expenses

Research and Development Expenses

Research and development expenses increased by £10.2 million to £39.2 million for the year ended January 31, 2019, from £29.0 million for the year ended January 31, 2018. This was due to increased expenditure related to the Group's CDI program, antibiotic pipeline development activities, and research and development related staffing and facilities costs, offset by decreased expenditure related to the discontinued DMD program.

In more detail, investment in the CDI program increased by £12.3 million to £17.9 million for the year ended January 31, 2019, from £5.6 million for the year ended January 31, 2018. This increase primarily related to clinical preparatory activities and manufacturing activities related to the Phase 3 clinical trials of ridinilazole that commenced in February 2019. Investment in the Group's antibiotic pipeline development activities was £1.9 million for the year ended January 31, 2019, compared to £0.1 million for the year ended January 31, 2018, which reflects activities post the completion of the acquisition of Discuva Limited that included the proprietary Discuva Platform in December 2017.

Expenses related to the DMD program decreased by £6.5 million to £9.5 million for the year ended January 31, 2019, from £16.0 million for the year ended January 31, 2018. This was driven by the decision to discontinue development of ezutromid in June 2018, which resulted in a decrease in the clinical and manufacturing costs, as well as a reduction in next and future generation utrophin modulation program research activities.

Other research and development expenses increased by £2.5 million to £9.8 million during the year ended January 31, 2019, as compared to £7.3 million during the year ended January 31, 2018, which was due to an increase in staff and facilities costs related to the CDI and antibiotic development teams, a non-cash charge related to the acceleration of share-based payment expenses resulting from the surrender of share option awards and a non-cash charge for amortization of the proprietary Discuva Platform.

General and Administration Expenses

General and administration expenses increased by £0.3 million to £12.3 million for the year ended January 31, 2019, from £12.0 million for the year ended January 31, 2018. This increase was primarily due to a non-cash charge for the acceleration of share-based payment expenses resulting from the surrender of share option awards, a loss on recognition of contingent consideration payable relating to the acquisition of Discuva Limited, offset by a net positive movement in exchange rate variances.

Impairment of Goodwill and Intangible Assets

As a result of discontinuing the development of ezutromid, the Group recognized an impairment charge during the year ended January 31, 2019, of £4.0 million relating to the utrophin program intangible asset and goodwill associated with the acquisition of MuOx Limited.

Finance Income

Finance income was £2.8 million for the year ended January 31, 2019. This related primarily to the remeasurement of the Group’s financial liabilities on funding arrangements relating to DMD-related US not for profit organizations following the discontinuation of the development of ezutromid in June 2018. Finance income was £3.1 million for the year ended January 31, 2018. This related primarily to the derecognition of the Group's financial liability on the Wellcome Trust funding arrangement, after the Group and the Wellcome Trust entered into a revenue sharing agreement in October 2017.

Finance Cost

Finance costs recognized during the year ended January 31, 2019, relate to the unwinding of the discounts associated with financial liabilities on funding arrangements and provisions. Finance costs were £0.4 million for the year ended January 31, 2019, compared to £1.2 million for the year ended January 31, 2018. This decrease was due to a reduction in the unwinding of the discount following the remeasurement of the financial liabilities on funding arrangements relating to DMD-related US not for profit organizations to £nil following the discontinuation of the development of ezutromid in June 2018.

Income Tax Credit

The income tax credit for the year ended January 31, 2019, was £2.5 million as compared to £3.8 million for the year ended January 31, 2018. This change in income tax credit was driven by a reduction in the Group's accrued UK research and development tax credit, as there are insufficient losses to surrender for the year ended January 31, 2019, due to the recognition of all remaining deferred revenue related to the Sarepta agreement following the Group's decision to discontinue the development of ezutromid in June 2018, to be eligible to receive a full research and development tax credit. This movement was offset by the release of deferred tax liabilities associated with the impairment of goodwill and amortization of intangible assets.

The Group's net corporation tax receivable includes research and development tax credits receivable on qualifying expenditure in respect of previous financial years. The Group anticipates that it will receive these research and development tax credit payments in the first half of 2019, after receiving confirmation of intention to pay from the HM Revenue & Customs, or HMRC, in March 2019.

Profit / (Losses)

Profit before income tax was £5.0 million for the year ended January 31, 2019, compared to a loss before income tax of £24.0 million for the year ended January 31, 2018. The profit recorded for the year ended January 31, 2019, was due to the recognition of all remaining deferred revenue related to the Sarepta agreement following the Group's decision to discontinue the development of ezutromid in June 2018. This recognition of deferred revenues did not impact the Group's cash flows.

Net profit was £7.5 million for the year ended January 31, 2019, with a basic and diluted profit per share of 9 pence compared to a net loss of £20.2 million for the year ended January 31, 2018, with a basic and diluted loss per share of 31 pence.

Comparison of Years Ended January 31, 2018, and 2017

The following table summarizes the results of our operations for the years ended January 31, 2018, and 2017, together with the changes to those items:

	Year ended January 31,		Change 2018 vs. 2017
	2018 (Adjusted*)	2017	Increase/(Decrease)
	(in thousands, except percentages)		
Revenue	£ 12,360	£ 2,304	£ 10,056 —
Other operating income	2,725	72	2,653 3,684.7 %
Operating expenses			
Research and development	(28,970)	(18,952)	10,018 52.9
General and administration	(11,999)	(8,277)	3,722 45.0
Operating loss	(25,884)	(24,853)	1,031 4.1
Finance income	3,096	8	3,088 38,600.0
Finance cost	(1,164)	(862)	302 35.0
Loss before income tax	(23,952)	(25,707)	(1,755) 6.8
Income tax credit	3,762	4,336	(574) (13.2)
Loss for the year	£ (20,190)	£ (21,371)	£ (1,181) 5.5 %

* See Note 3 - 'Changes to accounting policies - Adoption of IFRS 15 *Revenue from contracts with customers*' within the financial statements filed as part of this Annual Report.

Revenue

Revenue of £12.4 million was recognized during the year ended January 31, 2018 (adjusted), compared to £2.3 million recognized during the year ended January 31, 2017. This increase was principally due to income received pursuant to our exclusive license and collaboration agreement with Sarepta. During the year ended January 31, 2018, £6.9 million relating to the upfront payment of $40.0 million (£32.8 million) from Sarepta received in October 2016 was recognized compared to £2.3 million for the year ended January 31, 2017. During the year, an aggregate of £9.2 million of the upfront payment has been recognized while the remaining £23.6 million is classified as deferred revenue and will continue to be recognized as revenue over the development period. Revenue recognized during the year ended January 31, 2018, also reflects the recognition of £4.8 million of revenue relating to the receipt of the development milestone of £17.2 million ($22.0 million) and £0.3 million of income recognized in respect of specified DMD research and development costs funded by Sarepta pursuant to our license and collaboration agreement. In addition, revenue of £0.1 million was recognized during the year ended January 31, 2018, in respect of our exclusive license and commercialization agreement with Eurofarma. Under the

terms of the agreement, we received an upfront payment of $2.5 million (£1.9 million) from Eurofarma in December 2017. We have assessed the agreement, and we believe the development services to be indistinguishable from the grant of the license and as a result the upfront payment has been initially reported as deferred revenue on the Consolidated Statement of Financial Position and is being recognized as revenue over the development period. Revenue of £0.3 million was recognized during the year ended January 31, 2018, pursuant to the research collaboration agreement between our subsidiary Discuva Limited and Roche. Under the terms of the agreement, £9.0 million was received by Discuva Limited from Roche in February 2014 and is being recognized over the research services period.

Other Operating Income

Other operating income increased by £2.6 million to £2.7 million during the year ended January 31, 2018, from £0.1 million during the year ended January 31, 2017. This increase resulted primarily from the recognition of £1.8 million pursuant to our contract with BARDA that was awarded in September 2017 and £0.9 million resulting from the derecognition of a part of our financial liabilities on funding arrangements.

Operating Expenses

Research and Development Expenses

Research and development expenses increased by £10.0 million to £29.0 million for the year ended January 31, 2018, from £19.0 million for the year ended January 31, 2017. This increase was due to increased spending related to both our DMD and CDI programs. During the year ended January 31, 2018, expenses related to our DMD program increased by£6.5 million to £16.0 million from £9.5 million for the year ended January 31, 2017. This increase included £2.6 million related to our ezutromid clinical activities, £1.5 million associated with manufacturing costs for our clinical trials and

£2.4 million related to research associated with our future generation utrophin modulator program. During the year ended January 31, 2018, expenses related to our CDI program increased by £1.5 million to £5.6 million from £4.1 million for the year ended January 31, 2017. This increase was primarily due to planning activities relating to the two Phase 3 clinical trials of ridinilazole. During the year ended January 31, 2018, other research and development expenses increased by £2.0 million to £7.4 million from £5.4 million for the year ended January 31, 2017. This increase was due to a£1.4 million increase in staffing costs, a £0.3 million increase in internal regulatory costs and a £0.3 million increase in supplier contracting costs relating to research and development.

General and Administration Expenses

General and administration expenses increased by £3.7 million to £12.0 million for the year ended January 31, 2018, from £8.3 million for the year ended January 31, 2017. This increase was due to a net negative movement in exchange rate variances of £1.5 million, an increase of £1.3 million in staff related costs, an increase of £0.6 million in overhead and facility related costs and an increase of £0.3 million in share-based payment expense.

Finance Income

Finance income was £3.1 million for the year ended January 31, 2018, and related primarily to the de-recognition of a part of our financial liabilities on funding arrangements, specifically the remeasurements and discounts associated with the liabilities since initial recognition. Finance income recognized in comparative periods relates to bank interest received.

Finance Cost

Finance costs increased by £0.3 million to £1.2 million for the year ended January 31, 2018, from £0.9 million for the year ended January 31, 2017, and related to the unwinding of the discount and remeasurements on financial liabilities on funding arrangements.

Income Tax Credit

Our income tax credit decreased by £0.5 million to £3.8 million for the year ended January 31, 2018, from £4.3 million for the year ended January 31, 2017. This was driven by our lower level of net loss during the year ended January 31, 2018, as compared to the year ended January 31, 2017, which impacts the level of income tax credit receivable.

B. Liquidity and Capital Resources

Sources of liquidity

To date, we have financed our operations primarily through issuances of our ordinary shares and American Depositary Shares, or ADSs, payments to us under our license and collaboration agreement with Sarepta and our license and commercialization agreement with Eurofarma and development funding and other assistance from government entities, philanthropic, non-government and not for profit organizations and patient advocacy groups for our product candidates. In particular, we have received funding from BARDA, CARB-X, Innovate UK, Wellcome Trust and a number of not for profit organizations.

In March 2014, we received net proceeds of £20.5 million from the issuance and sale of 16,923,077 ordinary shares in a private placement outside the United States. In March 2015, in our initial public offering in the United States, we received net proceeds of $32.7 million (£21.9 million) from the issuance and sale of 3,967,500 ADSs which represent 19,837,500 ordinary shares. In October 2016, in connection with our entry into an exclusive license and collaboration agreement with Sarepta, we received an up-front payment of $40.0 million (£32.8 million) from Sarepta and we received a further $22.0 million (£17.2 million) in June 2017 as a development milestone from Sarepta following the first dosing of the last patient in our Phase 2 clinical trial of ezutromid. In September 2017, we received net proceeds of $18.2 million (£13.5 million) from the issuance and sale of 1,677,850 ADSs which represent 8,389,250 ordinary shares. In December 2017, in connection with our entry into an exclusive license and commercialization agreement with Eurofarma, we received an up-front payment of $2.5 million (£1.9 million) from Eurofarma. In March 2018, we received net proceeds of £14.1 million from the issuance and sale of 8,333,333 ordinary shares to investors in Europe. In January 2019, we received net proceeds of $24.4 million (£19.2 million) from the issuance and sale of 15,625,000 ADSs which represent 78,125,000 ordinary shares to a single investor, Mr. Robert W. Duggan.

Since our inception, we have incurred significant operating losses. We anticipate that we will continue to incur losses for at least the next several years. We expect that our research and development and general and administration expenses will continue to increase in connection with conducting clinical trials for our lead product candidate, ridinilazole, for the treatment of CDI, conducting preclinical research and development activities and seeking marketing approval for ridinilazole in the United States as well as other geographies where we retain commercialization rights.

In addition, our expenses will increase if and as we:

- continue the research and development of ridinilazole, as well as our preclinical program targeting infections caused by *Neisseria gonorrhoeae*;
- seek to identify and develop additional future product candidates, including through our bacterial genetics-based Discuva Platform for the discovery and development of new mechanism antibiotics, and specifically our discovery stage program against a group of bacteria that collectively are known as the ESKAPE pathogens;
- seek marketing approvals for any product candidates that successfully complete clinical development;
- ultimately establish a sales, marketing and distribution infrastructure in jurisdictions where we have retained commercialization rights and scale up external manufacturing capabilities to commercialize any product candidates for which we receive marketing approval;
- acquire or in-license other product candidates and technology;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, regulatory and scientific personnel;
- expand our physical presence; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts.

As of January 31, 2019, we had cash and cash equivalents of £26.9 million. We believe that our existing cash and cash equivalents, as well as the remaining amounts receivable from the $44.0 million we have been awarded under our contract with BARDA for the development of ridinilazole, the remaining amounts receivable from the $2.0 million of initial funding we have been awarded by CARB-X for our gonorrhea program, and the cost-sharing arrangement under our license and collaboration agreement with Sarepta, will be sufficient to enable us to fund our operating expenses and capital expenditure requirements through January 31, 2020. While these capital resources have allowed us to initiate our two Phase 3 clinical trials of ridinilazole, we do not expect to be able to complete these trials without additional capital.

We have based the foregoing estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. This estimate assumes, among other things, that we do not obtain any additional funding through grants and clinical trial support or through new collaboration arrangements. Our future capital requirements will depend on many factors, including:

- the progress, costs and results of clinical trials of ridinilazole for CDI;
- the number and development requirements of other future product candidates that we pursue;
- the costs, timing and outcome of regulatory review of ridinilazole and our other product candidates we develop;
- the costs and timing of commercialization activities, including product sales, marketing, distribution and manufacturing, for any of our product candidates that receive marketing approval;
- subject to receipt of marketing approval, revenue received from commercial sales of ridinilazole or any other product candidates;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property-related claims;
- our contract with BARDA and whether BARDA elects to pursue its designated options beyond the base period and first exercised option;
- our contract with CARB-X and whether CARB-X elects to pursue its designated options beyond the initial funding milestone;
- the amounts we receive from Eurofarma under our license and commercialization agreement, including for the achievement of development, commercialization and sales milestones and for product supply transfers;
- our ability to establish and maintain collaborations, licensing or other arrangements and the financial terms of such arrangements;
- the extent to which we acquire or invest in other businesses, products and technologies;
- the rate of the expansion of our physical presence; and
- the costs of operating as a public company in the United States in addition to in the United Kingdom.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, collaborations, strategic alliances, grants and clinical trial support from governmental entities and philanthropic, non-government and not for profit organizations and patient advocacy groups, debt financings, and marketing, distribution or licensing arrangements. We do not have any committed external source of funds other than amounts we may receive from BARDA, CARB-X and Eurofarma under our arrangements with them and the remaining cost-sharing payment we are entitled to receive from Sarepta under our collaboration agreement with them. As a result, we will need additional capital to fund our operations. Additional capital, when needed, 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, the ownership interest of our existing shareholders, including our ADS holders, will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing shareholders and ADS holders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends or other distributions. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Cash Flows

The following table summarizes the results of our cash flows for the years ended January 31, 2019, 2018 and 2017.

	Year ended January 31,			
	2019	2019	2018	2017
		(in thousands)		
Net cash (outflow) / inflow from operating activities	$ (35,195)	£ (26,795)	£ (14,689)	£ 12,141
Net cash outflow from investing activities	(411)	(313)	(5,242)	(80)
Net cash inflow from financing activities	43,919	33,437	13,905	413
Net increase / (decrease) in cash and cash equivalents	$ 8,313	£ 6,329	£ (6,026)	£ 12,474

Operating Activities

Net cash used in operating activities for the year ended January 31, 2019, was £26.8 million compared to £14.7 million for the year ended January 31, 2018. This increase of £12.1 million was primarily driven by an increase in operating costs of £6.4 million, a net reduction in cash received from licensing agreements and funding arrangements of £2.5 million and a negative movement in taxation cash flows of £3.2 million due to timing of receipt of our research and development tax credits receivable on qualifying expenditure in respect of previous financial years.

For the year ended January 31, 2018, net cash used by operating activities was £14.7 million. This compares to net cash generated from operating activities of £12.1 million for the year ended January 31, 2017. This net movement of £26.8 million was driven by an increase in research and development costs during the year ended January 31, 2018, and the receipt, during the year ended January 31, 2017, of a £32.8 million upfront payment as part of the exclusive collaboration and licensing agreement entered into with Sarepta in October 2016, which was partially offset by the receipt of the development milestone from Sarepta of £17.2 million during the year ended January 31, 2018, as well as the funding received from BARDA and the upfront payment received from Eurofarma during the year ended January 31, 2018.

Investing Activities

Net cash outflow in investing activities for the year ended January 31, 2019, was £0.3 million compared to £5.2 million for the year ended January 31, 2018. Net cash outflow from investing activities for the year ended January 31, 2019, represents contingent consideration paid and amounts paid to acquire property, plant and equipment and intangible assets, net of bank interest received on cash deposits.

Net cash outflow from investing activities for the year ended January 31, 2018, included £4.8 million used in the acquisition of Discuva Limited in December 2017, which is net of cash acquired as part of the transaction, and a further £0.5 million used to acquire property, plant and equipment and intangible assets mainly in relation to the relocation of our U.K. office in Oxford.

Net cash outflow for the year ended January 31, 2017, included the net amount of bank interest received on cash deposits less amounts paid to acquire property and equipment.

Financing Activities

Net cash inflow from financing activities for the year ended January 31, 2019, was £33.4 million. This includes £14.1 million of net proceeds received following our equity placing on the AIM market of the London Stock Exchange in March 2018, £19.2 million of net proceeds received following our private placement of ADSs in the United States in January 2019, and £0.1 million received following the exercise of restricted stock units and share options.

Net cash generated from financing activities for the year ended January 31, 2018, of £13.9 million included £13.5 million of net proceeds received following our underwritten public equity offering in September 2017, and £0.4 million received following the exercise of warrants and share options.

Net cash inflow from financing activities for the year ended January 31, 2017, relates to proceeds from the exercise of warrants and the exercise of share options.

C. Research and Development, Patents and Licenses, Etc.

For a discussion of our research and development activities, see “Item 4.B. Business” and “Item 5.A. Operating Results.”

D. Trend Information

Other than as disclosed elsewhere in this Annual Report, we are not aware of any trends, uncertainties, demands, commitments or events that are reasonably likely to have a material adverse effect on our revenues, profit (loss) from continuing operations, liquidity or capital resources, or that would cause the disclosed financial information not necessarily to be indicative of future operating results or financial conditions. For more information, see “Item 4.B. Business ,” “Item 5.A. Operating Results,” and “Item 5.B. Liquidity and Capital Resources.”

E. Off-Balance Sheet Arrangements

We do not have any, and during the periods presented we did not have any, off-balance sheet arrangements, other than the contractual obligations and commitments described below.

F. Tabular Disclosure of Contractual Obligations

The following table summarizes our contractual commitments and cash obligations as of January 31, 2019.

	Payments due by period				
	Total	Less than 1 Year	Between 1 and 3 Years	Between 3 and 5 Years	More than 5 Years
	(in thousands)				
Operating lease obligations	£ 1,080	£ 357	£ 723	£ —	—

We enter into operating leases in the normal course of our business.

Under various agreements, including those described below, we will be required to pay royalties and make milestone payments to third parties. See "Business —Our Collaborations and Funding Arrangements" in this Annual Report for additional information regarding these agreements. The preceding table excludes contingent payment obligations, such as royalties and milestones, which are described in more detail below, because the amount, timing and likelihood of payment are not known.

Discuva

Under a collaboration agreement that Discuva Limited, or Discuva, has with Roche, Roche is obligated to pay specified development, commercialization and sales milestone payments related to any compound developed under the platform that is or has been optioned by Roche. In connection with our acquisition of Discuva, we agreed to pay to former Discuva shareholders one-half of the economic benefit of any such payments received from Roche. In addition, certain employees, former employees and former directors of Discuva are eligible for payments from Discuva based on specified development and clinical milestones related to proprietary product candidates developed under the platform.

Wellcome Trust

In October 2012, we entered into a translation award funding agreement with The Wellcome Trust Limited, as trustee of the Wellcome Trust, to support a Phase 1 and a Phase 2 clinical trial of ridinilazole for the treatment of CDI. We refer to the translation award funding agreement as the translation award agreement. We refer to any compound or product that is covered by IP rights created under the translation award agreement or our prior agreement with the Wellcome Trust, or that is covered by IP rights to which we had rights prior to October 2009 and that relate to the activities under our agreements with the Wellcome Trust, as the award products.

In October 2017, we entered into a revenue sharing agreement with the Wellcome Trust as was required under the terms of the 2012 translational award agreement. Under the terms of the revenue sharing agreement: (i) if we commercialize ridinilazole, the Wellcome Trust is eligible to receive a low-single digit percentage of net revenue (as defined in the translation award agreement), and a one-time milestone payment of a specified amount if cumulative net revenues exceed a specified amount; (ii) if a third party commercializes ridinilazole, the Wellcome Trust is eligible to receive a mid-single digit percentage of the net revenues we receive from commercial sales by such third party, and a one-time milestone payment of a specified amount if cumulative net revenues we receive exceed a specified amount. In addition, following the first commercial sale by such third party, the Wellcome Trust is eligible to receive a one-time milestone payment equal to a low-single digit percentage of the aggregate amount of any pre-commercial payments we receive from third-party licensees prior to such commercial sale; and (iii) in the event of an assignment or sale of the assets or intellectual property pertaining to ridinilazole, the net proceeds we receive from such assignment or sale would be treated as net revenue under the revenue sharing agreement.

Under the revenue sharing agreement, it was agreed that any development funding or grant funding we receive from BARDA or other third parties, including licensees, would not be classified as net revenue or as a pre-commercial payment. In addition, under the revenue sharing agreement, the Wellcome Trust agreed to terminate all of its rights under the translation award agreement to develop or commercialize the award products or the related intellectual property in specified markets and in specified indications, in the event that we were not developing or commercializing the award products or such intellectual property for such markets or in such indications.

Following the license and commercialization agreement entered into with Eurofarma, an initial payment became due to the Wellcome Trust payable only upon commercialization of ridinilazole. The Wellcome Trust also agreed to terminate all of its rights under the translation award funding agreement pertaining to the exploitation of intellectual property related to the CDI program.

University College London

On March 23, 2010, we entered into a collaborative research agreement with the School of Pharmacy, University of London which was later novated on November 28, 2011 by the School of Pharmacy to University College London. As part of this agreement, and in consideration of their role in the development of the initial compound series from which ridinilazole was later identified, we agreed to pay the School of Pharmacy (now University College London) a low single-digit share of all revenue received by us in respect of ridinilazole, including any pre-commercial licensing revenue, up to a maximum of £1.0 million. Following the license and commercialization agreement entered into with Eurofarma, an initial payment was made to The School of Pharmacy of £0.04 million.

Other Contracts

In addition, we enter into contracts in the normal course of business with contract research organizations to assist in the performance of our research and development activities and other services and products for operating purposes. These contracts generally provide for termination on notice, and therefore are cancelable contracts and not included in the table of contractual obligations and commitments.

G. Safe Harbor

See "Forward Looking Statements."

Item 6: Directors, Senior Management and Employees

A. Directors and Senior Management

The following table sets forth the names, ages and positions of our senior management, key employees and directors as of the date of this Annual Report:

Name	Age	Position
Senior Management		
Glyn Edwards	63	Chief Executive Officer, Executive Director
David Roblin	52	Chief Operating Officer, Chief Medical Officer and President of Research and Development
Daniel Elger	48	Chief Commercial Officer, Senior Vice President of Research and Development
Key Employees		
Richard Vickers	43	Senior Vice President, Anti-Infectives
David Powell	50	Senior Vice President, Research
Melissa Strange	39	Vice President, Finance
Non-Employee Directors		
Frank Armstrong(2)(3)(4)	62	Non-Executive Chairman
Leopoldo Zambeletti (1)(2)(3)(4)	50	Non-Executive Director
Valerie Andrews(1)(2)(3)(4)	59	Non-Executive Director
David Wurzer(1)(3)(4)	60	Non-Executive Director

(1) Member of the Audit Committee.
(2) Member of the Remuneration Committee.
(3) Member of the Nominating and Corporate Governance Committee.
(4) An "independent director" as such term is defined in Rule 10A-3 under the Exchange Act.

Senior Management

Glyn Edwards has served as our Chief Executive Officer and a member of our board of directors since April 2012. Prior to joining our company, Mr. Edwards served as interim Chief Executive Officer of the BioIndustry Association, a U.K. trade organization, from November 2011 to June 2012, and Chief Executive Officer at Antisoma plc, a publicly traded biotechnology company specializing in the development of novel drugs for the treatment of cancer, from 1998 to 2011. Mr. Edwards also previously served as Vice President of Business Development at Therapeutic Antibodies Ltd. Mr. Edwards currently serves as a Non-Executive Director for OxSonics Limited, a U.K.-based ultrasound-based drug delivery company. Mr. Edwards received a BSc in biochemistry from Bristol University and a MSc in economics from the London

Business School. We believe that Mr. Edwards is qualified to serve as a member of our board of directors because of his extensive executive leadership and business development experiences in the life sciences industry.

David Roblin has served as our Chief Operating Officer, Chief Medical Officer and President of Research and Development since May 2017. He previously served as our Chief Operating Officer and President of Research and Development in a part-time capacity beginning in April 2017 and became full-time in June 2017. Dr. Roblin acted as a research and development adviser to us from 2014. Dr. Roblin has served as the Chief Operating Officer and Director of Scientific Translation at the Francis Crick Institute in London from 2014 to 2017. Prior to that, Dr. Roblin was Head of Research, Site Director and Chief Medical Officer for Europe R&D at Pfizer Inc. from 2008 to 2011 and was Head of Therapy Area for Anti-infectives at Bayer AG from 1997 to 1999. After Dr. Roblin left Pfizer Inc., he was Chief Medical Officer to a number of biotechnology companies including Creabilis SA where he held that role from 2011 until 2014. Dr Roblin has a degree in biochemistry from University College London and later qualified in medicine from St George's Hospital. He is a Fellow of the Royal College of Physicians and a Fellow of the Faculty of Pharmaceutical Medicine. He is an honorary Professor of Medicine at Swansea University and Professor of Translational Medicine at St George's. He is also a member of the board of directors of MedCity and Destiny Pharma Ltd and currently serves as a Non-Executive Director for Sosei Group Corporation, a Japanese-based clinical-stage biotechnology company. Before entering the life sciences industry, Dr Roblin practiced medicine for five years.

Daniel Elger has served as our Chief Commercial Officer since 2015; his role was widened in 2017 to Senior Vice President of Research and Development and Chief Commercial Officer, and he became an Executive Officer in February 2019. Before Summit, Dr. Elger was Chief Financial and Corporate Development Officer of Genkyotex SA, a Swiss biotech company, from 2014 to 2015; Chief Financial Officer of e-Therapeutics plc, a U.K. AIM-listed biotechnology company, from 2011 to 2014; and Vice President, Marketing and Communications of Antisoma plc, a U.K.- and U.S.-based oncology company listed on the London Stock Exchange, from 2002 to 2011. Dr. Elger earned his PhD in cancer biology from the University of Oxford and his BA in physiological sciences (medicine) also from the University of Oxford.

Key Employees

Richard Vickers joined our company in 2003 and has served as our Senior Vice President, Anti-Infectives, since February 2018. Prior to this date, and from October 2013, Dr. Vickers had previously served as our Chief Scientific Officer, Antimicrobials. During his time at our company, Dr. Vickers has worked in a variety of roles involved in the development and management of various antibacterial therapeutic programs, including our antibiotic program for the treatment of CDI. Prior to joining our company, Dr. Vickers undertook postdoctoral research studies with Professor Stephen Davies at the University of Oxford and held a Stipendiary Lectureship in organic chemistry at St. Catherine's College in Oxford. Dr. Vickers received a Ph.D. in organic chemistry from the University of Reading and a B.Sc. in chemistry from King's College London.

David Powell joined our company in 2016 and has served as our Senior Vice President, Research since February 2018. Prior to this date, and from June 2017, Dr. Powell served as our Head of Research. Prior to joining our company, Dr. Powell served at GlaxoSmithKline plc, or GSK, from 1995 to 2017, as Director and Head of the Crick-GSK Biomedical LinkLabs, based at GSK's U.K. R&D hub at Stevenage, U.K., and The Francis Crick Institute in London. Dr. Powell held a number of positions of increasing seniority in his time at GSK. As part of his work there, he participated in antibiotic discovery, assay development, high throughput screening design and implementation, and lead optimisation support. In his most recent role at GSK, he led a collaboration with the Crick Institute between 2014 and 2017, in addition to providing support to GSK's 'Discovery Partnerships with Academia' team which collaborated with academic groups in downstream drug discovery. He was awarded a BSc and MSc from the National University of Ireland Galway, before completing a PhD in biochemistry at Cardiff University.

Melissa Strange joined our company in November 2008 and has served as our Vice President, Finance since February 2018. In December 2018, Ms. Strange was appointed as our principal financial officer and principal accounting officer following the resignation of our former Chief Financial Officer. Prior to becoming our Vice President, Finance, Ms. Strange held the roles of Senior Director of Finance from February 2017 to January 2018, Director of Finance from June 2013 to January 2017 and Group Finance Controller from October 2009 to June 2013 and has been involved with a wide range of financial management and corporate activities. Ms. Strange has also acted as our Company Secretary since September 2014. Prior to joining Summit, Ms. Strange was Audit Manager for SRLV, a chartered accountants practice in London, from October 2007 to November 2008 and worked for Shaw Gibbs LLP, an Oxford based audit and accountancy practice in a number of positions, the most senior being Assistant to Partner during the period from April 2006 to September 2007 and earlier, from September 2001 to December 2004. Ms. Strange was Group Operational Auditor for Electrocomponents plc, a U.K.-based global distributor of industrial and electrical products, from January 2005 to March 2006. She was awarded an LLB (Hons) Law from Oxford Brookes University in 2000 and a Post Graduate Diploma in Legal Practice from the College of Law in 2001. Ms Strange is a Fellow of the Association of Chartered Certified Accountants having qualified in 2004.

Non-Employee Directors

Frank Armstrong has served as a member of our board of directors since November 2012 and Non-Executive Chairman since June 2013. Dr. Armstrong is currently President of Dr. Frank M Armstrong Consulting Limited, a position he has held since 2012. Prior to this, Dr. Armstrong led Medical Science and Innovation at Merck Serono, the biopharmaceutical division of Merck KGaA, from 2010 to 2011. Dr. Armstrong was also Head of Worldwide Product Development at Bayer AG from 1998 to 2001 and held various positions at ICI plc and Zeneca plc, now AstraZeneca plc, from 1985 to 1998. Dr. Armstrong has served as the Chief Executive Officer at five biotechnology companies, including Fulcrum Pharma plc, which is listed on AIM, CuraGen Corporation, a Nasdaq-listed company that was acquired by Celldex Therapeutics, Inc., Bioaccelerate Holdings Inc., Provensis Ltd. and Phoqus Pharmaceuticals plc. Dr. Armstrong is the Non-Executive Chairman of Faron Pharmaceuticals Oy and Caldan Therapeutics Ltd; a Non-Executive Director of TranScrip Partners LLP; a Member of the Strategic Advisory Board of HealthCare Royalty Partners and Epidarex Capital; and a Member of the Court of the University of Edinburgh. Dr. Armstrong served as Non-Executive Director of Mereo Biopharma Group plc, from 2015 to 2019, and Juniper Pharmaceuticals Inc., from 2013 to 2017. Dr. Armstrong received an honors degree in biochemistry and an MBChB(MD) in medicine from the University of Edinburgh in Scotland. He is a Fellow of the Royal College of Physicians, Edinburgh and a Fellow of the Faculty of Pharmaceutical Physicians. We believe that Dr. Armstrong is qualified to serve on our board of directors because of his extensive experience in the biotechnology industry and his medical background.

Leopoldo Zambeletti has served as a member of our board of directors since May 2014. Mr. Zambeletti has served as an independent strategic advisor to life sciences companies since 2013, focusing on mergers and acquisitions, out-licensing deals and financing strategy. Prior to this, Mr. Zambeletti worked in investment banking for 19 years, during which time he led the European Healthcare Investment teams at JP Morgan and at Credit Suisse. He is a Non-Executive Director of Faron Pharmaceuticals Oy, Tiziana Life Sciences plc, OKYO Pharma Plc, Philogen SpA, Nogra Pharma Ltd, DS Biopharma Ltd (formerly known as Dignity Services Ltd), Overjoy S.R.L and Afimmune Limited. He is also an advisor and co-founder to the U.S. medtech company Qardio. Mr. Zambeletti began his career as an accountant at KPMG. He received his degree in business administration from Bocconi University. We believe Mr. Zambeletti is qualified to serve on our board of directors because of his extensive experience in the finance and life sciences industries.

Valerie Andrews has served as a member of our board of directors since September 2014. Most recently, Ms. Andrews served from May 2011 until May 2014 as General Counsel at Vertex Pharmaceuticals Incorporated, a biopharmaceutical company focused on small molecule therapies for cystic fibrosis and other indications. From 2002 to May 2011, Ms. Andrews served in various legal roles at Vertex, including as Deputy General Counsel and Chief Compliance Officer. Prior to joining Vertex, Ms. Andrews was the Executive Director of Licensing for Massachusetts General Hospital and Brigham and Women's Hospital from September 2001 to March 2002. From 1989 to 2001, Ms. Andrews served as a corporate lawyer at Hill & Barlow PC, where she became a partner in 1997. In her professional roles, Ms. Andrews has garnered expertise in areas including corporate strategy, strategic transactions, corporate governance, executive compensation, risk management, and compliance. Ms. Andrews served as a Non-Executive Director of Juniper Pharmaceuticals Inc. from 2005 until 2015. Ms. Andrews received a B.A. in chemistry and psychology from Duke University and a J.D. from Boston College. We believe Ms. Andrews is qualified to serve on our board of directors because of her extensive skills in business and legal matters related to the pharmaceuticals industry.

David M. Wurzer has served as a member of our board of directors since February 2015. Mr. Wurzer is currently the Executive Vice President and Chief Investment Officer at Connecticut Innovations, a state-funded venture capital fund, where he previously served as Senior Managing Director and Managing Director. Prior to joining Connecticut Innovations in November 2009, Mr. Wurzer served as Executive Vice President, Treasurer and Chief Financial Officer at CuraGen Corporation from 1997 to 2008. He also held numerous positions at Value Health Inc. from 1991 to 1997, including Senior Vice President, Treasurer and Chief Financial Officer. Mr. Wurzer is a Non-Executive Director of Standard Diversified, Inc. (formerly known as Standard Diversified Opportunities, Inc.), Thetis Pharmaceutical LLC, ReNetX Bio, Inc. (formerly known as Axerion Therapeutics, Inc.) and Bioasis Technologies, Inc.; from 2017 to 2018 he was a Non-Executive Director of Natural Polymer Devices, Inc., from 2016 to 2018 he was a Non-Executive Director of My Gene Counsel LLC and from 2010 to 2015 he was a Non-Executive Director of Response Genetics Inc. Mr. Wurzer is a Certified Public Accountant and began his career with Coopers & Lybrand, which is now part of PricewaterhouseCoopers. He received a B.B.A. from the University of Notre Dame. We believe Mr. Wurzer is qualified to serve on our board of directors because of his extensive experience in the pharmaceutical and biotechnology industries and his finance and accounting background.

B. Compensation

The following discussion provides the amount of compensation paid, and benefits in kind granted, by us and our subsidiaries to our directors and senior management for services provided in all capacities to us or our subsidiaries for the year ended January 31, 2019, as well as the amount contributed by us into money purchase plans for the year ended January 31, 2019, to provide pension benefits to our directors and senior management.

Directors' and Senior Management Compensation

For the year ended January 31, 2019, the table below sets out the compensation paid to our directors and senior management.

Compensation for Year Ended January 31, 2019

Name	Salary and Bonus / Fees	Taxable Benefits[1]	Pension Benefit	Total
Glyn Edwards *Chief Executive Officer and Executive Director*	£ 627,000	£ 1,577	£ 21,432	£ 650,009
Erik Ostrowski[2] *Former Chief Financial Officer*	$ 398,188	—	$ 14,959	$ 413,147
David Roblin *Chief Operating Officer, Chief Medical Officer and President of Research & Development*	£ 482,282	£ —	£ 21,115	£ 503,397
Frank Armstrong *Non-Executive Chairman*	£ 75,000	£ 3,519	—	£ 78,519
Barry Price [3] *Former Non-Executive Director*	£ 24,125	£ 2,161	—	£ 26,286
Stephen Davies [3] *Former Non-Executive Director*	£ 27,889	—	—	£ 27,889
Leopoldo Zambeletti *Non-Executive Director*	£ 40,278	£ 582	—	£ 40,860
Valerie Andrews *Non-Executive Director*	£ 58,378	£ 1,101	—	£ 59,479
David Wurzer *Non-Executive Director*	£ 50,796	£ 1,911	—	£ 52,707

(1) Taxable benefits represent the value of the personal benefits granted, which include private medical insurance and life assurance for senior management and travel costs (and associated income tax and national insurance contributions which were settled on behalf of the Non-Executive Directors) for attendance at board meetings for the Non-Executive Directors. Amounts included are based on the taxable benefits reported in the year ended January 31, 2019, to HM Revenue & Customs.
(2) Mr. Ostrowski left our company in December 2018.
(3) Mr. Price and Professor Davies stepped down from the board of directors and left our company in September 2018.

Total compensation set out in the table above does not include any amounts for the value of options to acquire our ordinary shares or restricted stock units granted to or held by the directors and senior management, which is described in "Compensation—Outstanding Equity Awards, Grants and Option Exercise" in this Annual Report.

Bonuses

Our Executive Director, Chief Operating Officer and Chief Medical Officer and President of R&D are eligible for annual bonuses at the discretion of our board and, in the case of our Executive Director, our remuneration committee. Annual bonuses are based on achievement of strategic and financial measures and personal performance objectives. Mr. Edwards, our Chief Executive Office and Executive Director, is eligible for annual bonus potential of 150% of his gross base salary to be paid in share options, cash or a combination of both at the discretion of our board. In January 2019, Mr. Edwards was awarded a bonus representing 100% of his gross base salary, which was paid in cash in February 2019. Dr. Roblin, our Chief Operating Officer, Chief Medical Officer and President of R&D, is eligible for a discretionary annual bonus in an amount up to 50% of his annual base salary, as determined by our board of directors. In January 2019, Dr. Roblin was awarded a bonus representing 50% of his annual base salary at the discretion of the board. The bonus was paid in cash in February 2019. Mr. Ostrowski, our former Chief Financial Officer who left the company on December 28, 2018, would have been eligible for a discretionary annual bonus in an amount up to 50% of his annual base salary, as determined by our board of directors. However, Mr Ostrowski forfeited his eligibility to receive a bonus upon leaving the business, therefore no bonus was paid.

Outstanding Options As of January 31, 2019, for Directors and Senior Management

Outstanding Equity Awards, Grants and Option Exercise

During the year ended January 31, 2019, options to purchase 7,733,609 ordinary shares were awarded to our directors and senior management. The table below sets out information on outstanding options granted to our directors and senior management as of January 31, 2019.

Name	Date of grant	At February 1, 2018	Granted during the period	Exercised during the period	Lapsed or surrendered during the period	At January 31, 2019 [1]	Price per share (£)	Date from which exercisable	Expiration date
Glyn Edwards	May 10, 2012	150,046	—	—	—	150,046	0.60	Note 1	May 10, 2022
Chief Executive Officer and Executive Director	January 31, 2013	72,973	—	—	—	72,973	0.20	Note 2	January 31, 2023
	December 18, 2013	76,364	—	—	—	76,364	0.20	Note 3	December 18, 2023
	July 15, 2014	600,000	—	—	(600,000)	—	1.26	Note 4	July 15, 2024
	June 16, 2015	887,333	—	—	(887,333)	—	1.43	Note 8	June 16, 2025
	June 23, 2016	110,576	—	—	—	110,576	0.01	Note 10	June 23, 2026
	April 11, 2017	762,764	—	—	(762,764)	—	1.85	Note 11	April 11, 2027
	July 18, 2017	135,478	—	—	(135,478)	—	1.83	Note 11	July 18, 2027
	October 24, 2017	198,776	—	—	(198,776)	—	1.80	Note 11	October 24, 2027
	April 20, 2018	—	458,978	—	(458,978)	—	2.05	Note 11	April 20, 2028
	April 20, 2018	—	900,000	—	(900,000)	—	2.05	Note 11	April 20, 2028
	October 19, 2018	—	2,375,309	—	—	2,375,309	0.30	Note 12	October 19, 2028
		2,994,310	3,734,287	—	(3,943,329)	2,785,268			
Erik Ostrowski[1]	June 23, 2014	400,000	—	—	(400,000)	—	1.48	Note 13	June 23, 2024
Former Chief Financial Officer	June 16, 2015	400,000	—	—	(400,000)	—	1.43	Note 8	June 16, 2025
	June 23, 2016	250,000	—	—	(250,000)	—	1.05	Note 11	June 23, 2026
	July 18, 2017	68,062	—	—	(68,062)	—	1.83	Note 12	July 18, 2027
	October 24, 2017	98,495	—	—	(98,495)	—	1.80	Note 12	October 24, 2027
	April 20, 2018	—	160,000	—	(160,000)	—	2.05	Note 11	April 20, 2028
	April 20, 2018	—	800,000	—	(800,000)	—	2.05	Note 11	April 20, 2028
	October 19, 2018	—	1,439,661	—	(1,439,661)	—	0.30	Note 11	October 19, 2028
		1,216,557	2,399,661	—	(3,616,218)	—			
David Roblin	July 15, 2014	100,000	—	—	—	100,000	0.80	Note 4	July 15, 2024
Chief Operating Officer, Chief Medical Officer and President of R&D	June 16, 2015	25,000	—	—	(25,000)	—	1.43	Note 8	June 16, 2025
	June 23, 2016	17,500	—	—	(17,500)	—	1.05	Note 14	June 23, 2026
	April 11, 2017	324,324	—	—	(324,324)	—	1.85	Note 11	April 11, 2027
	July 18, 2017	164,384	—	—	(164,384)	—	1.83	Note 11	July 18, 2027
	April 20, 2018	—	160,000	—	(160,000)	—	2.05	Note 11	April 20, 2028
	October 19, 2018	—	1,439,661	—	—	1,439,661	0.30	Note 12	October 19, 2028
		631,208	1,599,661	—	(691,208)	1,539,661			
Barry Price[2]	April 7, 2011	13,981		(13,981)	—	—	0.65	Note 6	April 7, 2021
Former Non-Executive Director	July 15, 2014	17,500	—	(17,500)	—	—	1.26	Note 7	July 15, 2024
	June 16, 2015	25,000	—	—	(25,000)	—	1.43	Note 9	June 16, 2025
		56,481	—	(31,481)	(25,000)	—			
Frank Armstrong	July 15, 2014	37,500	—	—	(37,500)	—	1.26	Note 5	July 15, 2024
Non-Executive Director	June 16, 2015	50,000	—	—	(50,000)	—	1.43	Note 9	June 16, 2025
		87,500	—	—	(87,500)	—			
Stephen Davies[2]	July 15, 2014	17,500	—	(17,500)	—	—	1.26	Note 7	July 15, 2024
Former Non-Executive Director	June 16, 2015	25,000	—	—	(25,000)	—	1.43	Note 9	June 16, 2025
		42,500	—	(17,500)	(25,000)	—			
Leopoldo Zambeletti	June 16, 2015	25,000	—	—	(25,000)	—	1.43	Note 9	June 16, 2025
Non-Executive Director		25,000	—	—	(25,000)	—			
Valerie Andrews	June 16, 2015	25,000	—	—	(25,000)	—	1.43	Note 9	June 16, 2025
Non-Executive Director		25,000	—	—	(25,000)	—			
David Wurzer	June 16, 2015	25,000	—	—	(25,000)	—	1.43	Note 9	June 16, 2025
Non-Executive Director		25,000	—	—	(25,000)	—			

(1) Mr. Ostrowski left our company in December 2018.
(2) Mr. Price and Professor Davies stepped down from the board of directors and left our company in September 2018.

During the year ended January 31, 2019, restricted stock units in the form of nominal cost options, or RSUs, to purchase 814,256 ordinary shares were awarded to our non-executive directors. The table below sets out information on outstanding RSUs granted to our current non-executive directors as of January 31, 2019 (or for the period ended September 20, 2018 for Mr. Price and Professor Davies).

Name	Date of grant	At February 1, 2018	Granted during the period	Exercised during the period	At January 31, 2019 [1]	Price per share (£)	Date from which exercisable	Expiration date
Frank Armstrong	June 18, 2017	41,096	—	(41,096)	—	0.01	Note 14	December 31, 2018
Non-Executive Director	October 24, 2017	41,666	—	(41,666)	—	0.01	Note 15	December 31, 2018
	April 20, 2018	—	36,585	—	36,585	0.01	Note 16	December 31, 2019
	January 11, 2019	—	288,461	—	288,461	0.01	Note 17	December 31, 2020
		82,762	325,046	(82,762)	325,046			
Leopoldo Zambeletti	June 18, 2017	19,179	—	(19,179)	—	0.01	Note 14	December 31, 2018
Non-Executive Director	October 24, 2017	19,444	—	(19,444)	—	0.01	Note 15	December 31, 2018
	April 20, 2018	—	17,073	—	17,073	0.01	Note 16	December 31, 2019
	January 11, 2019	—	134,615	—	134,615	0.01	Note 17	December 31, 2020
		38,623	151,688	(38,623)	151,688			
Valerie Andrews	June 18, 2017	19,179	—	(19,179)	—	0.01	Note 14	December 31, 2018
Non-Executive Director	October 24, 2017	19,444	—	(19,444)	—	0.01	Note 15	December 31, 2018
	April 20, 2018	—	17,073	—	17,073	0.01	Note 16	December 31, 2019
	January 11, 2019	—	134,615	—	134,615	0.01	Note 17	December 31, 2020
		38,623	151,688	(38,623)	151,688			
David Wurzer	June 18, 2017	19,179	—	(19,179)	—	0.01	Note 14	December 31, 2018
Non-Executive Director	October 24, 2017	19,444	—	(19,444)	—	0.01	Note 15	December 31, 2018
	April 20, 2018	—	17,073	—	17,073	0.01	Note 16	December 31, 2019
	January 11, 2019	—	134,615	—	134,615	0.01	Note 17	December 31, 2020
		38,623	151,688	(38,623)	151,688			
Barry Price[1]	June 18, 2017	19,179	—	(19,179)	—	0.01	Note 14	December 31, 2018
Former Non-Executive Director	October 24, 2017	19,444	—	—	19,444	0.01	Note 15	December 31, 2018
		—	17,073	—	17,073	0.01	Note 16	December 31, 2019
		38,623	17,073	(19,179)	36,517			
Stephen Davies[1]	June 18, 2017	19,179	—	(19,179)	—	0.01	Note 14	December 31, 2018
Former Non-Executive Director	October 24, 2017	19,444	—	—	19,444	0.01	Note 15	December 31, 2018
		—	17,073	—	17,073	0.01	Note 16	December 31, 2019
		38,623	17,073	(19,179)	36,517			

(1) Mr. Price and Professor Davies stepped down from the board of directors and left our company in September 2018.

1. These options vested and became exercisable on May 10, 2015, following the satisfaction of the performance conditions relating to the share price.
2. These deferred bonus options vested and became exercisable on July 31, 2013. These options were awarded as a bonus for the financial year ended January 31, 2013.
3. These deferred bonus options vested and became exercisable on June 18, 2014. These options were awarded as a bonus for the financial year ended January 31, 2014.
4. These options vested on March 13, 2017, following the satisfaction of the performance conditions relating to the share price. One-third of the options became exercisable on March 13, 2017, and the remaining options became exercisable on July 15, 2017. These options were voluntarily surrendered on October 5, 2018.
5. These options vested on March 13, 2017, following the satisfaction of the performance conditions relating to the share price. One-third of the options became exercisable on March 13, 2017, and the remaining options became exercisable on July 15, 2017. These options were voluntarily surrendered on January 11, 2019.
6. These options were awarded to Dr. Price whilst he was interim Executive Chairman, vested and became exercisable on April 8, 2014, following the satisfaction of the performance conditions relating to the share price. These options were exercised on April 23, 2018.
7. These options vested on March 13, 2017, following the satisfaction of the performance conditions relating to the share price. One-third of the options became exercisable on March 13, 2017, and the remaining options became exercisable on July 15, 2017. These options were exercised on April 23, 2018.
8. These options failed to meet the performance condition relating to share price and therefore lapsed.

9. These options remained unvested and were voluntarily surrendered on April 8, 2018.
10. These deferred bonus options vested and became exercisable on July 21, 2016. These options were awarded as a part settlement of the bonus for the financial year ended January 31, 2016.
11. These options remained unvested and were voluntarily surrendered in October 2018.
12. These options were subject to achievement of performance conditions pertaining to corporate and program development milestones. These options will vest on October 19, 2021, if the performance condition is met on or before that date.
13. These options failed to meet the performance condition relating to share price and therefore lapsed.
14. This award was exercised by all non-executive directors on July 18, 2018.
15. This award was exercised by all non-executive directors on October 24, 2018. This was a postponed equity award from the financial year ended January 31, 2017, as we ended our practice of making annual share option awards to non-executive directors.
16. This award expires on December 31, 2019, unless this falls within a restricted trading period, in which case it is expected that the award would be exercised in the next available trading period and no later than December 31, 2020.
17. This award expires on December 31, 2020, unless this falls within a restricted trading period, in which case it is expected that the award would be exercised in the next available trading period and no later than December 31, 2021.

We periodically grant share options to employees, including executive officers, to incentivize employees, and align their interests with shareholders as outlined in our remuneration policy that was approved by our shareholders at the 2017 annual general meeting. We intend to grant additional options subject to a cap, as previously agreed with shareholders, of up to 15% of total issued share capital in any ten-year period.

Pension Benefits

We operate a defined contribution pension scheme which is available to all employees of our group. For the year ended January 31, 2019, we paid a total of £21,432 in lieu of pension contributions in respect of our Executive Director and £21,115 in respect of our Chief Medical Officer and President of Research and Development. In addition, for the year ended January 31, 2019, we made payments of $14,959 into our former Chief Financial Officer's 401(k) plan.

Employment Agreements and Letters of Appointment

Non-Executive Directors

Our non-executive directors have each entered into a letter of appointment with us. Each non-executive director's letter of appointment provides for a continuous term for each non-executive director until termination of the letter of appointment. The letters of appointment automatically terminate if the relevant non-executive director is not re-elected to office by the shareholders, is removed from office by a resolution of the shareholders, vacates his or her office, is adjudged bankrupt or enters into any composition or arrangement with his or her creditors, is guilty of misconduct or commits a serious persistent breach of his or her appointment letter, or is unable to perform his or her duties under the appointment for 90 days in aggregate in any period of 12 months. The letters of appointment may also be terminated by mutual agreement or effective immediately upon written notice by one party to the other at any time. Each letter of appointment also includes confidentiality provisions for the protection our confidential information.

Each non-executive director, with the exception of Dr. Armstrong, Mr. Wurzer and Ms. Andrews, received £35,000 per annum for payment for services provided to us. Dr. Armstrong receives £75,000 per annum, which includes payment for services as chairman of our board of directors. Mr. Wurzer receives $67,000 per annum and Ms. Andrews receives $77,000 per annum, in each case, as payment for services provided to us and includes payment for services as chair of the audit and remuneration committees. respectively. Mr. Zambeletti receives an additional £5,000 per annum for each committee he sits on. Under the letters of appointment, each non-executive director is also entitled to reimbursement for all reasonable expenses incurred in connection with his or her duties as a non-executive director and that are in line with our expense policy.

Senior Managers

Glyn Edwards, Chief Executive Officer

Mr. Edwards was appointed as the chief executive officer by a service agreement dated April 4, 2012, which continues unless terminated. This agreement originally required six months' written notice by us or by Mr. Edwards. In an amendment to this agreement dated June 18, 2018, it was agreed that either party could terminate the agreement with 12 months' notice. We may also terminate the agreement with immediate effect by paying a sum in lieu of notice equal to the basic fixed salary which Mr. Edwards would have been entitled to receive during the notice period (and which shall not include payment in

respect of benefits). We may otherwise terminate the agreement with immediate effect at any time without notice or payment in lieu of notice for certain circumstances including material breach of the agreement, serious misconduct, serious incompetence or negligence, criminal convictions or bankruptcy. The agreement originally included a garden leave clause for a maximum of two months but this was extended to 12 months in the amendment to this agreement and there is no provision for compensation in addition to the contractual notice period.

Under his service agreement, Mr. Edwards initially received a salary of £200,000 per annum payable in arrears by equal monthly installments plus reasonable expenses. Effective in February 2019, Mr. Edwards' salary increased to £322,766 per annum. Mr. Edwards' service agreement also provides for a monthly pension contribution equal to 7.0% of salary, increasing to 8% from April 1, 2019, private medical cover (including cover for his spouse) and life assurance (for four times his gross salary). A share option package, as agreed by the chairman of our remuneration committee, will be awarded to Mr. Edwards subject to the rules of our share option scheme. Under his service agreement, Mr. Edwards is prohibited from engaging in any type of business in competition with the business of our group, procuring orders from or doing business with any person who has done or proposed to do business with our group, and endeavoring to entice away from our group any senior manager or director engaged by our group, for a period of 12 months from the date of termination of his agreement. Mr. Edwards is also subject to confidentiality and protection of intellectual property provisions.

David Roblin, Chief Operating Officer, Chief Medical Officer and President of Research and Development

Dr. Roblin was appointed as the Chief Operating Officer and President of Research and Development pursuant to a letter of employment with Summit (Oxford) Limited dated November 25, 2016, which became effective on December 16, 2017, and was further updated September 1, 2018, and continues unless terminated with twelve months' written notice by us or by Dr. Roblin. In May 2017, Dr. Roblin assumed the role of Chief Medical Officer. Under his letter of employment, Dr. Roblin initially received a salary of £300,000 per annum. Effective in February 2019, Dr. Roblin's salary increased to £318,270 per annum. Dr. Roblin was initially eligible to receive an additional £30,000 per annum for the purposes of assuring a second place of residence near Oxford; effective September 1, 2018, he no longer receives this allowance, however we do cover the cost of his travel and accommodation expenses for traveling to the office.

Dr. Roblin's employment agreement provides for a monthly pension contribution (or payments in lieu thereof) equal to 7.0% of salary, increasing to 8% from April 1, 2019, private medical coverage for him and his spouse and life insurance coverage equal to an amount that is four times his gross base salary. Pursuant to the employment agreement, a share option package equal to twice his base salary, as agreed by the chairman of our remuneration committee, was awarded to Dr. Roblin after he began working for us full-time. Under his employment agreement, Dr. Roblin is prohibited from engaging in any type of business in competition with the business of our group, procuring orders from or doing business with any person who has done or proposed to do business with our group, and endeavoring to entice away from our group any senior manager or director engaged by our group, for a period of six months from the date of termination of his letter of employment. Dr. Roblin is also subject to confidentiality and protection of intellectual property obligations under his employment letter.

Dr. Roblin is eligible to receive a discretionary bonus in an amount up to 50% of his annual base salary and an annual share option award subject to performance conditions, in each case, as determined by our board of directors.

Daniel Elger, Chief Commercial Officer and Senior Vice President of Research and Development

Dr. Elger was appointed as the Chief Commercial Officer pursuant to a letter of employment with Summit (Oxford) Limited dated June 4, 2015, updated February 1, 2019, which continues unless terminated with six months' written notice by us or by Dr. Elger. Under his letter of employment, Dr. Elger initially received a pro rata salary of £200,000 per annum and prior to February 1, 2019, received a salary of £255,000. Effective from February 1, 2019, Dr. Elger's salary increased to £262,650 per annum in line with Dr. Elger joining the Executive Committee.

Dr. Elger is eligible to receive a discretionary bonus in an amount up to 50% of his annual base salary and an annual share option award subject to performance conditions, in each case, as determined by our board of directors. Dr. Elger's employment agreement provides for a monthly pension contribution (or payments in lieu thereof) equal to 7% of salary, increasing to 8% from April 1, 2019, private medical coverage for him and his family and life insurance coverage equal to an amount that is four times his gross base salary.

Under his employment agreement, Dr. Elger is prohibited from engaging in any type of business in competition with the business of our group, procuring orders from or doing business with any person who has done or proposed to do business with our group, and endeavoring to entice away from our group any senior manager or director engaged by our group, for a period of six months from the date of termination of his letter of employment. Mr. Elger is also subject to confidentiality and protection of intellectual property obligations under his employment letter.

Equity Compensation Arrangements

2016 Long Term Incentive Plan

Our 2016 Long Term Incentive Plan, which we refer to as the Incentive Plan, was adopted on January 21, 2016. Under the Incentive Plan, our board may grant conditional awards, options, cash conditional awards and cash options to any of our employees, including executive directors, and the employees of our subsidiaries. The Incentive Plan is administered by our board, which has full authority, consistent with the Incentive Plan, to administer the Incentive Plan, including the authority to interpret and construe any provision of the Incentive Plan and to adopt regulations for administering the Incentive Plan. Decisions of the board are final and binding on all parties. References to our board in this summary shall include any duly authorized committee of our board.

Our board may grant awards to any employees eligible to receive awards under the Incentive Plan in its discretion, subject to the rules of the Incentive Plan and such additional terms as the board may determine. However, the grant of an award is subject to obtaining any approval or consent required by any relevant authority and any other applicable laws or regulations. Awards must be granted by deed (or in such other written form as the board determines) and, as soon as reasonably practicable after the date on which an award is granted, the participant must be notified of the terms of his or her award.

A conditional award is a right to acquire shares subject to and in accordance with the rules of the Incentive Plan with no exercise period. An option is a right to acquire shares subject to and in accordance with the rules of the Incentive Plan during a specified exercise period not to exceed ten years from the date the option is granted. A cash conditional award is a right to receive a cash payment equal to the market value (as determined by the board) of a number of notional shares underlying the vested portion of the award on the vest date. A cash option is a right to receive a cash payment equal to the market value (as determined by the board) of a number of notional shares underlying the vested portion of the award the date of exercise less the aggregate exercise price payable (if any).

Vesting of Awards

Unless the board determines otherwise, the vesting of an award granted under the Incentive Plan is subject to the satisfaction of a performance condition. Subject to the terms of the Incentive Plan that apply upon a cessation of a participant's employment and upon certain corporate events, the performance condition will be measured over the performance period which, unless the board determines otherwise, will be at least three years. Performance conditions may be amended or substituted by the board if one or more events occur which cause the board to consider that an amended or substituted performance condition would be more appropriate and would not be materially less difficult to satisfy than the original performance condition to which the award was subject.

As soon as reasonably practicable after the end of the performance period relating to an award that is subject to a performance condition, our board will determine if and to what extent the performance condition has been satisfied. To the extent that the performance condition has not been satisfied in full, the remainder of the award will lapse immediately. Subject to the terms of the Incentive Plan that apply upon a cessation of a participant's employment and upon certain corporate events, an award that is subject to a performance condition will vest on the later of the date on which the board determines that the performance condition has been satisfied and the third anniversary of the date of grant of the award (or such other date determined by the board and communicated to the participant). An award that is not subject to the satisfaction of a performance condition will vest on the third anniversary of the date of grant (or such other date determined by the board and communicated to the participant). We refer to the date on which an award would normally vest, whether or not it is subject to the achievement of a performance condition, as the normal vesting date. Notwithstanding the foregoing, if there are share dealing restrictions (imposed by the company's share dealing code, the rules of the London Stock Exchange, or any other applicable laws or regulations) on the applicable normal vesting date, the award will vest on the date the dealing restrictions are lifted.

The Incentive Plan provides that if a participant dies prior to the date on which an award vests, a number of shares subject to such award will, unless the board determines otherwise, vest as soon as practicable following the participant's death. The number of shares that vest in such circumstance will depend, unless the board determines otherwise, on the extent to which any applicable performance condition has been satisfied at the date of death and the period of time that has elapsed since the start of the applicable performance period or, if the award is not subject to a performance condition, since the date of grant of the award, or such other period as the board determines. To the extent that an award does not vest in full, the remainder will lapse immediately.

In addition, the Incentive Plan provides that if a participant ceases to hold office or employment with any group member (as such term is defined in the Incentive Plan) prior to the date on which an award vests as a result of ill-health, injury or disability; redundancy or retirement; upon the company for which the participant works ceasing to be a group member or the transfer of an undertaking or part-undertaking in which the participant is employed to a company not in our group; or any other reason at the board's discretion (except where a participant is summarily dismissed), the board may determine that an award will vest as soon as practicable following the date of the participant's cessation of office or employment (or on such other date as determined by the board). Otherwise, the award will vest on the normal vesting date. In either case, the number of shares that will vest will depend, unless the board determines otherwise, on the extent to which any applicable performance condition has been satisfied at the date of cessation of office or employment and the period of time that has

elapsed since the start of the applicable performance period or, if the award is not subject to a performance condition, since the date of grant of the award, or such other period as the board determines. To the extent that an award does not vest in full, the remainder will lapse immediately. If a participant ceases to hold office or employment with a group member for any other reason prior to the vesting date, his or her award will lapse at such time.

Exercise of Options

Generally, options must be exercised while the participant holds office or employment with a member of our group. In the event, however, that a participant ceases to hold office or employment with a member of our group as a result of ill-health, injury or disability; redundancy or retirement; upon the company for which the participant works ceasing to be a member of our group or the transfer of an undertaking or part-undertaking in which the participant is employed to a company not in our group; or any other reason at the board's discretion (except where a participant is summarily dismissed) prior to the date on which the award becomes exercisable, the option may be exercised, subject to it lapsing upon certain corporate events, for a period of six months (or such other period as the board may determine) commencing on the date the award vests (as described above). If a participant ceases to hold office or employment with a member of our group on or after the vesting date of the option as a result of the participant's resignation or an event described in the preceding sentence on or after the date on which the award becomes exercisable, the option may be exercised, subject to it lapsing upon certain corporate events, for a period of six months (or such other period as the board may determine) from the date of such cessation.

If a participant dies before his or her vested option has been exercised, the participant's personal representatives may exercise the option for 12 months (or such other period as the board may determine) after the later of the date of the participant's death and the date on which the award becomes exercisable.

All awards lapse in prescribed circumstances, including upon the tenth anniversary of the date of grant; the expiry of the period (if any) allowed for the satisfaction of any performance condition without such condition having been satisfied; on the day on which a participant ceases to hold office or employment with a group member (with the exception of the carve outs detailed in the Incentive Plan and described above); the expiry of the period during which an option may be exercised following the participant's death or cessation of office or employment with a group member; on the bankruptcy of the participant; or at such time the participant attempts to transfer, assign, charge or otherwise dispose of his or her award in any way (other than in the event of the participant's death, to his personal representatives).

Dividend Equivalent

The board may decide at any time prior to the issue or transfer of the shares in respect of an award that has vested that the participant will receive an amount (in cash and/or additional shares) equal in value to any dividends that would have been paid on those shares on such terms and over such period (ending no later than the vesting date of the award) as the board may determine. This amount may assume the reinvestment of dividends (on such basis as the board may determine) and may exclude or include special dividends.

Cash Equivalent/Net Settlement

Unless our board has determined that this rule will not apply to all or any portion of an award, at any time prior to the date on which shares in respect of an award that has been vested or exercised have been issued or transferred to a participant, the board may determine that the participant will receive: (i) in lieu of ordinary shares, a cash payment equal to the market value (as determined by the board) of the number of shares that would otherwise have been issued or transferred to the participant, less, in the case of an option, the aggregate exercise price payable (if any); or (ii) a reduced number of shares, which reduced number of shares will be equal to the market value (as determined by the board) of the number of shares that would otherwise have been issued or transferred to the participant, less (if the board so determines) any deductions (including, but not limited to any tax or similar liabilities) as may be required by law in respect of the award and, in the case of an option, the aggregate exercise price payable (if any).

Limits

The board may not grant an award that would cause the number of ordinary shares allocated under the Incentive Plan and under any other employee share plan adopted by the company (including the 2005 EMI Scheme described below) to exceed a number equal to 15% of our ordinary share capital in issue at that time. The Incentive Plan sets forth rules for determining when shares are treated as allocated under the Incentive Plan and makes clear that the number of shares allocated does not include shares in respect of which the right to acquire such shares lapses or is released or shares allocated in respect of awards which are then satisfied in cash.

The Incentive Plan also includes an individual participant limit: no eligible employee may be granted an award which would, at the time of grant, cause the market value (as determined by the board) of all the shares subject to awards granted to the participant in a particular financial year of the company to exceed ten times the participant's annual base salary. If any award exceeds this limit, it will be scaled back accordingly.

Reduction of Awards and Clawback

The board may, in its discretion, determine at any time prior to the vesting of an award to reduce (including to zero) the number of shares to which an award relates and/or impose further conditions on an award where there has been a material misstatement of our group's audited financial results; a material failure of risk management by us; serious reputational damage to us, any member of our group or a relevant business unit; material misconduct on the part of the participant or any other circumstances which the board considers to be similar in their nature or effect.

The board may also, in its discretion, determine that at any time after the vesting of an award prior to the later of the second anniversary of vesting and the fifth anniversary of the date of grant (or such longer period as is required by SEC rules that are applicable to us) to take the action described in the preceding paragraph (if an option has not yet been exercised or if shares or cash have not yet been delivered to the participant following the vesting of a conditional award or exercise of an option); require a participant or former participant to make a cash payment to us in respect of some or all of the shares or cash delivered to him or her under the award; and/or require a participant or former participant to transfer for no consideration some or all of the shares delivered to him or her under the award, where there has been a material misstatement of our group's audited financial results or material misconduct on the part of the participant. The board will have discretion to determine the basis on which the amount of cash or shares is calculated including whether, and the extent to which, any tax or social security liability is applicable to the award.

The board may decide to reduce (including to zero) the number of shares to which an award relates or may relate; impose further conditions on an award; and/or require a participant to transfer for no consideration some or all of the shares delivered to such participant under an award or make a cash payment to us in respect of some or all of the shares delivered to such participant under an award to effect the recovery of sums paid or shares delivered under any provisions similar to the rules described in the preceding paragraphs which are included in any bonus plan or share plan (other than the Incentive Plan) operated by any member of our group.

Corporate Events

In certain specified circumstances involving a change of control of our company, all awards which have not yet vested will vest at the time of the change of control or an earlier date, to the extent determined by the board in its discretion, taking into account, unless the board determines otherwise, the extent to which any performance condition has, in the board's opinion, been satisfied and the period of time that has elapsed from the grant date to the date of the change of control (or the date of cessation of office or employment, if earlier). To the extent an award does not vest (or is not exchanged, as described below) it will lapse immediately. Vested options will be exercisable for three months (or such other period as our board may determine) from the date of the change of control, after which time all options will lapse. Notwithstanding the foregoing, an award will not vest but will be exchanged for a new award which, in the opinion of the board, is equivalent to the original award, but relates to shares in a different company, if an offer to exchange the award is made and accepted by the participant; there is an Internal Reorganisation (as that term is defined in the Incentive Plan) unless the board determines that the award should nevertheless vest as described above upon the Internal Reorganisation; or the board decides (before the relevant event) that an existing award will automatically be exchanged.

Awards may also vest upon or become exercisable for a specified period following the occurrence of certain other corporate events, including, for example, if a person becomes bound or entitled to acquire shares pursuant to certain provisions of U.K. company law; if the company is affected by a demerger, delisting, special dividend or other event. The board may also provide for the vesting of awards that have not yet vested or permit exercise of vested options within a specified period following the date on which we pass a resolution for a voluntary winding up of our company.

Variation of Share Capital

In the event of any variation of the share capital of the company or a demerger, delisting, special dividend or other event which may, in the opinion of the board, affect the current or future value of shares, the number of shares that may be allocated under the Incentive Plan, the number of shares subject to an award, any performance condition and/or the exercise price of an option may be adjusted in such manner as the board determines.

Amendments

The board may at any time amend the rules of the Incentive Plan or, except as otherwise provided in the Incentive Plan, the terms of any award. An amendment that is to the material disadvantage of the existing rights of a participant will not be made unless the participant has approved the amendment and no amendment will be made that would prevent the Incentive Plan from being an employees' share scheme under U.K. law.

Termination

The Incentive Plan will terminate, and no award may be granted under the Incentive Plan, after the tenth anniversary of adoption by the Board. The Incentive Plan may also be terminated at any earlier time by the passing of a resolution by the board or an ordinary resolution of the company in general meeting. Termination of the Incentive Plan will be without prejudice to the existing rights of participants.

Schedule 2—Company Share Option Plan

The purpose of the Company Share Option Plan, or CSOP, is to enable us to grant CSOP options to eligible U.K. employees in accordance with the Income Tax (Earnings and Pensions) Act 2003, Schedule 4 (commonly known as the Enterprise Management Incentive Scheme provisions). Substantially all the rules of the Incentive Plan apply to CSOP options, but there are a number of differences, including that there is no cash or dividend equivalent or ability to net settle a CSOP option; the eligibility rules are more limited; and the value of awards under the CSOP is subject to lower limits than those in the Incentive Plan.

Schedule 3—U.S. Participants

We have in place rules governing awards granted to our U.S. employees which have been adapted from the Incentive Plan. The rules are substantially the same as the Incentive Plan, but are designed to ensure that awards granted under the Incentive Plan comply with or are exempt from Section 409A of the U.S. Internal Revenue Code.

Non-Executive Director Restricted Stock Unit Awards

On July 18, 2017, at our annual general meeting of shareholders, our shareholders approved our Directors' Remuneration Policy, which provided for an annual grant of restricted stock units, or RSUs, to our non-executive directors. This annual grant of RSUs to our non-executive directors was designed to replace our prior practice of making annual awards of share options to non-executive directors. Following approval of the policy at our 2017 annual general meeting, we have entered into a restricted stock unit agreement, or RSU agreement, with each of our non-executive directors as part of an annual grant of RSUs. Each of these agreements provides for a grant of RSUs in the form of nominal cost options to purchase our ordinary shares.

Vesting and Settlement

Under the RSU agreements, the RSUs vest in full on the first anniversary of the date of grant. Vested RSUs will lapse and be forfeited if not exercised by December 31 of the calendar year in which they vested in full, subject to certain limited exceptions.

At any time prior to the date on which shares in respect of an RSU have been issued or transferred, the board may determine that the holder will receive, in lieu of ordinary shares, a cash payment equal to the market value of the number of shares that would otherwise have been issued or transferred to the holder or American Depositary Shares, or ADSs, equal to the market value of the number of shares that would otherwise have been issued or transferred to the holder, in each case, less any deductions (including, but not limited to any tax or similar liabilities) as may be required by law in respect of the RSU and the aggregate exercise price payable.

If a holder dies prior to the date on which the RSU vests, the RSU will vest in full as of the date of such holder's death. If a holder dies before his or her vested RSU has been exercised, the holder's personal representatives may exercise the RSU on or before December 31 in the calendar year in which it vested, after which time it will lapse. If the holder ceases to be a non-executive director of the company for any reason other than death, the RSU will continue to vest and become exercisable, and subject to forfeiture, in accordance with its terms.

Dividend Equivalent

The board may decide at any time prior to the issue or transfer of the shares following the exercise of an RSU that the holder will receive an amount (in cash and/or additional shares and/or additional ADSs) equal in value to any dividends that would have been paid on those shares on such terms and over such period (ending no later than the vesting date of the RSU) as the board may determine. This amount may assume the reinvestment of dividends (on such basis as the board may determine) and may exclude or include special dividends.

Reduction of RSU Award and Clawback

The board may, in its discretion, determine at any time prior to the vesting of an RSU to reduce (including to zero) the number of shares to which the RSU relates and/or impose further conditions on the RSU where there has been a material misstatement of our group's audited financial results; a material failure of risk management by us, any member of our group or a relevant business unit; serious reputational damage to us, any member of our group or a relevant business unit; material misconduct on the part of the holder or any other circumstances which the board considers to be similar in their nature or effect.

The board may also, in its discretion, determine that at any time after the vesting of an RSU prior to the later of the second anniversary of vesting and the fifth anniversary of the date of grant (or such longer period as is required by SEC rules that are applicable to us) to take the action described in the preceding paragraph (if a vested RSU has not yet been exercised or if shares or cash have not yet been delivered to the holder following the exercise of the RSU); require the holder to make a cash payment to us in respect of some or all of the shares or cash delivered to him or her under the RSU; and/or require the holder to transfer for no consideration some or all of the shares delivered to him or her under the RSU, where there has been a

material misstatement of our group's audited financial results or material misconduct on the part of the holder. The board will have discretion to determine the basis on which the amount of cash or shares is calculated including whether, and the extent to which, any tax or social security liability is applicable to the RSU.

Corporate Events

In certain specified circumstances involving a change of control of our company, all RSUs which have not yet vested will vest at the time of the change of control. To the extent an RSU does not vest (or is not exchanged, as described below), it will lapse immediately. A vested RSU will be exercisable until December 31 of the calendar year in which it vested after which time it will lapse. Notwithstanding the foregoing, an RSU will not vest but will be exchanged for a new RSU which, in the opinion of the board, is equivalent to the original RSU, but relates to shares in a different company, if an offer to exchange the RSU is made and accepted by the holder; there is an Internal Reorganisation (as that term is defined in the RSU agreement) unless the board determines that the RSU should nevertheless vest as described above upon the Internal Reorganisation; or the board decides (before the relevant event) that an existing RSU will automatically be exchanged.

RSUs may also vest upon or become exercisable for a specified period following the occurrence of certain other corporate events, including, for example, if a person becomes bound or entitled to acquire shares pursuant to certain provisions of U.K. company law; or if the company is affected by a demerger, delisting, special dividend or other event. The board may also provide for the vesting of RSUs that have not yet vested or change the period of time during which any vested RSUs may be exercised (provided such period does not end later than December 31 of the calendar year of the vesting) following the date on which we pass a resolution for a voluntary winding up of our company.

Variation of Share Capital

In the event of any variation of the share capital of the company or a demerger, delisting, special dividend or other event which may, in the opinion of the board, affect the current or future value of shares, the number of shares subject to the RSU and/or the exercise price of the RSU, the RSU may be adjusted in such manner as the board determines.

Amendments

The board may at any time amend the terms of the RSU by written agreement with the holder of the RSU.

2005 EMI Scheme Rules

Our 2005 EMI Scheme Rules were adopted on December 1, 2005. Under the scheme, we may grant enterprise management incentive options, known as approved options, to those eligible bona fide employees and directors who qualify under applicable U.K. tax law and, to the extent that our employees and directors do not qualify for approved options, unapproved options may be granted to such eligible bona fide employees and directors. Options can no longer be granted under this scheme. As at January 31, 2019, 776,756 options remain in existence and exercisable under this scheme (including those options awarded under the rules as amended for U.S. employees).

Exercise of Options

Vesting of options is subject to such performance conditions as shall be set out in the agreement granting an option pursuant to the scheme and shall be otherwise determined by the board in accordance with the scheme. An approved option must be capable of being exercised within the period of ten years from the date of grant. Performance conditions may be amended, relaxed or waived by us if an event occurs which would cause us to consider that an amended performance condition would be a fairer measure of performance provided that such amended targets are no more and no less difficult to satisfy than they were prior to amendment.

Generally, options must be exercised while the participant is an eligible employee or director. In the event, however, that a participant ceases to be an eligible employee or director as a result of ill-health, injury, or disability; redundancy, retirement or pregnancy; upon the company for which the participant works ceasing to be a member of our group; or the transfer of an undertaking or part-undertaking in which the participant is employed to a company not in our group, the option may be exercised during the period commencing on the date he ceases to be an eligible employee or director and ending on 12 months thereafter. If a participant dies while he is an eligible employee or director, the participant's personal representatives may exercise the option for 12 months after the participant's death. All options lapse in prescribed circumstances, including: upon the tenth anniversary of the date of grant; the expiry of the period (if any) allowed for the satisfaction of any performance condition without such condition having been satisfied or becomes, in our opinion, incapable of being satisfied; on the day on which a participant ceases to be an eligible employee or director (with the exception of the carve outs detailed in the scheme); on the bankruptcy of the participant; or on the occurrence of a takeover.

Ordinary shares allotted under the scheme rank equally with the ordinary shares in issue at the date of allotment of the option shares. If and for so long as the ordinary shares are listed on AIM or any other exchange, we shall apply for ordinary shares allotted under the scheme to be admitted to the relevant exchange.

Limits

The maximum number of ordinary shares which may on any day be placed under option under the scheme, when added to the number of ordinary shares allocated for subscription for the preceding ten years under any employee share scheme, shall not exceed 15% of our ordinary share capital immediately prior to that day. Approved options are also subject to individual participant limits in accordance with the scheme and as provided for under relevant U.K. tax law. Lapsed options shall be disregarded for these purposes.

Takeovers and Liquidations

In certain specified circumstances involving a change of control, as specified in accordance with U.K. tax law, an option may automatically vest or otherwise be determined to vest by our board of directors. Where an option vests by reason of a change of control, the exercise of the option shall be conditional upon the change of control occurring. Our board of directors may, in certain circumstances, determine that an option shall lapse upon the change of control or six months thereafter.

Options may also be exercisable for the relevant period in the event of certain court sanctioned restructurings or amalgamations of us or if another company becomes bound or entitled to acquire our ordinary shares pursuant to certain provisions of U.K. companies law. Our board of directors may also permit exercise of the options within a period following the date on which we pass a resolution for voluntary winding up.

In the event of a person obtaining control of us as a result of a takeover offer or court sanctioned restructuring or amalgamation or qualifying exchange of shares within the relevant U.K. laws, the participant may, by agreement with the acquiring company, release options in consideration for the grant of a new option with respect to the acquiring company's shares.

Variation of Share Capital

In the event of any capitalization, rights issue, consolidation, subdivision, reduction or other variation of our share capital the number of ordinary shares comprised in an option and the exercise price in respect of the ordinary shares shall be varied as the directors determine and our auditors confirm to be fair and reasonable. Limitations apply to the extent to which any such adjustments may reduce the price at which ordinary shares may be purchased pursuant to the exercise of an option and no adjustment will take effect until it has been approved by the United Kingdom tax authorities in accordance with applicable U.K. tax law.

Amendments

Our board of directors may waive or amend the scheme subject to certain limitations which require approval of our shareholders.

Scheme Rules Governing Options Awarded to U.S. Employees

We have in place rules governing options awarded to our U.S. employees which have been adapted from our 2005 EMI Scheme Rules. The rules of the scheme are substantially the same as the 2005 EMI Scheme Rules.

Options Granted Outside the 2005 EMI Scheme Rules

Certain of our consultants who are not eligible employees of companies in our group for the purposes of our option scheme rules, and therefore, are not eligible to participate in our option schemes as detailed above, have been granted options to acquire our shares pursuant to separate unapproved option agreements. These options are generally on comparable terms to options granted under the 2005 EMI Scheme Rules.

Limitations on Liability and Indemnification Matters

To the extent permitted by the U.K. Companies Act 2006, 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. We have entered into a deed of indemnity with each of our directors and executive officers.

C. Board Practices

Board Composition

Our board of directors currently consists of five members, a non-executive chairman, one executive director and three non-executive directors.

Under Nasdaq listing standards, a director will only qualify as an "independent director" if, in the opinion of the listed company's board of directors, that person does not have a relationship that would interfere with the exercise of independent

judgment in carrying out the responsibilities of a director. Our board of directors has determined that all of our directors, other than Mr. Edwards, qualify as independent directors under Rule 5605(a)(2) of the Nasdaq listing standards.

Corporate Governance and Committees of the Board

Corporate Governance

Our board of directors is responsible for overall corporate governance and for supervising the general affairs and business of our company and its subsidiaries. As an AIM-listed company, we are subject to the continuing requirements of the AIM Rules for Companies as published by the London Stock Exchange plc from time to time. We are not required to comply with the U.K. Corporate Governance Code by virtue of being an AIM-listed company. From September 28, 2018, a change to the AIM Rules required AIM listed companies to adopt a recognized corporate governance code. On this date, we formally adopted the Quoted Companies Alliance Corporate Governance Code to comply with this requirement.

Our board is responsible to our shareholders for the proper management of our company and its subsidiaries and setting the overall direction and strategy of our group, reviewing scientific, operational and financial performance, and advising on management appointments. All key operational and investment decisions are subject to board approval.

There is a clear separation of the roles of chief executive officer and non-executive chairman. The chairman is responsible for overseeing the running of our board, ensuring that no individual or group dominates our board's decision-making and ensuring that the non-executive directors are properly briefed on matters. The chief executive officer has the responsibility for implementing the strategy of our board and managing the day-to-day business activities of our group.

Under our articles of association, all of our directors are subject to election by shareholders at the first annual general meeting after their appointment to our board and to re-election by shareholders at least once every three years. Accordingly, we plan to put one-third of the directors up for re-election each year and plan to put at least one of the directors up for re-election at the 2019 annual general meeting. The board considers a classified board structure and the practice of retiring by rotation every three years to be appropriate given that, as a biopharmaceutical company, the nature of our business is to carry out long-term research and development. Further details regarding the directors to be proposed for re-election will be detailed in the 2019 notice of annual general meeting that will be distributed to shareholders in accordance with our articles of association.

Committees of the Board

We have established an audit committee, a remuneration committee and a nominating and corporate governance committee and have adopted a charter for each of these committees.

Audit Committee

The members of our audit committee are Mr. Wurzer, Mr. Zambeletti and Ms. Andrews. Mr. Wurzer is the chair of the audit committee. Our audit committee's responsibilities include:

- appointing, approving the compensation of, and assessing the independence, objectivity and effectiveness of our registered public accounting firm;
- overseeing the work of our independent registered public accounting firm, including through the receipt and consideration of reports from that firm;
- monitoring the integrity of our financial statements by reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures;
- reviewing and monitoring our internal control over financial reporting, disclosure controls and procedures and code of business conduct;
- reviewing and monitoring the effectiveness of our internal audit function;
- overseeing our risk assessment and risk management policies;
- establishing policies regarding procedures for the receipt and retention of accounting related complaints and concerns;
- meeting independently with our internal auditing staff, if any, our independent registered public accounting firm and management; and
- reviewing and approving or ratifying any related person transactions.

All audit and non-audit services, other than *de minimis* non-audit services, to be provided to us by our independent registered public accounting firm must be approved in advance by our audit committee.

Our board of directors has determined that Mr. Wurzer is an "audit committee financial expert" as defined in Item 16A of Form 20-F.

In order to satisfy the independence criteria for audit committee members set forth in Rule 10A-3(b)(1) under the Exchange Act, each member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries. We believe that the composition of our audit committee meets the requirements for independence under current Nasdaq and SEC rules and regulations.

Remuneration Committee

The members of our remuneration committee are Ms. Andrews, Dr. Armstrong and Mr. Zambeletti. Ms. Andrews is the chair of the remuneration committee. Our remuneration committee's responsibilities include:

- reviewing and approving, or making recommendations to our board of directors with respect to, the compensation of our directors and executive management;
- overseeing an evaluation of our executive management; and
- overseeing and administering our employee share option scheme or equity incentive plans in operation from time to time.

In order to satisfy the independence criteria for remuneration committee members set forth in Rule 10C-1 under the Exchange Act, all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director's ability to be independent from management in connection with the duties of a remuneration committee member must be considered, including, but not limited to: (1) the source of compensation of the director, including any consulting advisory or other compensatory fee paid by such company to the director; and (2) whether the director is affiliated with the company or any of its subsidiaries or affiliates. We believe the composition of our remuneration committee meets the requirements for independence under current Nasdaq and SEC rules and regulations.

Nominating and Corporate Governance Committee

The members of our nominating and corporate governance committee are Dr. Armstrong, Mr. Zambeletti, Ms. Andrews and Mr. Wurzer. Dr. Armstrong is the chair of the nominating and corporate governance committee. Our nominating and corporate governance committee's responsibilities include:

- identifying individuals qualified to become members of our board;
- recommending to our board the persons to be nominated for election as directors and to each of our board's committees;
- overseeing a periodic evaluation of our board;
- reviewing and making recommendations to our board with respect to our board leadership structure;
- reviewing and making recommendations to our board with respect to management succession planning; and
- developing and recommending to our board corporate governance principles.

D. Employees

The number of our employees by geographic location and function as of the end of the period for our fiscal years ended January 31, 2019, 2018 and 2017 was as follows:

	2019	2018	2017
By Geography			
United Kingdom	52	54	28
North America	9	22	12
Total	61	76	40

	2019	2018	2017
By Function			
Research & Development	35	52	24
General & Administrative	26	24	16
Total	61	76	40

Our employees are not represented by any collective bargaining agreements, and we have never experienced a work stoppage. We believe our employee relations are good.

E. Share Ownership

For information regarding the share ownership of our directors and senior managers, see "Item 6.B. Compensation" and Item 7.A. Major Shareholders."

Item 7: Major Shareholders and Related Party Transactions

A. Major Shareholders

The following table sets forth information with respect to the beneficial ownership of our ordinary shares as of March 1, 2019, by:

- each of the members of our board of directors;
- each of our members of senior management; and
- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our ordinary shares.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our ordinary shares. Our ordinary shares subject to options or warrants that are currently exercisable or exercisable within 60 days of March 1, 2019, are considered outstanding and beneficially owned by the person holding the options or warrants for the purpose of calculating the percentage ownership of that person but not for the purpose of calculating the percentage ownership of any other person. Except as otherwise noted, the persons and entities in this table have sole voting and investing power with respect to all of the ordinary shares beneficially owned by them. Except as otherwise indicated in the table below, addresses of named beneficial owners are c/o Summit Therapeutics plc, 136a Eastern Avenue, Milton Park, Abingdon, Oxfordshire OX14 4SB, United Kingdom. All holders of our ordinary shares, including those shareholders listed below, have the same voting rights with respect to such shares.

	Ordinary shares beneficially owned	
Name of beneficial owner	Shares	%
Senior Management and Directors		
Glyn Edwards[1]	793,292	*
Erik Ostrowski[2]	—	—
David Roblin[3]	100,000	*
Daniel Elger	—	—
Frank Armstrong[4]	158,789	*
Leopoldo Zambeletti[5]	33,052	*
Valerie Andrews[6]	66,196	*
David Wurzer[7]	63,196	*
All current senior managers and directors as a group (7 persons)[8]	1,214,525	*
5% shareholders		
Robert W. Duggan	78,288,205	48.81%
Lansdowne Partners (UK) LLP[9]	21,143,500	13.18%
Polar Capital LLP[10]	5,322,946	3.31%

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* Less than one percent.

(1) Consists of (a) 409,959 ordinary shares underlying options that are exercisable as of March 1, 2019, or will become exercisable within 60 days after such date and (b) 383,333 ordinary shares.

(2) Mr. Ostrowski left our company in December 2018.

(3) Consists of 100,000 ordinary shares underlying options that are exercisable as of March 1, 2019, or will become exercisable within 60 days after such date.

(4) Consists of 36,585 ordinary shares underlying restricted stock units that are exercisable as of March 1, 2019, or will become exercisable within 60 days after such date and (b) 122,204 ordinary shares.

(5) Consists of (a) 17,073 ordinary shares underlying options that are exercisable as of March 1, 2019, or will become exercisable within 60 days after such date and (b) 15,979 ordinary shares.

(6) Consists of (a) 17,073 ordinary shares underlying options that are exercisable as of March 1, 2019, or will become exercisable within 60 days after such date and (b) 49,123 ordinary shares.

(7) Consists of (a) 17,073 ordinary shares underlying options that are exercisable as of March 1, 2019, or will become exercisable within 60 days after such date and (b) 46,123 ordinary shares.

(8) Consists of (a) 597,763 ordinary shares underlying options that are exercisable as of March 1, 2019, or will become exercisable within 60 days after such date and (b) 616,762 ordinary shares.

(9) These shares are registered in the name of HSBC Client Holdings Nominee (UK) Limited and HSBC Bank Plc Lansdowne Markets. Lansdowne Partners (UK) LLP may be deemed to have voting and dispositive power over the ordinary shares. Investment decisions with respect to the ordinary shares held by Lansdowne Partners (UK) LLP can be made by Stuart Roden, Peter Davies and Jonathan Regis. The address of Lansdowne Partners (UK) LLP is 15 Davies Street, London, W1K 3AG.

(10) This information is based on information contained in a TR-1 Notification sent to us on January 9, 2019, by Polar Capital LLP.

Bank of New York Mellon, or BNY Mellon, is the holder of record for the company's ADR program, pursuant to which each ADS represents five ordinary shares. As of March 1, 2019, BNY Mellon held 112,561,345 ordinary shares representing 70.2% of the issued share capital held at that date. As of March 1, 2019, we had three holders of record with an address in the United States, and such holders held less than one percent of our outstanding ordinary shares. The number of holders of record or registered holders in the United States is not representative of the number of beneficial holders or of the residence of beneficial holders.

To our knowledge, other than as provided in the table above, our other filings with the SEC and this Annual Report, there has been no significant change in the percentage ownership held by the principal shareholders listed above since March 1, 2019.

B. Related Party Transactions

Since February 1, 2018, we have engaged in the following transactions with our directors, executive officers or holders of 5% or more of our ordinary shares, or affiliates of our directors, executive officers or holders of more than 5% of our ordinary shares that are required to be described in this Annual Report pursuant to Item 7.B. of Form 20-F.

Private Placement in the U.K.

In March 2018, we completed a placement of an aggregate of 8,333,333 ordinary shares to investors in Europe at a purchase price of 180 pence per ordinary share. In connection with such placement, an affiliate of Lansdowne Partners (UK) LLP, a holder of more than 5% of our ordinary shares, subscribed for 2,083,000 ordinary shares.

Transactions with Mr. Robert W. Duggan

Securities Purchase Agreement

On January 9, 2019, we completed a private placement with Mr. Robert W. Duggan, who subscribed for an aggregate of 15,625,000 of our ADSs, representing an aggregate of 78,125,000 ordinary shares, par value £0.01 per share, at a subscription price of $1.60 per ADS. In connection with such transaction, Mr. Duggan became a holder of ADSs representing more than 5% of our ordinary shares. Pursuant to a securities purchase agreement he entered into with us, Mr. Duggan also agreed not to sell, transfer or otherwise dispose of any ADSs, ordinary shares or any options, warrants or other securities or rights convertible into or exercisable or exchangeable for our ordinary shares, subject to certain limited exceptions, until the earliest to occur of (i) the date on which (x) the ADSs cease to be registered pursuant to Section 12 of the Exchange Act and (y) our ordinary shares cease to be listed on AIM; (ii) the date that is one year after the closing date (as defined below); and (iii) the date on which we and Mr. Duggan mutually agree in writing to terminate this restriction.

Relationship Agreement

On December 14, 2018, we entered into a relationship agreement with Mr. Duggan and Cairn Financial Advisers LLP, a limited liability partnership incorporated in England and Wales with the Registrar of Companies of England and Wales, as our nominated adviser, to regulate our relationship with Mr. Duggan and to limit Mr. Duggan's influence over our corporate actions and activities and the outcome of general matters pertaining to us. Pursuant to the relationship agreement, Mr. Duggan has agreed to, and has agreed to ensure that any of his associates (within the meaning of the definition of "related party" contained in the AIM Rules) and any person who holds shares of ours on his behalf (together, his "affiliates") shall among other things: (i) conduct all transactions with us on arm's length terms and on a normal commercial basis, including in accordance with the related party rules set out in the AIM Rules; (ii) exercise his voting rights to ensure that we are capable of carrying on our business and making decisions independently of Mr. Duggan and his affiliates; and (iii) abstain

from voting in respect of any resolution containing any transaction, agreement or arrangement involving us or any of our subsidiary undertakings to which Mr. Duggan or any of his affiliates is a party. The obligations and restrictions on Mr. Duggan will terminate upon Mr. Duggan ceasing to be beneficially entitled to ordinary shares representing at least 20% of the voting rights attaching to our ordinary shares or the ordinary shares ceasing to be admitted to trading on AIM and the ADSs ceasing to be admitted to trading on the Nasdaq Stock Exchange. The relationship agreement became effective immediately prior to the closing date.

Registration Rights Agreement

In connection with the closing of the subscription, we entered into a registration rights agreement with Mr. Duggan pursuant to which we agreed to use commercially reasonable efforts to prepare and file a registration statement covering the resale by Mr. Duggan of the ADSs purchased by him in the subscription promptly following the date that is 180 days after January 9, 2019, or the closing date, but no later than 210 days after the closing date. Under such registration rights agreement, we have agreed to use commercially reasonable efforts to cause such registration statement to become effective as soon as practicable after its filing and to keep such registration statement continuously effective, subject to certain limited exceptions, until the earliest of the date on which all ADSs covered by such registration statement have been sold or may be resold pursuant to Rule 144 of the Securities Act of 1933 without restriction, or the fifth anniversary of the closing date. Under such registration rights agreement, we have agreed to be responsible for all fees and expenses incurred in connection with the registration of the ADSs, excluding underwriter discounts, commissions or fees, and each party will grant the other customary indemnification rights in connection with the registration and resale of the ADSs.

C. Interests of Experts and Counsel

Not applicable.

Item 8: Financial Information

A. Consolidated Financial Statements and Other Financial Information

See “Item 18. Financial Statements.”

B. Significant Changes

There have been no significant changes since January 31, 2019.

C. Dividends

We have never declared or paid any dividends and currently intend to retain all available earnings generated by our operations for the development and growth of our business. We do not currently anticipate paying any cash dividends on our shares.

Item 9: The Listing

A. Listing Details

Our ordinary shares have been trading on AIM, a market operated by the London Stock Exchange plc, or AIM, under the symbol “SUMM” since October 14, 2004, and our American Depositary Shares, or ADSs, have been trading on the Nasdaq Global Market under the symbol “SMMT” since March 5, 2015.

B. Plan of Distribution

Not applicable.

C. Markets

Our ordinary shares are listed on AIM under the symbol “SUMM” and our ADSs are listed on the Nasdaq Global Market under the symbol “SMMT.”

D. Selling Shareholders

Not applicable.

E. Dilution

Not applicable.

F. Expenses of the Issue

Not applicable.

Item 10: Additional Information

A. Share Capital

Not applicable.

B. Memorandum and Articles of Association

We incorporate by reference into this Annual Report the description of our amended articles of association contained in our Registration Statement on Form F-1 (File No. 333-201807) originally filed with the SEC on January 30, 2015, as amended.

C. Material Contracts

Except as otherwise disclosed in this Annual Report (including the exhibits hereto), we are not currently, and have not been in the last two years, party to any material contract, other than contracts entered into in the ordinary course of business.

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 our articles of association on the right of non-residents to hold or vote shares.

E. Taxation

Taxation in the United Kingdom

The following is a general summary of certain U.K. tax considerations relating to the ownership and disposal of our ordinary share or ADS and does not address all possible tax consequences relating to an investment in our ordinary share or ADS. It is based on U.K. tax law and generally published HM Revenue & Customs, or HMRC, practice as of the date of this Annual Report, both of which are subject to change, possibly with retrospective effect. A U.K. tax year runs from April 6th in any year to April 5th in the following year.

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

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

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

This summary further assumes that a holder of ADSs is the beneficial owner of the underlying ordinary shares for U.K. direct tax purposes.

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

Taxation of Dividends

Withholding Tax

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

Income Tax

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

A dividend received by individual U.K. Holders will be subject to U.K. income tax. The system of grossing up dividends has been abolished from April 2016 and replaced with a simple rate of tax on dividends. The rate of U.K. income tax that is chargeable on dividends received in the tax year 2018/19 or 2019/20 by an individual U.K. Holder who is (i) an additional rate taxpayer is 38.1%, (ii) a higher rate taxpayer is 32.5%, and (iii) a basic rate taxpayer is 7.5%. An individual U.K. Holder may be entitled to a tax-free dividend allowance (in addition to their personal allowance) of £2,000 for each tax year starting from the tax year 2018/19. This dividend allowance will not reduce an individual's total income tax for U.K. purposes. This means that while the relevant individual does not need to pay U.K. income tax on their first £2,000 of dividend income received, dividends within the dividend allowance will still count towards the relevant individual's basic of higher rate bands. An individual's dividend income is treated as the top slice of their total income that is chargeable to U.K. income tax. Dividends which are covered by an individual's personal income tax allowance do not count towards and are ignored for the dividend allowance.

Corporation Tax

A U.K. Holder within the charge to U.K. corporation tax may be entitled to exemption from U.K. corporation tax in respect of dividend payments in respect of an ordinary share. If the conditions for the exemption are not satisfied, or such U.K. Holder elects for an otherwise exempt dividend to be taxable, U.K. corporation tax will be chargeable on the dividend. The rate of U.K. corporation tax is currently 19% and is expected to reduce to 17% with effect from April 1, 2020. If potential investors are in any doubt as to their position, they should consult their own professional advisers.

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

Taxation of Disposals

U.K. Holders

A disposal or deemed disposal of an ordinary share or ADS by an individual U.K. Holder may, depending on his or her individual circumstances, give rise to a chargeable gain or to an allowable loss for the purpose of U.K. capital gains tax. The principal factors that will determine the capital gains tax position on a disposal of an ordinary share or ADS are the extent to which the holder realizes any other capital gains in the tax year in which the disposal is made, the extent to which the holder has incurred capital losses in that or any earlier tax year and the level at which the annual exempt amount for U.K. capital gains tax (the "annual exempt amount") is set by the U.K. government for that tax year. The annual exempt amount for the 2018/19 tax year is £11,700 increasing to £12,000 for the 2019/20 tax year. If, after all allowable deductions, an individual U.K. Holder's total taxable income for the relevant tax year exceeds the basic rate income tax limit, a taxable capital gain accruing on a disposal of an ordinary share or an ADS is taxed at the rate of 20%. In other cases, a taxable capital gain accruing on a disposal of our ordinary share or ADS may be taxed at the rate of 10% or the rate of 20% or at a combination of both rates.

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

A disposal (or deemed disposal) of an ordinary share or ADS by a corporate U.K. Holder may give rise to a chargeable gain or an allowable loss for such holder for the purpose of U.K. corporation tax. Such a holder should be entitled to an indexation allowance, which applies to reduce a capital gain to the extent that such a gain arises due to inflation. The allowance may reduce a chargeable gain but will not create or increase an allowable loss. The indexation allowance was frozen with effect from December 31, 2017, such that for disposals on or after January 1, 2018, the indexation allowance figure only covers the movement in the "retail price index" to December 31, 2017.

Any gain or loss in respect of currency fluctuations over the period of holding an ordinary share or an ADS is also brought into account on a disposal.

Non-U.K. Holders

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

A corporate holder of an ordinary share or ADS that is not a U.K. Holder will not be liable for U.K. corporation tax on chargeable gains realized on the disposal of an ordinary share or ADS unless it carries on a trade in the U.K. through a permanent establishment to which the ordinary share or ADS is attributable. In these circumstances, a disposal (or deemed disposal) of an ordinary share or ADS by such holder may give rise to a chargeable gain or an allowable loss for the purposes of U.K. corporation tax.

Inheritance Tax

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

Stamp Duty and Stamp Duty Reserve Tax

The U.K. stamp duty, or stamp duty, and U.K. stamp duty reserve tax, or SDRT, treatment of the issue and transfer of, and the agreement to transfer, an ordinary share outside a depositary receipt system or a clearance service is discussed in the paragraphs under "*General*" below. The stamp duty and SDRT treatment of such transactions in relation to such systems is discussed in the paragraphs under "*Depositary Receipt Systems and Clearance Services*" below.

General

An agreement to transfer an ordinary share would normally give rise to a charge to SDRT at the rate of 0.5% of the amount or value of the consideration payable for the transfer. SDRT is, in general, payable by the purchaser. However, since April 28, 2014, no SDRT or stamp duty is chargeable in respect of shares that are admitted to trading on a 'recognized growth market' and not listed on any 'recognized stock exchange' ("AIM Exemption"). As the company's ordinary shares are admitted to trading on AIM (which qualifies as a 'recognized growth market') and not listed on any market that would qualify as a 'recognized stock exchange,' a transfer of an ordinary share is presently exempt from the charge to SDRT.

Subject to the above noted AIM Exemption, a transfer of an ordinary share would be subject to stamp duty at the rate of 0.5% of the consideration given for the transfer (rounded up to the next £5). The purchaser is liable to HMRC for the payment of the stamp duty (if any). Under current HMRC guidance, no stamp duty should be payable on a written instrument transferring an ADS or on a written agreement to transfer an ADS, on the basis that an ADS is not regarded as either "stock" or a "marketable security" for U.K. stamp duty purposes.

If a duly stamped transfer completing an agreement to transfer is produced within six years of the date on which the agreement is made (or, if the agreement is conditional, the date on which the agreement becomes unconditional) any SDRT already paid is generally repayable, normally with interest, and any SDRT charge yet to be paid is canceled to avoid a double charge as the stamp duty has been paid.

Depositary Receipt Systems and Clearance Services

The Court of Justice of the European Union in C-569/07 *HSBC Holdings Plc, Vidacos Nominees Limited v The Commissioners of Her Majesty's Revenue & Customs* and the First-tier Tax Tribunal decision in *HSBC Holdings Plc and the Bank of New York Mellon Corporation v The Commissioners of Her Majesty's Revenue & Customs*, have considered the provisions of the E.U. Council Directive 69/335/EEC, which was subsequently substituted by the E.U. Council Directive 2008/7/EEC ("E.U. Directives"). Following these decisions HMRC has publicly confirmed that issues or transfers of shares of U.K. incorporated companies, such as us, to a clearance service (such as, in our understanding, DTC) or a depositary receipt system (such as, in our understanding, Bank of New York Mellon Corporation) will not be chargeable to U.K. SDRT at 1.5% where that issue or transfer is an integral part of a raising of new capital.

It was announced as part of the U.K. Budget 2017 by the U.K. government that the 1.5% stamp duty and SDRT charge will not be reintroduced on the issue of shares by U.K. incorporated companies (and transfers of such shares where the transfer is integral to new capital raising) into clearance services and depositary receipt systems following the U.K.'s exit from the European Union ("Brexit" and "E.U.", respectively). However, there remains some uncertainty as to how under the provisions of the U.K.'s European Union (Withdrawal) Act 2018 ("Withdrawal Act") the rights and restrictions arising under the E.U. Directives before Brexit will continue to be recognized and available under U.K. domestic law (and to be enforced, allowed and followed accordingly) after Brexit. There is therefore some uncertainty whether any future issue or transfer of our ordinary shares into a clearance service or depositary receipt system (even where any such issue or transfer is integral to the raising of new capital by the company) will or will not be exempt from stamp duty and SDRT at 1.5%. It should also be noted that the Withdrawal Act ends the supremacy of E.U. law in the U.K. from the date of Brexit. Therefore, following Brexit, the U.K. government could potentially introduce new U.K. legislation with the effect that a future issue or transfer of our ordinary shares following (i) Brexit and (ii) any such change of U.K. law into a clearance service or depositary receipt system (even where such an issue or transfer is an integral part of the raising of new capital by the company) may potentially become chargeable to 1.5% stamp duty or SDRT. However, as long as the company's ordinary shares continue to be admitted to trading on AIM and not to be listed on any market that would qualify as a 'recognized stock exchange,' it is our understanding that the AIM Exemption should continue to exempt future issues and transfers of the company's ordinary shares into clearance services or depositary receipt systems from any 1.5% stamp duty and SDRT charge, including following a Brexit event.

Subject to the AIM exemption, where an ordinary share is transferred (i) to, or to a nominee for, a person whose business is or includes the provision of clearance services or (ii) to, or to a nominee for a person whose business is or includes issuing depositary receipts and that transfer is not integral to the raising of new capital by the company, stamp duty or SDRT would generally be chargeable at the rate of 1.5% of the amount or value of the consideration given or, in certain circumstances, the value of the shares.

There is an exception from the 1.5% charge on the transfer to, or to a nominee , a clearance service where the clearance service has made and maintained an election under section 97A(1) of the Finance Act 1986, which has been approved by HMRC. If such an election were made by a clearance service, subject to the AIM exemption, SDRT at the rate of 0.5% of the amount or value of the consideration payable for the transfer would arise on any transfer of an ordinary share into such a clearance service and on subsequent agreements to transfer such share within such clearance service. It is our understanding that DTC has not to date made an election under section 97A(1) of the Finance Act of 1986.

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

The Proposed Financial Transactions Tax

The European Commission has published a proposal for a Directive for a common Financial Transactions Tax, or FTT, in Belgium, Germany, Greece, Spain, France, Italy, Austria, Portugal, Slovenia and Slovakia (described below as the "participating Member States").

The proposed FTT has very broad scope and could, if introduced in its current form, apply to certain dealings in ordinary shares (including secondary market transactions) in certain circumstances.

Under current proposals, the FTT could apply in certain circumstances to persons both within and outside of the participating Member States. Generally, it would apply to certain dealings in the company's ordinary shares where at least

one party is a financial institution, and at least one party is established in a participating Member State. A financial institution may be, or be deemed to be, "established" in a participating Member State in a broad range of circumstances, including (i) by transacting with a person established in a participating Member State or (ii) where the financial instrument which is subject to the dealings is issued in participating Member State.

The FTT proposal remains subject to negotiation between the participating Member States. Further, the legality of the FTT proposal is at present uncertain. It may therefore be altered prior to any implementation, the timing of which remains unclear. Additional E.U. Member States may decide to participate. The FTT proposal remains only a proposal and little progress has been made in recent years; the impact of an FTT on us and holders of our ordinary shares and ADSs is made more uncertain following the U.K.'s decision to withdraw from the E.U. Prospective holders of ordinary shares or ADSs are advised to seek their own professional advice in relation to the FTT.

Taxation in the United States

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

This section summarizes the material U.S. federal income tax consequences to U.S. holders, as defined below, of an investment in the ADSs. This summary addresses only the U.S. federal income tax considerations for U.S. holders that acquire and hold the ADSs as capital assets. **Each prospective investor should consult a professional tax advisor with respect to the tax consequences of the acquisition, ownership or disposition of the ADSs**. This summary does not address tax considerations applicable to a holder of ADSs that may be subject to special tax rules including, without limitation, the following:

- banks or other financial institutions;
- insurance companies;
- brokers, dealers or traders in securities, currencies, or notional principal contracts;
- grantor trusts;
- tax-exempt entities, including an "individual retirement account" or "Roth IRA" retirement plan;
- regulated investment companies or real estate investment trusts;
- persons that hold the ordinary shares as part of a hedge, straddle, conversion, constructive sale or similar transaction involving more than one position;
- persons required to accelerate the recognition of any item of gross income with respect to the ADSs as a result of such income being recognized on an applicable financial statement;
- an entity classified as a partnership and persons that hold the ordinary shares through partnerships or certain other pass-through entities;
- holders (whether individuals, corporations or partnerships) that are treated as expatriates for some or all U.S. federal income tax purposes;
- persons who acquired the ADSs as compensation for the performance of services;
- persons who are resident, or ordinarily resident, in a foreign country;
- persons holding the ADSs in connection with a trade or business conducted outside of the United States;
- a U.S. holder who holds the ADSs through a financial account at a foreign financial institution that does not meet the requirements for avoiding withholding with respect to certain payments under Sections 1471 through 1474 of the Internal Revenue Code of 1986, as amended, or the Code;
- holders that own (or are deemed to own) 10% or more of our voting shares, measured by either voting power or value; and
- holders that have a "functional currency" other than the U.S. dollar.

Further, this summary does not address alternative minimum tax, gift or estate considerations, U.S. state or local tax matters or the indirect effects on the holders of equity interests in entities that own the ADSs. In addition, this discussion does not consider the U.S. tax consequences to holders of ADSs that are not "U.S. holders" (as defined below).

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

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

If a partnership holds ordinary shares or ADSs, the tax treatment of a partner will generally depend upon the status of the partner and upon the activities of the partnership; those rules are not discussed in this summary.

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

The discussion below assumes that the representations contained in the deposit agreement governing the ADSs are true and that the obligations in the deposit agreement and any related agreement will be complied with in accordance with their terms.

Ownership of ADSs

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

Distributions

Subject to the discussion under "*Passive Foreign Investment Company Considerations*" below, the gross amount of any distribution actually or constructively received by a U.S. holder with respect to ordinary shares will be taxable to the U.S. holder as a dividend to the extent of such U.S. holder's pro rata share of our current and accumulated earnings and profits as determined under U.S. federal income tax principles. Distributions in excess of such pro rata share of our earnings and profits will be non-taxable to the U.S. holder to the extent of, and will be applied against and reduce, the U.S. holder's adjusted tax basis in the ordinary shares. Distributions in excess of the sum of such pro rata share of our earnings and profits and such adjusted tax basis will generally be taxable to the U.S. holder as capital gain from the sale or exchange of property. However, since we do not calculate our earnings and profits under U.S. federal income tax principles, it is expected that any distribution will be reported as a dividend, even if that distribution would otherwise be treated as a non-taxable return of capital or as capital gain under the rules described above. The amount of any distribution of property other than cash will be the fair market value of that property on the date of distribution. A corporate U.S. holder will not be eligible for any dividends-received deduction in respect of a dividend received with respect to ordinary shares.

Subject to the discussion below regarding the "Medicare tax," qualified dividends received by non-corporate U.S. holders (*i.e.*, individuals and certain trusts and estates) are currently subject to a maximum income tax rate of 20%. This reduced income tax rate is applicable to dividends paid by "qualified foreign corporations" to non-corporate U.S. holders that meet the applicable requirements, including a minimum holding period (generally, at least 61 days without protection from the risk of loss during the 121-day period beginning 60 days before the ex-dividend date). A non-United States corporation (other than a corporation that is classified as a "passive foreign investment company," or PFIC, for the taxable year in which the dividend is paid or the preceding taxable year) generally will be considered to be a qualified foreign corporation (a) 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 provision, or (b) with respect to any dividend it pays on shares of stock which are readily tradable on an established securities market in the United States. Our ADSs are listed on the Nasdaq Global Market, which is an established securities market in the United States, and we expect the ADSs to be readily tradable on the Nasdaq Global Market. However, there can be no assurance that the ADSs will be considered readily tradable on an established securities market in the United States in later years. The company, which is incorporated under the laws of the United Kingdom, believes that it qualifies as a resident of the United Kingdom for the purposes of, and 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 Capital Gains, signed on July 24, 2001, or the U.S.-U.K. Tax Treaty, although there can be no assurance in this regard.

Further, the IRS has determined that the U.S.-U.K. Tax Treaty is satisfactory for purposes of the qualified dividend rules and that it includes an exchange-of-information program. Based on the foregoing, we expect to be considered a qualified foreign corporation under the Code. Accordingly, dividends paid by us to non-corporate U.S. holders with respect to shares that meet the minimum holding period and other requirements are expected to be treated as "qualified dividend income." However, as discussed above, dividends paid by us will not qualify for the 20% maximum U.S. federal income tax rate if we are treated, for the tax year in which the dividends are paid or the preceding tax year, as a PFIC for U.S. federal income tax purposes, as discussed below.

The U.S. Treasury Department has announced its intention to issue rules regarding when and to what extent holders of ADSs will be permitted to rely on certifications from issuers to establish that dividends paid on shares to which such ADSs relate are treated as qualified dividends. Because such procedures have not yet been issued, it is not clear whether we will be able to comply with them.

Dividends received by a U.S. holder with respect to ordinary shares generally will be treated as foreign source income for the purposes of calculating that holder's foreign tax credit limitation. For these purposes, dividends distributed by us generally will constitute "passive category income" (but, in the case of some U.S. holders, may be allocated to a different category of income).

Sale or Other Disposition of Ordinary Shares

A U.S. holder will generally recognize gain or loss for U.S. federal income tax purposes upon the sale or exchange of ordinary shares in an amount equal to the difference between the U.S. dollar value of the amount realized from such sale or exchange and the U.S. holder's tax basis for those ordinary shares. Subject to the discussion under "*Passive Foreign Investment Company Considerations*" below, this gain or loss will generally be a capital gain or loss and will generally be treated as from sources within the United States. Such capital gain or loss will be treated as long-term capital gain or loss if the U.S. holder has held the ordinary shares for more than one year at the time of the sale or exchange. Long-term capital gains of non-corporate U.S. holders may be eligible for a preferential tax rate; the deductibility of capital losses is subject to limitations. For a cash basis taxpayer, units of foreign currency paid or received are translated into U.S. dollars at the spot rate on the settlement date of the purchase or sale. In that case, no foreign currency exchange gain or loss will result from currency fluctuations between the trade date and the settlement date of such a purchase or sale. An accrual basis taxpayer, however, may elect the same treatment required of cash basis taxpayers with respect to purchases and sales of the ADSs that are traded on an established securities market, provided the election is applied consistently from year to year. Such election may not be changed without the consent of the IRS. For an accrual basis taxpayer who does not make such election, units of foreign currency paid or received are translated into U.S. dollars at the spot rate on the trade date of the purchase or sale. Such an accrual basis taxpayer may recognize exchange gain or loss based on currency fluctuations between the trade date and settlement date. Any foreign currency gain or loss a U.S. holder realizes will be U.S. source ordinary income or loss.

Medicare Tax

An additional 3.8% tax, or "Medicare Tax," is imposed on all or a portion of the "net investment income" (which includes taxable dividends and net capital gains, adjusted for deductions properly allocable to such dividends or net capital gains) received by (i) U.S. holders that are individuals with modified adjusted gross income of over $200,000 ($250,000 in the case of joint filers, $125,000 in the case of married individuals filing separately) and (ii) certain trusts or estates.

Passive Foreign Investment Company Considerations

A corporation organized outside the United States generally will be classified as a passive foreign investment company, or PFIC, for U.S. federal income tax purposes in any taxable year in which, after applying the applicable look-through rules, either: (i) at least 75% of its gross income is passive income; or (ii) on average at least 50% of the gross value of its assets is attributable to assets that produce passive income or are held for the production of passive income. In arriving at this calculation, a pro rata portion of the income and assets of each corporation in which we own, directly or indirectly, at least a 25% interest, as determined by the value of such corporation, must be taken into account. Passive income for this purpose generally includes dividends, interest, royalties, rents and gains from commodities and securities transactions.

We believe that we were not a PFIC for any previous taxable year. Based on our estimated gross income, the average value of our gross assets, and the nature of the active businesses conducted by our "25% or greater" owned subsidiaries, we do not believe that we will be classified as a PFIC in the current taxable year. Our status for any taxable year will depend on our assets and activities in each year, and because this is a factual determination made annually after the end of each taxable year, there can be no assurance that we will not be considered a PFIC for the current taxable year or any future taxable year. The market value of our assets may be determined in large part by reference to the market price of the ADSs and our ordinary shares, which is likely to fluctuate (and may fluctuate considerably given that market prices of life sciences

companies can be especially volatile). In addition, the composition of our income and assets will be affected by how, and how quickly, we spend the cash we raise in this offering.

If we were a PFIC for any taxable year during which a U.S. holder held ordinary shares, under the "default PFIC regime" (i.e., in the absence of one of the elections described below) gain recognized by the U.S. holder on a sale or other disposition (including a pledge) of the ordinary shares would be allocated ratably over the U.S. holder's holding period for the ordinary shares. The amounts allocated to the taxable year of the sale or other disposition and to any year before we became a PFIC would be taxed as ordinary income. The amount allocated to each other taxable year would be subject to tax at the highest rate in effect for individuals or corporations, as appropriate, for that taxable year, and an interest charge would be imposed on the resulting tax liability for that taxable year. Similar rules would apply to the extent any distribution in respect of ordinary shares exceeds 125% of the average of the annual distributions on ordinary shares received by a U.S. holder during the preceding three years or the holder's holding period, whichever is shorter.

In the event we were treated as a PFIC, the tax consequences under the default PFIC regime described above could be avoided by either a "mark-to-market" or "qualified electing fund" election. A U.S. holder making a mark-to-market election (if the eligibility requirements for such an election were satisfied) generally would not be subject to the PFIC rules discussed above, except with respect to any portion of the holder's holding period that preceded the effective date of the election. Instead, the electing holder would include in ordinary income, for each taxable year in which we were a PFIC, an amount equal to any excess of (a) the fair market value of the ordinary shares as of the close of such taxable year over (b) the electing holder's adjusted tax basis in such ordinary shares. In addition, an electing holder would be allowed a deduction in an amount equal to the lesser of (a) the excess, if any, of (i) the electing holder's adjusted tax basis in the ordinary shares over (ii) the fair market value of such ordinary shares as of the close of such taxable year or (b) the excess, if any, of (i) the amount included in ordinary income because of the election for prior taxable years over (ii) the amount allowed as a deduction because of the election for prior taxable years. The election would cause adjustments in the electing holder's tax basis in the ordinary shares to reflect the amount included in gross income or allowed as a deduction because of the election. In addition, upon a sale or other taxable disposition of ordinary shares, an electing holder would recognize ordinary income or loss (not to exceed the excess, if any, of (a) the amount included in ordinary income because of the election for prior taxable years over (b) the amount allowed as a deduction because of the election for prior taxable years).

Alternatively, a U.S. holder making a valid and timely "QEF election" generally would not be subject to the default PFIC regime discussed above. Instead, for each PFIC year to which such an election applied, the electing holder would be subject to U.S. federal income tax on the electing holder's pro rata share of our net capital gain and ordinary earnings, regardless of whether such amounts were actually distributed to the electing holder. However, because we do not intend to prepare or provide the information that would permit the making of a valid QEF election, that election will not be available to U.S. holders.

If we were considered a PFIC for the current taxable year or any future taxable year, a U.S. holder would be required to file annual information returns for such year, whether or not the U.S. holder disposed of any ordinary shares or received any distributions in respect of ordinary shares during such year.

Backup Withholding and Information Reporting

U.S. holders generally will be subject to information reporting requirements with respect to dividends on ordinary shares and on the proceeds from the sale, exchange or disposition of ordinary shares that are paid within the United States or through U.S.-related financial intermediaries, unless the U.S. holder is an "exempt recipient." In addition, U.S. holders may be subject to backup withholding (at a 24% rate) on such payments, unless the U.S. holder provides a taxpayer identification number and a duly executed IRS Form W-9 or otherwise establishes an exemption. Backup withholding is not an additional tax, and the amount of any backup withholding will be allowed as a credit against a U.S. holder's U.S. federal income tax liability and may entitle such holder to a refund, provided that the required information is timely furnished to the IRS.

Foreign Account Tax Compliance Act, or FATCA, and Related Provisions

Under certain circumstances, in accordance with proposed Treasury regulations issued in December 2018, the company or its paying agent may be required, pursuant to the FATCA provisions of the Code (or analogous provisions of non-U.S. law) and regulations or pronouncements thereunder, any "intergovernmental agreement" entered into pursuant to those provisions or any U.S. or non-U.S. fiscal or regulatory legislation, rules, guidance notes or practices adopted pursuant to any such agreement, to withhold U.S. tax at a rate of 30% on all or a portion of payments of dividends or other corporate distributions which are treated as "foreign passthru payments" made on or after the date that is two years after the date of publication of future final regulations defining the term "foreign passthru payment," if such payments are not exempt from such withholding. The company believes, and this discussion assumes, that the company is not a "foreign financial institution" for purposes of FATCA.

Foreign Asset Reporting

In addition, certain individuals who are U.S. Holders may be required to file IRS Form 8938 to report the ownership of "specified foreign financial assets" if the total value of those assets exceeds an applicable threshold amount (subject to certain exceptions). For these purposes, a specified foreign financial asset may include not only a financial account (as defined for these purposes) maintained by a non-U.S. financial institution, but also stock or securities issued by a non-U.S. corporation (such as the company). Certain U.S. entities may also be required to file IRS Form 8938 in the future.

F. Dividends and Paying Agents

Not applicable.

G. Statement by Experts

Not applicable.

H. Documents on Display

We are subject to the informational requirements of the Exchange Act. Accordingly, we are required to file reports and other information with the SEC, including annual reports on Form 20-F and reports on Form 6-K. The SEC maintains an Internet website that contains these reports and other information about issuers, like us, that file electronically with the SEC. The address of that website is www.sec.gov.

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

I. Subsidiary Information

Not applicable.

Item 11: Quantitative and Qualitative Disclosures About Market Risk

Our activities expose us to a variety of financial risks: foreign currency risk, interest rate risk, credit risk and liquidity risk. Our principal financial instrument comprises cash and cash equivalents, and this is used to finance our operations. We have various other financial instruments such as other receivables and trade and other payables that arise directly from our operations. The category of loans and receivables contains only other receivables, shown on the face of the Statement of Financial Position, all of which mature within one year. We have compared fair value to book value for each class of financial asset and liability and no difference was identified. Further information is included in note 22 to our consolidated financial statements appearing at the end of this Annual Report. We have a policy, which has been consistently followed, of not trading in financial instruments.

Foreign Currency Risk

Foreign currency risk refers to the risk that the value of a financial commitment or recognized asset or liability will fluctuate due to changes in foreign currency rates. Our net income and financial position, as expressed in pounds sterling, are exposed to movements in foreign exchange rates against the U.S. dollar and the euro. The main trading currencies are pounds sterling, the U.S. dollar, and the euro. We are exposed to foreign currency risk as a result of operating transactions, capital raises in the United States, payment in U.S. dollars under our funding agreements with BARDA and CARB-X, our license and commercialization agreement with Eurofarma and our license and collaboration agreement with Sarepta, and the translation of foreign bank accounts. We monitor our exposure to foreign exchange risk. Exposures are generally managed through natural hedging via the currency denomination of cash balances and any impact currently is not material to us.

Interest Rate Risk

We do not hold any derivative instruments to manage interest rate risk.

Credit Risk

We consider all of our material counterparties to be creditworthy. We consider the credit risk for each of our counterparties to be low and do not have a significant concentration of credit risk at any of our counterparties. We had £1.7 million of trade receivables outstanding at January 31, 2019, from Sarepta.

Liquidity Risk

We have funded our operations since inception primarily through the issuance of equity securities. We have also received funding from our license and collaboration agreement with Sarepta and our license and commercialization agreement with Eurofarma, as well as philanthropic, non-government and not for profit organizations and patient advocacy groups and grant funding from government entities, including BARDA. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of public or private equity or debt financings or other sources. Adequate additional financing may not be available to us on acceptable terms, or at all. Our inability to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy.

Item 12: Description of Securities other than Equity Securities

A. Debt Securities.

Not applicable.

B. Warrants and Rights.

Not applicable.

C. Other Securities.

Not applicable.

D. American Depositary Shares.

Fees and Expenses

The following table shows the fees and charges that a holder of our ADSs may have to pay, either directly or indirectly. The majority of these costs are set by the depositary and are subject to change:

Persons depositing or withdrawing shares or ADS holders must pay:	For:
$5.00 (or less) per 100 ADSs (or portion of 100 ADSs)	Issuance of ADSs, including issuances resulting from a distribution of shares or rights or other property Cancellation of ADSs for the purpose of withdrawal, including if the deposit agreement terminates
$.05 (or less) per ADS	Any cash distribution to ADS holders
A fee equivalent to the fee that would be payable if securities distributed to you had been shares and the shares had been deposited for issuance of ADSs	Distribution of securities distributed to holders of deposited securities (including rights) that are distributed by the depositary to ADS holders
$.05 (or less) per ADS per calendar year	Depositary services
Registration or transfer fees	Transfer and registration of shares on our share register to or from the name of the depositary or its agent when you deposit or withdraw shares
Expenses of the depositary	Cable, telex and facsimile transmissions (when expressly provided in the deposit agreement) Converting foreign currency to U.S. dollars
Taxes and other governmental charges the depositary or the custodian has to pay on any ADSs or shares underlying ADSs, such as stock transfer taxes, stamp duty or withholding taxes	As necessary
Any charges incurred by the depositary or its agents for servicing the deposited securities	As necessary

The depositary collects its fees for delivery and surrender 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 may collect any of its fees by deduction from any cash distribution payable (or by selling a portion of securities or other property distributable) to ADS holders that are obligated to pay those fees. The depositary may generally refuse to provide fee-attracting services until its fees for those services are paid.

From time to time, the depositary may make payments to us to reimburse us for costs and expenses generally arising out of establishment and maintenance of the ADS program, waive fees and expenses for services provided to us by the depositary or share revenue from the fees collected from ADS holders. In performing its duties under the deposit agreement, the depositary may use brokers, dealers or other service providers that are affiliates of the depositary and that may earn or share fees or commissions.

Payment of Taxes

You will be responsible for any taxes or other governmental charges payable on your ADSs or on the deposited securities represented by any of your ADSs. The depositary may refuse to register any transfer of your ADSs or allow you to withdraw the deposited securities represented by your ADSs until those taxes or other charges are paid. It may apply payments owed to you or sell deposited securities represented by your American Depositary Shares to pay any taxes owed and you will remain liable for any deficiency. If the depositary sells deposited securities, it will, if appropriate, reduce the number of ADSs to reflect the sale and pay to ADS holders any proceeds, or send to ADS holders any property, remaining after it has paid the taxes.

PART II

Item 13: Defaults, Dividend Arrearages and Delinquencies

None.

Item 14: Material Modifications to the Rights of Security Holders and Use of Proceeds

A. Not applicable.

B. Not applicable.

C. Not applicable.

D. Not applicable.

E. Not applicable.

Item 15: Controls and Procedures

A. Disclosure Controls and Procedures.

We have carried out an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) under the supervision and the participation of the company's management, which is responsible for the management of the internal controls, and which includes our Chief Executive Officer (our principal executive officer) and our Vice President of Finance (our principal financial officer). The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Securities Exchange Act of 1934 is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Securities Exchange Act of 1934 is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. There are inherent limitations to the effectiveness of any system of disclosure controls and procedures, including the possibility of human error and the circumvention or overriding of the controls and procedures. Accordingly, even effective disclosure controls and procedures can only provide reasonable assurance of achieving their control objectives. Based upon our evaluation of our disclosure controls and procedures as of January 31, 2019, our Chief Executive Officer and Vice President of Finance concluded that, as of such date, our disclosure controls and procedures were effective at a reasonable level of assurance.

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

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Our internal control over financial reporting is a process designed, under the supervision of the Chief Executive Officer (our principal executive officer) and the Vice President of Finance (our principal financial officer), to provide reasonable assurance regarding the reliability of financial reporting and the preparation of our financial statements for external reporting purposes in accordance with International Financial Reporting Standards.

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

Our management has assessed the effectiveness of internal control over financial reporting as of January 31, 2019, based on the Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) 2013. Based on this assessment, our management has concluded that our internal control over financial reporting as of January 31, 2019, was effective.

C. Attestation Report of the Registered Public Accounting Firm

This report does not include an attestation report of our registered public accounting firm as we are an emerging growth company.

D. Changes in Internal Control Over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the fiscal year ended January 31, 2019, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 16A: Audit Committee Financial Expert

The members of our audit committee are Mr. Wurzer, Mr. Zambeletti and Ms. Andrews. Mr. Wurzer is the chair of the audit committee. Each of our audit committee members satisfies the independence requirements of Rule 5605(a)(2) of the Nasdaq Stock Market Marketplace Rules and the independence requirements of Rule 10A-3(b)(1) under the Exchange Act. Our board of directors has determined that Mr. Wurzer is an "audit committee financial expert" as defined in Item 16A of Form 20-F.

Item 16B: Code of Ethics

Our Code of Business Conduct and Ethics is applicable to all of our employees, officers and directors and is available on our website at www.summitplc.com. Our Code of Business Conduct and Ethics provides that our directors and officers are expected to avoid any action, position or interest that conflicts with the interests of our company or gives the appearance of a conflict. Our directors and officers have an obligation under our Code of Business Conduct and Ethics to advance our company's interests when the opportunity to do so arises. We expect that any amendment to this code, or any waivers of its requirements, will be disclosed on our website. Information contained on, or that can be accessed through, our website is not incorporated by reference into this Annual Report, and you should not consider information on our website to be part of this Annual Report.

Item 16C: Principal Accountant Fees and Services

The following table sets forth, for each of the years indicated, the aggregate fees billed to us for services rendered by PricewaterhouseCoopers LLP, our independent registered public accounting firm.

	Year Ended January 31,	
	2019	2018
	(in thousands)	
Audit Fees	£ 279	£ 341
Audit-Related Fees [1]	115	118
Tax Fees [2]	25	23
All Other Fees [3]	—	—
Total	£ 419	£ 482

(1) For the year ended January 31, 2019, audit-related fees includes assurance reporting in connection with our registration statement on Form F-3 that was filed with the U.S. Securities and Exchange Commission on May 15, 2018. For the year ended January 31, 2018, audit-related fees includes assurance reporting in connection with our underwritten public offering in September 2017.

(2) Fees relate to the aggregated fees for services rendered on tax compliance, tax advice and tax planning.

(3) No fees incurred in this category.

The audit committee is responsible for the appointment, replacement, compensation, evaluation and oversight of the work of the independent auditors. As part of this responsibility, the audit committee pre-approves all audit and non-audit services performed by the independent auditors in order to assure that they do not impair the auditor's independence from the company.

Item 16D: Exemptions from the Listing Standards for Audit Committees

Not applicable.

Item 16E: Purchases of Equity Securities by the Issuer and Affiliated Purchasers

Not applicable.

Item 16F: Change in Registrant's Certifying Accountant

Not applicable.

Item 16G: Corporate Governance

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

- We do not follow Nasdaq's quorum requirements applicable to meetings of shareholders. Such quorum requirements are not required under U.K. law. In accordance with generally accepted business practice, our articles of association provide alternative quorum requirements that are generally applicable to meetings of shareholders.

- We do not follow Nasdaq's requirements that non-management directors meet on a regular basis without management present. Our board of directors may choose to meet in executive session at their discretion.

- We do not follow Nasdaq's requirements to seek shareholder approval for the implementation of certain equity compensation plans, the issuances of ordinary shares under such plans, or in connection with certain private placements of equity securities. In accordance with U.K. law, we are not required to seek shareholder approval to allot ordinary shares in connection with applicable employee equity compensation plans. We will follow U.K. law with respect to any requirement to obtain shareholder approval prior to any private placements of equity securities, including those that may result in a change of control.

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

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

Item 16H: Mine Safety Disclosure

Not applicable.

PART III

Item 17: Financial Statements

We have elected to provide financial statements pursuant to Item 18.

Item 18: Financial Statements

The financial statements are filed as part of this Annual Report beginning on page F-1.

Item 19: Exhibits

Exhibit No.	Description
1.1	Articles of Association of Summit Therapeutics plc (incorporated by reference to Exhibit 3.1 to the Company's Registration Statement on Form F-1 (File No. 333-201807), as amended, filed with the Securities and Exchange Commission on February 20, 2015)
2.1	Specimen certificate evidencing ordinary shares of Summit Therapeutics plc (incorporated by reference to Exhibit 4.5 to the Company's Registration Statement on Form F-1 (File No. 333-201807), filed with the Securities and Exchange Commission on January 30, 2015)
2.2	Form of Deposit Agreement among Summit Therapeutics plc, The Bank of New York Mellon, as depositary, and all Owners and Holders of ADSs issued thereunder (incorporated by reference to Exhibit 4.1 to the Company's Registration Statement on Form F-1 (File No. 333-201807), as amended, filed with the Securities and Exchange Commission on February 20, 2015)
2.3	Form of American Depositary Receipt (included in Exhibit 2.2) (incorporated by reference to Exhibit 4.2 to the Company's Registration Statement on Form F-1 (File No. 333-201807), as amended, filed with the Securities and Exchange Commission on February 20, 2015)
2.4	Registration Rights Agreement, dated January 9, 2019, by and among Summit Therapeutics plc and Robert W. Duggan (incorporated by reference to Exhibit 2.1 to the Company's Report on Form 6-K (File No. 001-36866), filed with the Securities and Exchange Commission on January 10, 2019)
4.1†	Translation Award Funding Agreement, entered into as of October 19, 2012, by and between the Wellcome Trust Limited and Summit Therapeutics plc (incorporated by reference to Exhibit 10.3 to the Company's Registration Statement on Form F-1 (File No. 333-201807), as amended, filed with the Securities and Exchange Commission on February 27, 2015)
4.2	Service Agreement, effective as of January 14, 2015, by and between Cambridge Innovation Center and Summit Therapeutics Inc. (incorporated by reference to Exhibit 10.10 to the Company's Registration Statement on Form F-1 (File No. 333-201807), as amended, filed with the Securities and Exchange Commission on February 20, 2015)
4.3	2005 Enterprise Management Incentive Scheme (incorporated by reference to Exhibit 10.11 to the Company's Registration Statement on Form F-1 (File No. 333-201807), filed with the Securities and Exchange Commission on January 30, 2015)
4.4	Letter of Appointment, dated November 20, 2014, by and between Summit Therapeutics Inc. and Valerie Andrews (incorporated by reference to Exhibit 10.12 to the Company's Registration Statement on Form F-1 (File No. 333-201807), filed with the Securities and Exchange Commission on January 30, 2015)
4.5	Letter of Appointment, dated November 21, 2012, by and between Summit Therapeutics plc and Frank Armstrong (incorporated by reference to Exhibit 10.13 to the Company's Registration Statement on Form F-1 (File No. 333-201807), filed with the Securities and Exchange Commission on January 30, 2015)
4.6	Letter of Appointment, dated April 16, 2014, by and between Summit Therapeutics plc and Leopoldo Zambeletti (incorporated by reference to Exhibit 10.16 to the Company's Registration Statement on Form F-1 (File No. 333-201807), filed with the Securities and Exchange Commission on January 30, 2015)
4.7	Letter of Appointment, dated February 18, 2015, by and between Summit Therapeutics plc and David Wurzer (incorporated by reference to Exhibit 10.17 to the Company's Registration Statement on Form F-1 (File No. 333-201807), as amended, filed with the Securities and Exchange Commission on February 20, 2015)
4.8	Form of Deed of Indemnity (incorporated by reference to Exhibit 10.18 to the Company's Registration Statement on Form F-1 (File No. 333-201807), as amended, filed with the Securities and Exchange Commission on February 20, 2015)
4.9	2016 Long Term Incentive Plan (incorporated by reference to Exhibit 4.22 to the Company's Annual Report on Form 20-F (File No. 001-36866), filed with the Securities and Exchange Commission on May 12, 2016)
4.10†	License and Collaboration Agreement, dated October 3, 2016, by and between Summit (Oxford) Ltd. and Sarepta Therapeutics, Inc. (incorporated by reference to Exhibit 4.23 to the Company's Annual Report on Form 20-F (File No. 001-36866), filed with the Securities and Exchange Commission on March 30, 2017)
4.11	Lease, dated February 17, 2017, by and among MEPC Milton Park No. 1 Limited, MEPC Milton Park No. 2 Limited and Summit Therapeutics plc (incorporated by reference to Exhibit 4.25 to the Company's Annual Report on Form 20-F (File No. 001-36866), filed with the Securities and Exchange Commission on March 30, 2017)

Exhibit No.	Description
4.12†	Agreement, dated September 5, 2017, by and between Summit (Oxford) Limited and the U.S. Department of Health and Human Services Biomedical Advanced Research and Development Authority (BARDA) (incorporated by reference to Exhibit 4.26 to the Company's Annual Report on Form 20-F (File No. 001-36866), filed with the Securities and Exchange Commission on April 13, 2018)
4.13*+	Amendment of Solicitation/Modification of Contract (0001), dated June 19, 2018, to Agreement, dated September 5, 2017, by and between Summit (Oxford) Limited and the U.S. Department of Health and Human Services Biomedical Advanced Research and Development Authority (BARDA)
4.14*+	Amendment of Solicitation/Modification of Contract (0002), dated August 14, 2018, to Agreement, dated September 5, 2017, by and between Summit (Oxford) Limited and the U.S. Department of Health and Human Services Biomedical Advanced Research and Development Authority (BARDA)
4.15*+	Amendment of Solicitation/Modification of Contract (0003), dated February 14, 2019, to Agreement, dated September 5, 2017, by and between Summit (Oxford) Limited and the U.S. Department of Health and Human Services Biomedical Advanced Research and Development Authority (BARDA)
4.16†	License and Commercialization Agreement, dated December 18, 2017, by and between Summit (Oxford) Ltd. and Eurofarma Laboratórios S.A. (incorporated by reference to Exhibit 4.27 to the Company's Annual Report on Form 20-F (File No. 001-36866), filed with the Securities and Exchange Commission on April 13, 2018)
4.17†	Share Purchase Agreement, dated December 23, 2017, by and among Summit Therapeutics plc and the shareholders of Discuva Limited (incorporated by reference to Exhibit 4.28 to the Company's Annual Report on Form 20-F (File No. 001-36866), filed with the Securities and Exchange Commission on April 13, 2018) (1)
4.18†	Transfer Incentive Agreement, dated December 23, 2017, by and among Discuva Limited and certain of its managers (incorporated by reference to Exhibit 4.29 to the Company's Annual Report on Form 20-F (File No. 001-36866), filed with the Securities and Exchange Commission on April 13, 2018)
4.19	Lease, dated December 22, 2017, by and between Merrifield Centre Ltd and Discuva Limited (incorporated by reference to Exhibit 4.31 to the Company's Annual Report on Form 20-F (File No. 001-36866), filed with the Securities and Exchange Commission on April 13, 2018)
4.20†	Equity and Revenue Sharing Agreement, dated October 16, 2017, by and between Summit (Oxford) Limited and the Wellcome Trust Limited (incorporated by reference to Exhibit 4.32 to the Company's Annual Report on Form 20-F (File No. 001-36866), filed with the Securities and Exchange Commission on April 13, 2018)
4.21	Form of Non-Executive Director Restricted Stock Unit (RSU) Agreement (incorporated by reference to Exhibit 4.33 to the Company's Annual Report on Form 20-F (File No. 001-36866), filed with the Securities and Exchange Commission on April 13, 2018)
4.22	Securities Purchase Agreement, dated December 14, 2018, by and among Summit Therapeutics plc and Robert W. Duggan (incorporated by reference to Exhibit 10.1 to the Company's Report on Form 6-K (File No. 001-36866), filed with the Securities and Exchange Commission on December 17, 2018)
4.23	Relationship Agreement, dated December 14, 2018, by and among Summit Therapeutics plc, Robert W. Duggan and Cairn Financial Advisers LLP (incorporated by reference to Exhibit 10.2 to the Company's Report on Form 6-K (File No. 001-36866), filed with the Securities and Exchange Commission on December 17, 2018)
8.1*	Subsidiaries of Summit Therapeutics plc
12.1*	Certification of Chief Executive Officer pursuant to Securities Exchange Act Rules 13a-14(a) and 15d-14(a) as adopted pursuant to §302 of the Sarbanes-Oxley Act of 2002
12.2*	Certification of Vice President of Finance (Principal Financial Officer) pursuant to Securities Exchange Act Rules 13a-14(a) and 15d-14(a) as adopted pursuant to §302 of the Sarbanes-Oxley Act of 2002
13.1*	Certification of Chief Executive Officer and Vice President of Finance (Principal Financial Officer) pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002
15.1*	Consent of PricewaterhouseCoopers LLP
101.INS*	XBRL Instance Document
101.SCH*	XBRL Taxonomy Extension Schema Document
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document

101.LAB*	XBRL Taxonomy Extension Label Linkbase Document

Exhibit No.	Description
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document

*	Filed herewith.
†	Confidential treatment has been granted as to certain portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission.
+	Confidential treatment has been requested as to certain portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission.
(1)	The schedules and exhibits to the Share Purchase Agreement have been omitted. A copy of any omitted schedule or exhibit will be furnished to the Securities and Exchange Commission upon request.

SIGNATURES

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

SUMMIT THERAPEUTICS PLC

By:	/s/ Glyn Edwards
Name:	Glyn Edwards
Title:	Chief Executive Officer

Date: March 29, 2019

SUMMIT THERAPEUTICS PLC

Index to Financial Statements

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Shareholders of Summit Therapeutics plc

Opinion on the Financial Statements

We have audited the accompanying Consolidated Statement of Financial Position of Summit Therapeutics plc and its subsidiaries (the "Company") as of January 31, 2019, and January 31, 2018, and the related Consolidated Statements of Comprehensive Income, of changes in equity and of cash flows for each of the three years in the period ended January 31, 2019, including the related notes (collectively referred to as the "Consolidated Financial Statements"). In our opinion, the Consolidated Financial Statements present fairly, in all material respects, the financial position of the Company as of January 31, 2019, and January 31, 2018, and the results of its operations and its cash flows for each of the three years in the period ended January 31, 2019, in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board.

Basis for Opinion

These Consolidated Financial Statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's Consolidated Financial Statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

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

Emphasis of matter

As discussed in Note 1 to the Consolidated Financial Statements, the Company will require additional financing to fund planned future operations. Management's plans in regard to this matter are described in Note 1.

/s/ PricewaterhouseCoopers LLP
Reading, United Kingdom
March 27, 2019

We have served as the Company's auditor since 2013.

Consolidated Statement of Financial Position
At January 31, 2019 and 2018

	Note	**January 31, 2019**	January 31, 2018 (Adjusted*)
		£000	£000
ASSETS			
Non-current assets			
Goodwill	14	**1,814**	2,478
Intangible assets	15	**10,604**	14,785
Property, plant and equipment	16	**616**	809
		13,034	18,072
Current assets			
Trade and other receivables	17	**13,547**	11,134
Current tax receivable		**6,328**	4,654
Cash and cash equivalents		**26,858**	20,102
		46,733	35,890
Total assets		**59,767**	53,962
LIABILITIES			
Non-current liabilities			
Deferred revenue	19	**(831)**	(27,270)
Financial liabilities on funding arrangements	21	**—**	(3,090)
Provisions for other liabilities and charges	23	**(1,851)**	(1,641)
Deferred tax liability	24	**(1,675)**	(2,379)
		(4,357)	(34,380)
Current liabilities			
Trade and other payables	18	**(8,865)**	(8,932)
Deferred revenue and income	19	**(3,374)**	(13,834)
Contingent consideration	20	**(629)**	—
		(12,868)	(22,766)
Total liabilities		**(17,225)**	(57,146)
Net assets / (liabilities)		**42,542**	(3,184)
EQUITY			
Share capital	25	**1,604**	736
Share premium account		**92,806**	60,237
Share-based payment reserve		**1,148**	6,743
Merger reserve		**3,027**	3,027
Special reserve		**19,993**	19,993
Currency translation reserve		**56**	37
Accumulated losses reserve		**(76,092)**	(93,957)
Total equity / (deficit)		**42,542**	(3,184)

* See Note 3 - 'Changes to accounting policies - Adoption of IFRS 15 *Revenue from contracts with customers*.'

The accompanying notes form an integral part of these Consolidated Financial Statements.

Consolidated Statement of Comprehensive Income
For the year ended January 31, 2019, 2018 and 2017

	Note	**Year ended January 31, 2019**	Year ended January 31, 2018 (Adjusted*)	Year ended January 31, 2017
		£000	£000	£000
Revenue	5	**43,012**	12,360	2,304
Other operating income	6	**15,156**	2,725	72
Operating expenses				
Research and development	8	**(39,174)**	(28,970)	(18,952)
General and administration	8	**(12,342)**	(11,999)	(8,277)
Impairment of goodwill and intangible assets	9	**(3,985)**	—	—
Total operating expenses		**(55,501)**	(40,969)	(27,229)
Operating profit / (loss)		**2,667**	(25,884)	(24,853)
Finance income	11	**2,788**	3,096	8
Finance costs	11	**(424)**	(1,164)	(862)
Profit / (loss) before income tax		**5,031**	(23,952)	(25,707)
Income tax	12	**2,496**	3,762	4,336
Profit / (loss) for the year		**7,527**	(20,190)	(21,371)
Other comprehensive income / (loss)				
Items that may be reclassified subsequently to profit or loss				
Exchange differences on translating foreign operations		**19**	(13)	29
Total comprehensive profit / (loss)		**7,546**	(20,203)	(21,342)
Basic and diluted earnings / (loss) per ordinary share from operations	13	**9 p**	**(31) p**	**(35) p**

* See Note 3 - 'Changes to accounting policies - Adoption of IFRS 15 *Revenue from contracts with customers*.'

The accompanying notes form an integral part of these Consolidated Financial Statements.

Consolidated Statement of Cash Flows

For the year ended January 31, 2019, 2018 and 2017

	Note	Year ended January 31, 2019	Year ended January 31, 2018 (Adjusted*)	Year ended January 31, 2017
		£000s	£000s	£000s
Cash flows from operating activities				
Profit / (loss) before income tax		**5,031**	(23,952)	(25,707)
		5,031	(23,952)	(25,707)
Adjusted for:				
Gain on remeasurement or derecognition of financial liabilities on funding arrangements	6,21	**(539)**	(908)	—
Loss on recognition of contingent consideration payable	20	**754**	—	—
Finance income	11	**(2,788)**	(3,096)	(8)
Finance costs	11	**424**	1,164	862
Unrealized foreign exchange (gain) / loss		**(408)**	1,960	711
Depreciation	16	**309**	140	48
Amortization of intangible fixed assets	15	**829**	106	10
Loss on disposal of assets	8	**43**	40	—
Increase / (decrease) in provisions	23	**19**	(60)	12
Research and development expenditure credit	6	**(333)**	(23)	(3)
Impairment of goodwill and intangible assets	14,15	**3,985**	—	—
Share-based payment	7	**4,743**	1,607	1,379
Adjusted profit / (loss) from operations before changes in working capital		**12,069**	(23,022)	(22,696)
(Increase) / decrease in trade and other receivables		**(2,218)**	(8,993)	492
(Decrease) / increase in deferred revenue		**(36,898)**	10,577	30,527
Increase in trade and other payables		**93**	3,375	813
Cash (used by) / generated from operations		**(26,954)**	(18,063)	9,136
Taxation received		**159**	3,374	3,005
Net cash (used by) / generated from operating activities		**(26,795)**	(14,689)	12,141
Investing activities				
Acquisition of subsidiaries net of cash acquired		**—**	(4,775)	—
Contingent consideration paid	20	**(192)**	—	—
Purchase of property, plant and equipment	16	**(119)**	(360)	(81)
Purchase of intangible assets	15	**(6)**	(119)	(7)
Interest received		**4**	12	8
Net cash used in investing activities		**(313)**	(5,242)	(80)
Financing activities				
Proceeds from issue of share capital		**34,648**	14,931	—
Transaction costs on share capital issued		**(1,313)**	(1,428)	—
Proceeds from exercise of warrants		**—**	10	107
Proceeds from exercise of share options		**102**	392	283
Cash received from funding arrangements accounted for as financial liabilities		**—**	—	23
Net cash generated from financing activities		**33,437**	13,905	413
Increase / (Decrease) in cash and cash equivalents		**6,329**	(6,026)	12,474
Effect of exchange rates on cash and cash equivalents		**427**	(1,934)	(716)
Cash and cash equivalents at beginning of the year		**20,102**	28,062	16,304
Cash and cash equivalents at end of the year		**26,858**	20,102	28,062

* See Note 3 - 'Changes to accounting policies - Adoption of IFRS 15 *Revenue from contracts with customers*.'

The accompanying notes form an integral part of these Consolidated Financial Statements.

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Consolidated Statement of Changes in Equity
Year ended January 31, 2019, 2018 and 2017

Year ended January 31, 2019

Group	Share capital £000s	Share premium account £000s	Share-based payment reserve £000s	Merger reserve £000s	Special reserve £000s	Currency translation reserve £000s	Accumulated losses reserve £000s	Total Equity £000s
At February 1, 2018 (as previously reported)	736	60,237	6,743	3,027	19,993	37	(80,898)	9,875
Change in accounting policy (full retrospective application (IFRS 15)	—	—	—	—	—	—	(13,059)	(13,059)
At February 1, 2018 (Adjusted*)	736	60,237	6,743	3,027	19,993	37	(93,957)	(3,184)
Profit for the year	—	—	—	—	—	—	7,527	7,527
Currency translation adjustment	—	—	—	—	—	19	—	19
Total comprehensive profit for the year	—	—	—	—	—	19	7,527	7,546
New share capital issued	864	33,784	—	—	—	—	—	34,648
Transaction costs on share capital issued	—	(1,313)	—	—	—	—	—	(1,313)
Share options exercised	4	98	—	—	—	—	—	102
Share-based payment	—	—	4,743	—	—	—	—	4,743
Transfer	—	—	(10,338)	—	—	—	10,338	—
At January 31, 2019	1,604	92,806	1,148	3,027	19,993	56	(76,092)	42,542

Year ended January 31, 2018

Group	Share capital £000s	Share premium account £000s	Share-based payment reserve £000s	Merger reserve £000s	Special reserve £000s	Currency translation reserve £000s	Accumulated losses reserve £000s	Total Equity £000s
At February 1, 2017	618	46,420	5,136	(1,943)	19,993	50	(73,767)	(3,493)
Loss for the year (Adjusted*)	—	—	—	—	—	—	(20,190)	(20,190)
Currency translation adjustment	—	—	—	—	—	(13)	—	(13)
Total comprehensive loss for the year (Adjusted*)	—	—	—	—	—	(13)	(20,190)	(20,203)
New share capital issued	84	14,847	—	—	—	—	—	14,931
Transaction costs on share capital	—	(1,428)	—	—	—	—	—	(1,428)
Issue of ordinary shares as consideration for a business combination	30	—	—	4,970	—	—	—	5,000
New share capital issued from exercise of warrants	1	9	—	—	—	—	—	10
Share options exercised	3	389	—	—	—	—	—	392
Share-based payment	—	—	1,607		—	—	—	1,607
At January 31, 2018 (Adjusted*)	736	60,237	6,743	3,027	19,993	37	(93,957)	(3,184)

Year ended January 31, 2017

Group	Share capital £000s	Share premium account £000s	Share-based payment reserve £000s	Merger reserve £000s	Special reserve £000s	Currency translation reserve £000s	Accumulated losses reserve £000s	Total Equity £000s
At February 1, 2016	613	46,035	3,757	(1,943)	19,993	21	(52,396)	16,080
Loss for the year	—	—	—	—	—	—	(21,371)	(21,371)
Currency translation adjustment	—	—	—	—	—	29	—	29
Total comprehensive loss for the year	—	—	—	—	—	29	(21,371)	(21,342)
New share capital issued from exercise of warrants	2	105	—	—	—	—	—	107
Share options exercised	3	280	—	—	—	—	—	283
Share-based payment	—	—	1,379		—	—	—	1,379
At January 31, 2017	618	46,420	5,136	(1,943)	19,993	50	(73,767)	(3,493)

* See Note 3 - 'Changes to accounting policies - Adoption of IFRS 15 *Revenue from contracts with customers*.'

The accompanying notes form an integral part of these Consolidated Financial Statements.

Share capital and premium

When shares are issued, the nominal value of the shares is credited to the share capital reserve. Any premium paid above the nominal value is credited to the share premium reserve. Ordinary shares of Summit Therapeutics plc have a nominal value of one penny per share.

Share-based payment reserve

The share-based payment reserve arises as the expense of issuing share-based payments is recognized over time (share option grants). The reserve reduces and transfers to accumulated losses reserve as share options are exercised, lapsed or surrendered, and the impact of the subsequent dilution of earnings crystallizes. The reserve may equally rise or might see any reduction offset, as new potentially dilutive share options are issued.

Merger reserve

A merger reserve arises as a result of certain requirements in the United Kingdom relating to business combination accounting. The merger reserve relates to the difference between the nominal value of Summit (Oxford) Limited and fair value of shares issued in business combinations using the acquisition method of accounting arising from the Group reconstruction in 2004 and the difference between the nominal value of Discuva Limited and fair value of shares issued in business combinations using the acquisition method of accounting arising from the acquisition in 2017.

Accumulated losses reserve

The accumulated losses reserve records the accumulated profits and losses, less any subsequent elimination of losses, of the Group since inception of the business. Where businesses or companies are acquired, only the profits or losses arising from the date of acquisition are included. When share options are exercised, lapsed or surrendered, the share-based payment reserve relating to those options is transferred to the accumulated losses reserve.

Special reserve

The special reserve was created during the consolidation and subdivision of the Company's share capital as part of a capital reorganization completed in September 2014. It represents the net balance of the cancellation of the deferred shares, the reduction of the share premium account and elimination of current losses from the accumulated deficit.

Currency translation reserve

The currency translation reserve records the foreign exchange difference that arises on the translation of the U.S. subsidiary, Summit Therapeutics Inc.

Notes to the Financial Statements

1. Basis of accounting

The principal accounting policies adopted by Summit Therapeutics plc and its subsidiaries in the preparation of these financial statements are set out below. These policies have been consistently applied to all the years presented, unless otherwise stated.

Basis of preparation

The Consolidated Financial Statements have been prepared in accordance with International Financial Reporting Standards and IFRS Interpretations Committee interpretations ('IFRS') as issued by the IASB. The Consolidated Financial Statements have been prepared on a going concern basis and under the historical cost convention modified by revaluation of financial assets and financial liabilities held at fair value through profit and loss. These Consolidated Financial Statements were authorized by the Board of Directors on March 27, 2019.

Going concern

The financial information in these financial statements has been prepared assuming the Group will continue on a going concern basis. Based on management's forecasts, the Group's existing cash and cash equivalents, anticipated payments from BARDA under its contract for the development of ridinilazole, anticipated payments from CARB-X under its contract for the development of its gonorrhea antibiotic candidate, and anticipated payments from the cost-sharing arrangement under its license and collaboration agreement with Sarepta are expected to be sufficient to enable the Group to fund its operating expenses and capital expenditure requirements through January 31, 2020. The Group will need to raise additional funding in order to support, beyond this date, its planned research and development efforts, potential commercialization related activities, if any of its product candidates receive marketing approval, as well as to support activities associated with operating as a public company in the United States and the United Kingdom. Should the Group be unable to raise additional funding, management has the ability to take mitigating action to fund its operating expenses and capital expenditure requirements in relation to its clinical development activities for only a short period beyond 12 months from the date of issuance of these financial statements. These circumstances represent a material uncertainty which may cast and raise significant doubt on the Group’s ability to continue as a going concern. These financial statements do not contain any adjustments that might result if the Group was unable to continue as a going concern.

The Group is evaluating various options to finance its cash needs through a combination of some, or all, of the following: equity offerings, collaborations, strategic alliances, grants and clinical trial support from government entities, philanthropic, non-government and not-for-profit organizations and patient advocacy groups, debt financings, and marketing, distribution or licensing arrangements. Whilst the Group believes that funds would be available in this manner before the end of January 2020, there can be no assurance that the Group will be able to generate funds, on terms acceptable to the Group, on a timely basis or at all, which would impact the Group’s ability to continue as a going concern. The failure of the Group to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on the Group’s business, results of operations and financial condition.

Use of estimates

The preparation of the financial statements, in conformity with IFRS, requires the use of estimates and assumptions that affect the reported amounts of assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Although these estimates are based on management’s best knowledge of the amount, event or actions, actual results may ultimately differ from those estimates. The areas involving higher degree of judgment or complexity, or areas where assumptions and estimates are significant to the Consolidated Financial Statements are disclosed in Note 2 ‘Critical accounting judgments and key sources of estimation uncertainty.’

Basis of consolidation

The Consolidated Financial Statements incorporate the financial statements of the Group and entities controlled by the Group made up to the reporting date. Control is achieved where the Company has the power to govern the financial and operating policies of an investee entity so as to obtain benefits from its activities.

The results of subsidiary undertakings acquired or disposed of in the year are included in the Consolidated Statement of Comprehensive Income from the effective date of acquisition or up to the effective date of disposal, as appropriate. Where necessary, adjustments are made to the financial statements of subsidiaries to bring the accounting policies used into line with those used by the Group.

All intra-group transactions, balances, income and expenses are eliminated on consolidation.

1. Basis of accounting (continued)

Revenue recognition

Revenue is accounted for in line with principles of IFRS 15 *Revenue from contracts with customers*.

Licensing agreements may consist of multiple elements and provide for varying consideration terms, such as upfront, development, regulatory and sales milestones, sales-based royalties and similar payments. Such arrangements are determined to be within the scope of IFRS 15 and are assessed under the five-step model of the standard to determine revenue recognition. The distinct performance obligations within the contract and the arrangement transaction price are identified. The fair value of the arrangement transaction price is allocated to the different performance obligations based on the relative stand-alone selling price of those services provided and the performance obligation activities to which the terms of the payments specifically relate to. The allocated transaction price is recognized over the respective performance period of each performance obligation. Amounts received in advance of the revenue recognition criteria being met are initially reported as deferred revenue on the Consolidated Statement of Financial Position and are recognized as revenue over the development period.

Development and regulatory approval milestone payments are included within the allocated transaction price only when it becomes highly probable that a significant reversal in the amount of cumulative revenue recognized will not occur. Revenues attributable to the development cost share element of a licensing agreement are also recognized over the performance period.

Sales-based royalty income and related milestone payments are recognized in the period when the related sales occur or when the relevant milestone is achieved, as the license granted is the predominant element of the performance obligation and the payments are inherently received once the development period is completed and the license granted is useable.

See Note 3 ‘Changes to accounting policies - Adoption of IFRS 15 *Revenue from contracts with customers*’ for details of the impact of the initial adoption of IFRS 15.

Business Combinations

The cost of an acquisition is measured as the fair value of the assets exchanged, equity instruments issued and liabilities incurred or assumed at the date of exchange. Identifiable assets acquired together with liabilities and contingent liabilities assumed in a business combination are measured initially at their fair values at the acquisition date. The excess of the cost of acquisition over the fair value of the identifiable net assets is recorded as goodwill. Goodwill is not amortized but is reviewed for impairment at least annually and more frequently whenever there is an indication of impairment.

Intangible Assets

In-process research and development that is separately acquired as part of a company acquisition or in-licensing agreement is capitalized even if they have not yet demonstrated technical feasibility, which is usually signified by regulatory approval. Amortization will commence when either products underpinned by the intellectual property rights or the rights themselves become available for use. Intangible assets not subject to amortization are tested for impairment at least annually or whenever there is an indicator of impairment.

The intangible asset relating to the acquired Discuva Platform capitalized as part of the acquisition of Discuva Limited in December 2017 is available for use. As such, it is subject to amortization over the period of the relevant associated patents.

Other intangible assets are amortized in equal installments over their useful estimated lives as follows:

All patents (once filed)	Over the period of the relevant patents (assumed to be 20 years)
Software licenses	3-5 years
Option over non-financial assets	Over the period of the relevant agreement

1. Basis of accounting (continued)

Impairment of assets

At each year end date, the Group reviews the carrying amounts of its tangible and intangible assets to determine whether there is any indication that those assets have suffered an impairment loss.

For the purposes of assessing impairment, assets are grouped at the lowest levels for which there are separately identifiable cash flows (cash-generating units).

An impairment loss is recognized for the amount by which the asset's or cash-generating unit's carrying amount exceeds its recoverable amount. The recoverable amount is the higher of fair value, reflecting market conditions less costs to sell, and value in use based on an internal discounted cash flow evaluation, where appropriate. Impairment losses recognized for cash-generating units are charged *pro rata* to the other assets in the cash generating unit. All tangible and intangible assets are subsequently reassessed for indications that an impairment loss previously recognized may no longer exist. See Note 15 'Intangible assets' for details.

Property, plant and equipment

Property, plant and equipment are stated at cost less depreciation. Cost comprises the purchase price plus any incidental costs of acquisition and commissioning. Depreciation is calculated to write-off the cost, less residual value, in equal annual installments over their estimated useful lives as follows:

Leasehold improvements	Over the period of the remaining lease
Laboratory equipment	2-10 years
Office and IT equipment	3-5 years

The residual value, if not insignificant, is reassessed annually.

Financial liabilities on funding arrangements

When entering into funding agreements with charitable and not for profit organizations, management is required to assess whether, based on the terms of the agreement, they can avoid a transfer of cash by settling using a non-financial obligation. Under IFRS, when such arrangements also give the counterparties rights over unexploited intellectual property, all or part of the funding agreement should be accounted for as a financial liability recognized in the Statement of Financial Position rather than as a charitable grant.

Financial liabilities are initially recognized at fair value using a discounted cash flow model with the difference between the fair value of the liability and the cash received considered to represent a charitable grant. The financial liabilities are subsequently measured at amortized cost using discounted cash flow models which calculate the risk adjusted net present values of estimated potential future cash flows for the relevant project. The financial liabilities are remeasured when there is a specific significant event that provides evidence of a significant change in the probability of successful development such as the completion of a phase of research or public reporting of significant interim data and changes in use or market for a product. The model is updated for changes in the clinical probability of success and other associated assumptions with the discount factor remaining unchanged within the model.

Provisions

Provisions are recognized when the Group has a present obligation (legal or constructive) as a result of a past event, where it is probable that an outflow of resources will be required to settle the obligation, and where a reliable estimate can be made of the amount of the obligation. If the effect of the time value of money is material, the expected future cash flows will be discounted using a pre-tax risk-free discount rate.

Other operating income

Other operating income includes income received and recognized from government agencies, philanthropic, non-government, not for profit organizations and patient advocacy groups which are accounted for in accordance with IAS 20, 'Accounting for Government Grants and Disclosure of Government Assistance.' Monies received through these means are held as deferred income in the Consolidated Statement of Financial Position and are released to the Consolidated Statement of Comprehensive Income as the underlying expenditure is incurred and to the extent the conditions of the grant are met.

1. Basis of accounting (continued)

Foreign currencies

Transactions in foreign currencies are recorded at the rate ruling at the date of the transaction. Monetary assets and liabilities denominated in foreign currencies are translated at the rate of exchange ruling at the year end date. All differences are taken to the Consolidated Statement of Comprehensive Income.

Assets and liabilities of subsidiaries that have a functional currency different from the presentation currency (Pound Sterling) are translated at the closing rate at the date of each statement of financial position presented. Income and expenses are translated at average exchange rates. Any resulting differences are recognized in other comprehensive income/(loss) in the Consolidated Statement of Comprehensive Income.

Employee benefits

All employee benefit costs, notably holiday pay, bonuses and contributions to Group or personal defined contribution pension schemes are charged to the Consolidated Statement of Comprehensive Income on an accruals basis.

Operating leases

Costs in respect of operating leases are charged to the Consolidated Statement of Comprehensive Income on a straight line basis over the lease term. Assets relating to lease incentives and dilapidation provisions are depreciated over the life of the lease and are included in property, plant and equipment as leasehold improvements.

Research and development

All ongoing research expenditure is currently expensed in the period in which it is incurred. Due to the regulatory environment inherent in the development of the Group's products, the criteria for development costs to be recognized as an asset, as set out in IAS 38 '*Intangible Assets,*' are not met until a product has received regulatory approval, and it is probable that future economic benefit will flow to the Group. The Group currently has no qualifying expenditure.

Cash and cash equivalents

Cash and cash equivalents include cash in hand and deposits held on call with the bank.

Share-based payments

In accordance with IFRS 2 '*Share-based Payment,*' share options and restricted stock units are measured at fair value at their grant date. The fair value for the majority of the options is calculated using the Black-Scholes formula and charged to the Consolidated Statement of Comprehensive Income on a straight-line basis over the expected vesting period. For those options issued with vesting conditions other than remaining in employment (for example, those conditional upon the Group achieving certain predetermined financial criteria) a simulation model has been used. At each year end date, the Group revises its estimate of the number of options that are expected to become exercisable. This estimate is not revised according to estimates of changes in market based conditions.

Current taxation

Income tax is recognized or provided at amounts expected to be recovered or paid using the tax rates and tax laws that have been enacted or substantively enacted at the year end date.

Current tax includes research and development tax credits which are calculated in accordance with the U.K. research and development tax credit regime applicable to small and medium sized companies. Research and development expenditure which is not eligible for reimbursement under the small and medium sized companies regime, such as expenditure incurred on projects for which we receive income, may be reimbursed under the U.K. Research and Development Expenditure Credit ('RDEC') scheme. Receipts under the RDEC scheme are presented within other operating income as they are similar in nature to grant income.

1. Basis of accounting (continued)

Deferred taxation

Deferred tax assets and liabilities are recognized where the carrying amount of an asset or liability in the Consolidated Statement of Financial Position differs from its tax base, except for differences arising on:

- the initial recognition of goodwill;
- the initial recognition of an asset or liability in a transaction which is not a business combination and at the time of the transaction affects neither accounting or taxable profit; and
- investments in subsidiaries and jointly controlled entities where the Group is able to control the timing of the reversal of the difference, and it is probable that the difference will not reverse in the foreseeable future.

Recognition of deferred tax assets is restricted to those instances where it is probable that taxable profit will be available against which the difference can be utilized.

The amount of the asset or liability is determined using tax rates that have been enacted or substantively enacted by the reporting date and are expected to apply when the deferred tax liabilities/(assets) are settled/(recovered).

Financial instruments

The Group recognizes financial assets and liabilities in the respective categories 'Financial assets at amortized cost' and 'Financial liabilities measured at amortized cost.' Financial assets at amortized cost are non-derivative financial assets which are held to collect the contractual cash flows on specified dates. They arise when the Group provides money, goods or services directly to the debtor with no intention of trading the receivable. They are included in current assets, except for maturities greater than 12 months after the year end date, which are classified as non-current assets. Other liabilities consist of trade and other payables, being balances arising in the course of normal business with suppliers, contractors and other service providers, and borrowings, being loans and hire purchase funds advanced for the refit of leasehold premises and the purchase of laboratory equipment, fixtures and fittings. Financial assets at amortized cost, and other liabilities are initially recorded at fair value, and thereafter at amortized cost, if the timing difference is deemed to impact the fair value of the asset or liability.

The Group assesses at each year end date the expected credit losses of a financial asset or a group of financial assets with consideration given to the risk of default occurring. Expected credit losses are the difference between the contractual cash flows due to the Group and the cash flows the Group expects to receive.

The Group does not hold or trade in derivative financial instruments.

Warrants

Warrants issued by the Group are recognized and classified as equity when upon exercise, the Company would issue a fixed amount of its own equity instruments (ordinary shares) in exchange for a fixed amount of cash or another financial asset.

Consideration received, net of incremental costs directly attributable to the issue of such new warrants, is shown in equity. Such warrants are not remeasured at fair value in subsequent reporting periods.

2. Critical accounting judgments and key sources of estimation uncertainty

The preparation of the Consolidated Financial Statements requires the Group to make judgments, estimates and assumptions that affect the application of accounting policies and the reported amounts of assets and liabilities, income and expense. Actual results may differ from those estimates.

Critical Judgments in Applying the Group's Accounting Policies

The following are the critical judgments, apart from those involving estimations, that the Directors have made in the process of applying the Group's accounting policies and that have the most significant effect on the amounts recognized in the Consolidated Financial Statements.

Financial liabilities on funding arrangements

Financial liabilities on funding arrangements are remeasured and the Group is required to apply judgment, when there is a specific significant event that provides evidence of a significant change in the probability of successful development such as the completion of a phase of research or changes in use or market for a product. All remaining financial liabilities have been remeasured to £nil during the financial year, see Note 21 'Financial liabilities on funding arrangements' for further details.

Revenue Recognition

The Group recognizes revenue from licensing fees, collaboration fees, development, regulatory and approval milestone fees, sales milestones and sales-based royalties. Agreements generally include a non-refundable upfront fee, milestone payments, the receipt of which is dependent upon the achievement of certain clinical, regulatory or commercial milestones, as well as royalties on product sales of licensed products, if and when such product sales occur. For these agreements, the Group is required to apply judgment as follows: the identification of the number of performance obligations within a contract, the allocation of the transaction price to those performance obligations and the timing of when milestone payments are included in the transaction price.

In relation to the license and collaboration agreement with Sarepta and the license and commercialization agreement with Eurofarma, the Group has assessed that the license to commercialize the Group's intellectual property is not distinct in the context of the contract and that there is a transformational relationship between the license and the research and development activities delivered as they are highly interrelated elements of the contract. The Group has therefore determined that there is one single performance obligation under IFRS 15 in relation to the license granted and research and development activities which is the transfer of a license for which the associated research and development activities are completed over time. In the case of the Sarepta agreement, management assessed that there were a number of further performance obligations being the research and clinical development activities relating to the future generation small molecule utrophin modulators, the license granted to commercialize in Latin America at the option of Sarepta, and the wind-down activities of terminated clinical trials. These performance obligations are separate and distinct from the transfer of a license for which the associated research and development activities are completed over time.

The allocation of the transaction price is based on the relative stand-alone selling price of those services provided and the performance obligation activities to which the terms of the payments specifically relate. Milestone payments and other variable consideration are only included in the transaction price allocated to a performance obligation when it becomes highly probable that a significant reversal in the amount of cumulative revenue recognized will not occur. The allocated transaction price is recognized over the respective performance period of each performance obligation.

As a result, the upfront payments, development milestones and development cost share income allocated to the license granted and research and development activities, which is the transfer of a license for which the associated research and development activities are completed over time, are initially reported as deferred revenue in the Consolidated Statement of Financial Position and are recognized as revenue over the development period.

See Note 3 'Changes to accounting policies -Adoption of IFRS 15 *Revenue from contracts with customers*' for details of the impact of the initial adoption of IFRS 15 and Note 5 'Revenue' for details of our contracts with customers.

Indications of asset impairment

The Group is required to exercise judgment as to whether there is any indication that its tangible and intangible assets have suffered an impairment loss when reviewing the carrying value of those assets. See Note 15 'Intangible assets' for details of the impairment reviews performed by the Group relating to this financial year.

2. Critical accounting judgments and key sources of estimation uncertainty (continued)

Key sources of estimation uncertainty

The key assumptions concerning the future, and other key sources of estimation uncertainty at the year end date that may have a risk of causing a material adjustment to the carrying amounts of assets and liabilities within the next financial year, are noted below.

Recognition of research and development expenditure and associated funding income

The Group recognizes expenditure incurred in carrying out its research and development activities and the associated funding income in line with management's best estimation of the work completed on each separately contracted study or activity. This includes the calculation of research and development accruals and prepayments at each period to account for expenditure that has been incurred and the associated funding income. This requires estimations of the expected costs to complete each study or activity and the estimation of the current stage of completion. In all cases, the full cost of each study or activity is expensed by the time the final report or where applicable, product, has been received. See Notes 17 'Trade and other receivables' and 18 'Trade and other payables' for further details of these estimates.

Assumed contingent liability

The Group's assumed contingent liability is recognized in the Consolidated Financial Statements at fair value as required by IFRS 3 *Business Combinations*. In determining the fair value of this liability, a number of assumptions need to be made by management which include significant estimates. See Note 23 'Provisions for other liabilities and charges and contingent liabilities.'

3. Changes to accounting policies

Adoption of IFRS 15 *Revenue from contracts with customers*

IFRS 15 establishes comprehensive guidelines for determining when to recognize revenue and how much revenue to recognize. The Group adopted this new standard effective February 1, 2018, as required, using the full retrospective transition method in accordance with IAS 8 *Accounting Policies, Changes in Accounting Estimates and Errors*.

The core principle in that framework is that a company should recognize revenue to depict the transfer of control of promised goods or services to the customer in an amount that reflects the consideration to which the company expects to be entitled in exchange for those goods or services. To determine revenue recognition for arrangements that a company determines are within the scope of IFRS 15, a company performs the following five steps: (i) identify the contract(s) with a 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) the company satisfies a performance obligation.

The Group assessed the effect of adoption of this standard as it relates to the license and collaboration agreement with Sarepta (the 'Sarepta Agreement') and the license and commercialization agreement with Eurofarma (the 'Eurofarma Agreement').

The Sarepta Agreement and the Eurofarma Agreement grant the rights in specific territories to commercialize products in the Group's utrophin modulator pipeline and ridinilazole, respectively, as well as the provision of the associated research and development activities. Such activities result in a service that is the output of the Group's ordinary activities. The Group assessed that the revenues from these agreements are in the scope of IFRS 15.

3. Changes to accounting policies (continued)

For both of these agreements, the Group assessed that the license to commercialize the Group's intellectual property is not distinct in the context of the contract and that there is a transformational relationship between the license and the research and development activities delivered as they are highly interrelated elements of the contract. The Group therefore determined that there is one single performance obligation under IFRS 15 in relation to the license granted and the research and development activities, which is the transfer of a license for which the associated research and development activities are completed over time. The transaction price of these agreements includes upfront payments, development and regulatory milestone payments, development cost share income, sales milestones and sales-based royalties. Milestone payments are included in the transaction price only when it becomes highly probable that a significant reversal in the amount of cumulative revenue recognized will not occur. The relevant transaction price elements are allocated to the performance obligation identified being the transfer of a license for which the associated research and development activities are completed over time. The revenues are recognized over the development period using an output method based on time elapsed, reflecting both the increase in value of the license and the progression of the research and development activities over the development period towards potential commercialization of the product. Sales milestones and sales-based royalties are not included in the Group's revenues when the associated clinical program is still in development. The predominant element of the performance obligation that the sales milestones and sales-based royalties relate to is the license granted and hence the revenues are recognized when the related sales occur.

The Sarepta Agreement also has a number of further performance obligations, including research and clinical development activities relating to the future generation small molecule utrophin modulators and the license granted to commercialize in Latin America, which is at the option of Sarepta. The development, regulatory and sales milestone payments allocated to the future generation candidate activities and Latin America license granted are contingent on future activities, and, as a result, would only be included in the transaction price and accounted for as revenue when it would be highly probable that a significant reversal in the amount of cumulative revenue recognized would not occur. The relevant sales-based royalties would be recognized when the related sales occur, as the license granted is the predominant element of the performance obligation. The development cost share income allocated to clinical trial wind-down activities, which is also a separate performance obligation within the Sarepta Agreement, are recognized using an input method based on costs incurred.

Due to the adoption of IFRS 15, the $22.0 million (£17.2 million) development milestone payment the Group received in May 2017 as part of the Sarepta Agreement, which had previously been recognized in full under IAS 18 during the Group's fiscal year ended January 31, 2018, was recognized as revenue over the development period. Similarly, development cost share income from Sarepta which commenced from January 1, 2018, under the agreement was recognized as revenue over the development period. As a result of this change, £13.1 million of income related to the Sarepta Agreement previously recognized as revenue during the year ended January 31, 2018, was classified as deferred revenue in the opening Statement of Financial Position as at February 1, 2018. The adjustment consisted of (i) £12.4 million related to the development milestone payment; and (ii) £0.7 million related to development cost share income related to Sarepta's share of research and development costs incurred in January 2018 (the first month that the cost share component of the agreement was in effect).

In June 2018, the Group announced the discontinuation of the development of ezutromid after its Phase 2 clinical trial, PhaseOut DMD, did not meet its primary or secondary endpoints. As a result, the Group updated the development period over which the Sarepta revenues allocated to the license and the research and development activities performance obligation were recognized, with the development period deemed to have concluded in June 2018 in line with when development of ezutromid was discontinued. This resulted in all revenues relating to the Sarepta Agreement that were previously deferred in the Statement of Financial Position being released in full during the year ended January 31, 2018. The Group continues to receive cost share income from Sarepta, at 45% of eligible costs, including for wind-down activities for the ezutromid clinical trial. This cost share income is recognized as revenue when such costs are incurred. The Group does not expect to receive any further milestone payments from Sarepta.

The Group's assessment resulted in there being no difference in the accounting treatment of the Eurofarma Agreement under IAS 18 and IFRS 15. Revenues recognized relating to the agreement during the year ended January 31, 2018, under IAS 18 related only to the upfront payment, which was initially reported as deferred revenue in the Statement of Financial Position and is being recognized as revenue over the development period. This is consistent with the accounting treatment under IFRS 15.

This change in accounting policy has been reflected retrospectively in the comparative Statement of Financial Position, the comparative Statement of Comprehensive Income, the comparative Statement of Cash Flows and the comparative Statement of Changes in Equity for the year ended January 31, 2018. The opening Statement of Financial Position as at February 1, 2017, is in line with comparative amounts disclosed in the financial statements for the year ended January 31, 2017, as there was no impact of this change in accounting policy on the Statement of Financial Position as at January 31, 2017.

3. Changes to accounting policies (continued)

The impact of this change in accounting policy on the comparatives to these financial statements was an increase in non-current and current deferred revenue, an increase in accumulated losses reserve, a reduction in revenue historically recognized, and a presentational change to the Statement of Cash Flows. The increase in non-current and current deferred revenue for the year ended January 31, 2018, and reduction in revenue recognized during the year ended January 31, 2018, relate to the difference between the accounting treatment of the Sarepta development milestone payment and development cost share income under IAS 18 and IFRS 15, as described above, which is recognized as revenue over the remainder of the determined development period.

Impact on Consolidated Statement of Financial Position	Original Year ended January 31, 2018 £000s	Adjusted Year ended January 31, 2018 £000s	Impact £000s
Non-current liabilities			
Deferred revenue	(18,033)	(27,270)	(9,237)
Current liabilities			
Deferred revenue	(10,012)	(13,834)	(3,822)
Equity			
Accumulated losses reserve	(80,898)	(93,957)	(13,059)

Impact on Consolidated Statement of Comprehensive Income	Original Year ended January 31, 2018 £000s	Adjusted Year ended January 31, 2018 £000s	Impact £000s
Revenue	25,419	12,360	(13,059)
Loss for the year	**(7,131)**	**(20,190)**	**(13,059)**

Impact on Consolidated Statement of Cash Flows	Original Year ended January 31, 2018 £000s	Adjusted Year ended January 31, 2018 £000s	Impact £000s
Loss before income tax	(10,893)	(23,952)	(13,059)
Adjusted for:			
(Decrease) / increase in deferred revenue	(2,482)	10,577	13,059
Impact on net cash used by operating activities	**(13,375)**	**(13,375)**	**—**

The Group will continue to monitor interpretations released by the IFRS Interpretations Committee and amendments to IFRS 15 and, as appropriate, will adopt these from the effective dates.

For details of revenue recognition during the year ended January 31, 2019, see Note 5 'Revenue.'

Adoption of IFRS 9 *Financial Instruments*

The Group adopted IFRS 9 *Financial Instruments* effective February 1, 2018. There has been no impact on the Group's net results or net assets for the year ended January 31, 2019, and 2018 as a result of adoption.

Impact assessment of IFRS 16 *Leases*

IFRS 16 specifies how to recognize, measure, present and disclose leases. The standard provides a single lessee accounting model, requiring lessees to recognize assets and liabilities for all leases unless the lease term is 12 months or less or the underlying asset has a low value. The standard is effective for reporting periods beginning on or after January 1, 2019, and replaces the accounting standard IAS 17 *Leases*. Two adoption methods are permitted for transition: retrospectively to all prior reporting periods presented in accordance with IAS 8 *Accounting Policies, Changes in Accounting Estimates and Errors*, with certain practical expedients permitted; or retrospectively with the cumulative effect of initially applying the standard recognized at the date of initial application.

3. Changes to accounting policies (continued)

At inception of a contract, a company assesses whether a contract is, or contains, a lease based on whether the contract conveys the right to control the use of an identified asset for a period of time in exchange for consideration. A right-of-use asset and a lease liability are recognized at the lease commencement date. The right-of-use asset is initially measured based on the initial amount of the lease liability adjusted for any lease payments made at or before the commencement date, plus any initial direct costs incurred and an estimate of costs to dismantle and remove the underlying asset or to restore the underlying asset or the site on which it is located, less any lease incentives received. The assets are depreciated to the earlier of the end of the useful life of the right-of-use asset or the lease term using the straight-line method. The lease term includes periods covered by an option to extend if it is reasonably certain to exercise that option and period covered by an option to terminate if it is reasonably certain not to exercise that option. The lease liability is initially measured at the present value of the lease payments that are not paid at the commencement date, discounted using the interest rate implicit in the lease or, if that rate cannot be readily determined, the applicable incremental borrowing rate. The lease liability is subsequently measured at amortized cost using the effective interest method and is remeasured when there is a change in future lease payments or if the assessment of whether a company will exercise a purchase, extension or termination option.

The Group has elected to adopt this new standard effective February 1, 2019, as required, using the full retrospective transition method in accordance with IAS 8 *Accounting Policies, Changes in Accounting Estimates and Errors*. Under this method, the Group will adjust its results for the years ended January 31, 2018, and 2019, and applicable interim periods, as if IFRS 16 had been effective for those periods. To date, the Group has assessed the effect of adoption of this standard as it relates to its leased properties in Oxford and Cambridge, U.K., and has concluded that any other contracts are not within the scope of IFRS 16 or are of low value, for which the Group has elected not to apply the requirement of IFRS 16. Currently, the Group anticipates the effects of adoption of IFRS 16 to be as described below. Estimated impacts from the adoption could differ upon the final adoption and implementation of the standard.

The adoption of IFRS 16 is not expected to have a significant impact on the Group's net results or net assets. The Group expects the accounting for the right-of-use asset and lease liability to be the most significant change in accounting for leases. The Group will no longer recognize a lease incentive accrual and will be required to reclassify some costs from research and development expenses and general and administration expenses to finance costs, being the interest expense on lease liabilities. In addition, some amounts previously presented as cash flows from operating activities in the Group's Consolidated Statement of Cash Flows will be presented as cash flows from financing activities.

The Group has performed an evaluation of the expected effect of adoption on the accounting for the U.K. leased properties. The Group currently estimates the effect to the financial statements for the year ended January 31, 2019, after the adoption of IFRS 16 will be an increase in both gross assets and liabilities of £0.9 million.

The quantitative amount provided above is an estimate of the expected effects of the Group's adoption of IFRS 16. This amount represents management's best estimates of the effects of adopting IFRS 16 at the time of the preparation of these financial statements. The actual quantitative effects of the adoption of IFRS 16 are subject to change from these estimates and such change may be significant, pending the completion of the Group's assessment in the first quarter to April 30, 2019.

The Directors do not expect that the adoption of the remaining standards and interpretations in future periods will have a material impact on the financial statements of the Group.

During the year ended January 31, 2019, the following additional new standards, amendments to standards or interpretations became effective for the first time. The adoption of these interpretations, standards or amendment to standards were either not relevant for the Group or have not led to any significant impact on the Group's financial statements.

International Accounting Standards (IAS/IFRS)	Effective Date
IFRS 9 Financial Instruments (as revised in 2014)	January 1, 2018
Amendment to IFRS 2 Share Based Payments, Classification and Measurement of Share-based Payment Transactions	January 1, 2018
Amendments resulting from Annual Improvements 2014–2016 Cycle	January 1, 2018
IFRIC 22 Foreign Currency Transactions and Advance Consideration	January 1, 2018

3. Changes to accounting policies (continued)

At the date of signing these Consolidated Financial Statements, the following standards, amendments and interpretations, which have not been applied in these financial statements, were in issue but not yet effective:

International Accounting Standards (IAS/IFRS)	Effective Date
IFRS 16 Leases	January 1, 2019
Amendments to IFRS 9 Financial Instruments, Prepayment Features with Negative Compensation	January 1, 2019
Amendments to IAS 19 Employee Benefits, Plan amendments, curtailments or settlements	January 1, 2019
Amendments resulting from Annual Improvements 2015–2017 Cycle	January 1, 2019
IFRIC 23 Uncertainty over Income Tax Treatments	January 1, 2019
Amendments to References to the Conceptual Framework in IFRS Standards	January 1, 2020
Amendments to IFRS 3 Business Combinations, Definition of a Business	January 1, 2020

4. Segmental reporting

The Summit Group comprises eleven legal entities, of which four are trading. These included the ten subsidiary companies and the Group holding company, Summit Therapeutics plc. The Group operates in one reportable segment: Drug Development. The chief operating decision-maker has been identified as the Executive Management Team consisting of the Chief Executive Officer, the Chief Financial Officer (prior to his departure in December 2018), the Chief Operating Officer and the Chief Commercial Officer. The Executive Management Team reviews the consolidated operating results regularly to make decisions about the financial and organizational resources and to assess overall performance.

The Drug Development segment covers Summit's research and development activities carried out by the Group, primarily comprising the CDI program, antibiotic pipeline research activities and the DMD program.

The corporate and other activities of Summit Therapeutics plc, Summit (Oxford) Limited, Summit Therapeutics Inc and Discuva Limited, which comprise the costs incurred in providing the facilities, finance, human resource and information technology services, are incurred by the main segment of the Group.

Substantially all of the Group's assets are held in the United Kingdom.

5. Revenue

	Year ended January 31, 2019	Year ended January 31, 2018 (Adjusted*)	Year ended January 31, 2017
	£000	£000	£000
Analysis of revenue by category:			
Licensing agreements	**42,766**	12,050	2,304
Research collaboration agreement	**246**	310	—
	43,012	12,360	2,304

Revenue recognized in the year consists of amounts received from the license and collaboration agreement with Sarepta Therapeutics, Inc., the license and commercialization agreement with Eurofarma Laboratórios S.A., and amounts received from a research collaboration agreement with F. Hoffmann-La Roche Ltd, which ended in February 2018. See Note 19 'Deferred revenue and income' for details of amounts deferred in the Consolidated Statement of Financial Position.

	Year ended January 31, 2019	Year ended January 31, 2018 (Adjusted*)	Year ended January 31, 2017
	£000	£000	£000
Analysis of revenue by geography:			
United States	**42,267**	12,008	2,304
Latin America	**499**	42	—
Europe	**246**	310	—
	43,012	12,360	2,304

The analysis of revenue by geography has been identified on the basis of the customer's geographical location.

* See Note 3 - 'Changes to accounting policies - Adoption of IFRS 15 *Revenue from contracts with customers.*'

5. Revenue (continued)

Sarepta Therapeutics, Inc.

On October 4, 2016, Summit announced its entry into an exclusive license and collaboration agreement with Sarepta Therapeutics, Inc. (‘Sarepta’), pursuant to which Summit granted Sarepta the exclusive right to commercialize products in the Group’s utrophin modulator pipeline in the European Union, Switzerland, Norway, Iceland, Turkey and the Commonwealth of Independent States (the 'Sarepta Agreement'). Such products included the Group’s former lead product candidate, ezutromid, and its pipeline of second generation and future generation small molecule utrophin modulators for the treatment of Duchenne muscular dystrophy. The Group also granted Sarepta an option to expand the licensed territory to include specified countries in Central and South America. The Group would retain commercialization rights in the rest of the world.

Under the Sarepta Agreement, the Group received from Sarepta an upfront payment of $40.0 million (£32.8 million), in October 2016, and a development milestone payment of $22.0 million (£17.2 million), in May 2017, which was payable after the first dosing of the last patient in PhaseOut DMD, its Phase 2 clinical trial of ezutromid. The terms of the contract were assessed under IFRS 15 *Revenue from contracts with customers*, and the upfront payment, first development milestone payment and relevant development cost share income are included in the transaction price which was reported as deferred revenue in the Consolidated Statement of Financial Position and recognized as revenue over the development period.

In June 2018, the Group announced the discontinuation of the development of ezutromid after PhaseOut DMD did not meet its primary or secondary endpoints. As a result, the Group has updated the development period over which the revenues are recognized, as described in Note 3 'Changes to accounting policies - Adoption of IFRS 15 *Revenue from contracts with customers*.' The development period was deemed to have concluded in June 2018 in line with when development of ezutromid was discontinued. This resulted in all revenues relating to the Sarepta Agreement that were previously deferred in the Statement of Financial Position being released in full to the Statement of Comprehensive Income.

As part of the Sarepta Agreement, the Group agreed to collaborate with Sarepta on the research and development of the licensed products pursuant to a joint development plan through a joint steering committee comprised of an equal number of representatives from each party. The Group had been solely responsible for all research and development costs for the licensed products until December 31, 2017. From January 1, 2018, the Group was responsible for 55% of the budgeted research and development costs related to the licensed products in the licensed territory, and Sarepta was responsible for 45% of such costs. Any costs in excess of 110% of the budgeted amount are borne by the party that incurred such costs. This development cost share income is recognized as part of licensing agreements revenue as the Group is acting as a principal in the scope of the research and development activities of the agreement. The Group continues to receive cost share income for both wind-down activities in relation to the ezutromid clinical trial and next and future generation utrophin modulation development activities. Such income is recognized as revenue using an input method based on costs incurred over the duration of the contract.

Eurofarma Laboratórios S.A.

On December 21, 2017, Summit announced it had entered into an exclusive license and commercialization agreement with Eurofarma Laboratórios S.A. ('Eurofarma'), pursuant to which the Group granted Eurofarma the exclusive right to commercialize ridinilazole in specified countries in South America, Central America and the Caribbean (the 'Eurofarma Agreement'). The Group has retained commercialization rights in the rest of the world.

Under the terms of the Eurofarma Agreement, the Group received an upfront payment of $2.5 million (£1.9 million) from Eurofarma. The terms of the contract have been assessed, and the Group believes the development services to be indistinguishable from the license and as a result the upfront payment was initially reported as deferred revenue in the Consolidated Statement of Financial Position and is being recognized as revenue over the development period. Accordingly, £0.5 million of revenue will be released during each subsequent financial year until all amounts have been realized in the Consolidated Statement of Comprehensive Income.

In addition, the Group will be entitled to receive an additional $3.75 million in development milestones upon the achievement of staged patient enrollment targets in the licensed territory in one of the Group's two planned Phase 3 clinical trials of ridinilazole. The Group is eligible to receive up to $21.4 million in development, commercial and sales milestones when cumulative net sales equal or exceed $100.0 million in the Eurofarma licensed territory. Each subsequent achievement of an additional $100.0 million in cumulative net sales will result in the Group receiving additional milestone payments, which, when combined with anticipated product supply transfer payments from Eurofarma paid to the Group in connection with a commercial supply agreement to be entered into between the two parties, will provide payments estimated to range from a mid- to high-teens percentage of cumulative net sales in the Eurofarma licensed territory. The Group estimates such product supply transfer payments from Eurofarma will range from a high single-digit to low double-digit percentage of cumulative net sales in the licensed territory.

6. Other operating income

	Year ended January 31, 2019	Year ended January 31, 2018	Year ended January 31, 2017
	£000	£000	£000
Analysis of other operating income by category:			
Income recognized in respect of BARDA	**13,091**	1,772	—
Grant income	**1,187**	13	56
Income on remeasurement or derecognition of financial liabilities on funding arrangements (Note 21)	**539**	908	—
Income recognized in respect of the Wellcome Trust	**—**	—	13
Research and development credit	**333**	23	3
Other income	**6**	9	—
	15,156	2,725	72

BARDA

In September 2017, the Group was awarded a funding contract worth up to $62 million by the Biomedical Advanced Research and Development Authority ('BARDA'), an agency of the U.S. government's Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response. The BARDA contract provides for a cost-sharing arrangement under which BARDA funds a specified portion of estimated costs for specified activities related to the continued clinical and regulatory development of ridinilazole for the treatment of CDI. Under the terms of the contract, the Group was initially eligible to receive $32 million from BARDA to fund, in part, obtaining regulatory approval for and commencing enrollment and dosing into the Group's two Phase 3 clinical trials of ridinilazole. In August 2018, the Group was awarded an additional $12 million upon exercise by BARDA of the first option work segment under the contract, which brought the total committed BARDA funding to $44 million. In addition, the Group is eligible for additional funding under the contract pursuant to two further independent option work segments, which may be exercised by BARDA in its sole discretion upon the achievement of certain development and other milestones for ridinilazole. If BARDA exercises its remaining option work segments in full, the total funding under the contract would increase up to $62 million.

Grant income includes income from funding arrangements with CARB-X and Innovate UK grants for the Group's antibiotic pipeline research and development activities.

CARB-X

In July 2018, the Group was granted a sub-award of up to $4.5 million from the Trustees of Boston University under the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator program, or CARB-X. Under the CARB-X award, the Group received an initial $2.0 million in funding from CARB-X in July 2018 that, in part, helped fund the selection of a preclinical candidate from the Group's lead gonorrhea series of clinical candidates. The remaining $2.5 million is split into two option segments, which may be exercised by CARB-X upon the achievement of certain development milestones. If exercised in full, this funding could support the development of the selected gonorrhea candidate through the end of a Phase 1 clinical trial.

Innovate UK

In January 2017, the Group's wholly owned subsidiary, Discuva Limited, was awarded a grant by Innovate UK worth up to £1.1 million. The grant helped to fund a specified portion of eligible costs incurred between January 2017 and December 2018 for activities related to the exploitation of transporters to develop novel antibiotics against Gram-negative bacteria.

7. Directors and employees

The average monthly number of employees of the Group, including Executive Directors, during the year was:

	Year ended January 31, 2019	Year ended January 31, 2018	Year ended January 31, 2017
Technical, research and development	**45**	34	23
Corporate and administration	**29**	26	21
	74	60	44

The average number of employees reflects an increase in the Group's workforce during the second half of the year ended January 31, 2018, and the first half of the year ended January 31, 2019, to support Phase 3 preparatory activities for ridinilazole and the clinical and regulatory development of ezutromid. The number of employees as at January 31, 2019, was 61 (January 31, 2018: 76). This decrease reflects the implementation of cost-cutting measures following the decision to discontinue ezutromid development in June 2018.

Their aggregate remuneration comprised:

	Year ended January 31, 2019	Year ended January 31, 2018	Year ended January 31, 2017
	£000	£000	£000
Wages and salaries	**8,268**	7,493	5,932
Social security costs	**844**	643	434
Other pension costs	**390**	350	332
Share-based payment	**4,743**	1,607	1,379
	14,245	10,093	8,077

Included within wages and salaries are termination benefits of £0.2 million (2018: £nil).

Key management of the Group are members of the Executive Management Team. Excluding the Chief Commercial Officer, who joined the Executive Management Team in February 2019, the aggregate amounts of key management compensation are set out below:

	Year ended January 31, 2019	Year ended January 31, 2018	Year ended January 31, 2017
	£000	£000	£000
Short-term employee benefits			
Wages and salaries	**1,406**	1,520	1,252
Social security costs	**168**	162	98
	1,574	1,682	1,350
Post-employment benefits			
Amounts paid in lieu of employer pension contributions	**43**	32	17
Other pension costs	**11**	14	11
	54	46	28
Share-based payment	**3,177**	705	327
Total remuneration	**4,805**	2,433	1,705

8. Loss before income tax

	Year ended January 31, 2019	Year ended January 31, 2018	Year ended January 31, 2017
	£000	£000	£000
Research and development			
Employee benefit expense	**6,264**	5,616	4,218
Share-based payment expense	**1,091**	327	374
Program related costs	**29,868**	21,810	13,605
Amortization of intangible assets	**829**	105	10
Other research and development costs	**1,122**	1,112	745
	39,174	28,970	18,952
General and administration			
Employee benefit expense	**3,238**	2,870	2,480
Share-based payment expense	**3,652**	1,280	1,005
Foreign exchange (gain) / loss	**(491)**	1,986	533
Depreciation of property, plant and equipment	**309**	141	48
Loss on disposal of assets	**43**	40	—
Other general and administration costs	**4,818**	5,613	4,211
Loss on contingent consideration	**754**	—	—
Royalty expense	**19**	69	—
	12,342	11,999	8,277

9. Impairment of goodwill and intangible assets

As a result of the Group's decision in June 2018 to discontinue development of ezutromid, management concluded that this was an indication of impairment and hence reviewed the intangible asset and goodwill associated with the acquisition of MuOx Limited which related to the utrophin program acquired. Based on this review, an impairment charge of £4.0 million was recognized, representing the full aggregate carrying value of the intangible asset of £3.3 million and goodwill of £0.7 million. See Note 15 *'Intangible assets'* for details of the valuation model and assumptions used as part of the review.

10. Auditors' remuneration

Services provided by the Group's auditors

During the year, the Group obtained the following services from the Group's auditors at the cost detailed below:

	Year ended January 31, 2019	Year ended January 31, 2018	Year ended January 31, 2017
	£000	£000	£000
Fees payable to the auditors and its associates for the audit of the Company and Consolidated Financial Statements	**160**	132	110
Fees payable to the auditors and its associates for other services:			
- Audit of the Company's subsidiaries[1]	**119**	209	120
- Audit-related assurance services	**—**	—	3
- Other assurance services[2]	**115**	118	163
- Tax compliance and advisory services	**25**	23	62
Total fees payable	**419**	482	458

(1) For the year ended January 31, 2018, fees payable for the Consolidated Financial Statements and fees payable for the Company's subsidiaries include audit services relating to the initial audit and business combination accounting for Discuva Limited. These were non-recurring fees.

(2) For the year ended January 31, 2019, other assurance services includes reporting in connection with the Company's registration statement on Form F-3 that was filed with the SEC on May 15, 2018. For the year ended January 31, 2018, other assurance services includes reporting in connection with the Company's underwritten public offering completed on September 18, 2017. These amounts were recognized directly in share premium. For the year ended January 31, 2017, other assurance services includes reporting in connection with the Company's registration statement on Form F-3 that was originally filed with the SEC on May 12, 2016.

11. Finance income and costs

	Note	**Year ended January 31, 2019**	Year ended January 31, 2018	Year ended January 31, 2017
		£000	£000	£000
Finance income				
Remeasurement or derecognition of financial liabilities on funding arrangements	21	**2,784**	3,085	—
Interest income on deposits		**4**	11	8
Finance income		**2,788**	3,096	8
Finance costs				
Unwinding of discount factor	21	**(424)**	(754)	(862)
Remeasurement of financial liabilities on funding arrangements	21	**—**	(410)	—
Finance costs		**(424)**	(1,164)	(862)

12. Income tax

	Year ended January 31, 2019	Year ended January 31, 2018	Year ended January 31, 2017
	£000	£000	£000
Analysis of credit in the period			
Current tax:			
Current tax income	**1,286**	3,767	4,245
Adjustments in respect of prior years	**506**	(5)	(9)
Total current tax	**1,792**	3,762	4,236
Total deferred tax	**704**	—	100
Total tax	**2,496**	3,762	4,336

The difference between the total tax shown above and the amount calculated by applying the standard rate of U.K. corporation tax to the loss before tax is as follows:

	Year ended January 31, 2019	Year ended January 31, 2018 (Adjusted*)	Year ended January 31, 2017
	£000	£000	£000
Profit / (loss) before tax	**5,031**	(23,952)	(25,707)
Profit / (loss) multiplied by the standard rate of corporation tax in the United Kingdom (Current tax) 19% (2018: 19.17%)	**956**	(4,592)	(5,141)
Adjustment for IFRS 15 restatement	**(2,481)**	2,504	—
Change in unrecognized tax losses	**820**	751	2,169
Non-deductible expenses	**1,797**	402	331
Tax relief for qualifying research and development expenditure	**(2,656)**	(3,043)	(1,699)
Prior year adjustments	**(506)**	5	9
Share options exercised	**(15)**	(40)	(84)
Overseas profits taxed at different rates	**292**	251	179
Change in rate of deferred tax	**(703)**	—	(100)
Total tax	**(2,496)**	(3,762)	(4,336)

* See Note 3 - 'Changes to accounting policies - Adoption of IFRS 15 *Revenue from contracts with customers*.'

There are no current tax liabilities as at January 31, 2019 (2018: nil; 2017: nil).

Tax relief for qualifying research and development expenditure relates to U.K. research and development tax credits claimed through the small or medium-

sized enterprise scheme ('SME') under the Finance Act 2015.

12. Income tax (continued)

The Finance (No 2) Act 2015, which provides for reductions in the main rate of corporation tax from 20% to 19% effective from April 1, 2017, and to 18% effective from April 1, 2020, was substantively enacted on October 26, 2015. Subsequently, the Finance Act 2016, which provides for a further reduction in the main rate of corporation tax to 17% effective from April 1, 2020, was substantively enacted on September 6, 2016. These rate reductions have been reflected in the calculation of deferred tax at the year end date.

The closing deferred tax liability at January 31, 2019, has been calculated at 17% reflecting the tax rate at which the deferred tax liability is expected to be reversed in future periods. Unrecognized deferred tax has been calculated at 17% reflecting the latest enacted rate. In respect of unrecognized deferred tax on losses, the new loss restriction rules effective from April 1, 2017, limit the amount of brought forward losses available to use against future taxable profits on a year by year basis to the extent that taxable profits exceed £5.0 million in each year. However, the losses will not lapse and therefore the full amount will be relieved over time provided there are sufficient profits against which the losses can be utilized.

Please see Note 24 'Deferred tax liability' for information on the unrecognized tax losses carried forward.

13. Earnings / (loss) per share

The calculation of earnings / (loss) per share is based on the following data:

	Year ended January 31, 2019	Year ended January 31, 2018 (Adjusted*)	Year ended January 31, 2017
	000s	000s	000s
Profit / (loss) for the year	**£ 7,527**	£ (20,190)	£ (21,371)
Weighted average number of ordinary shares for basic earnings / (loss) earnings per share	**85,702**	65,434	61,549
Effect of dilutive potential ordinary shares (share options and warrants)	**442**	—	—
Weighted average number of ordinary shares for diluted earnings per share	**86,144**	65,434	61,549
Basic earnings / (loss) per ordinary share from operations £	**0.09**	(0.31)	(0.35)
Diluted earnings / (loss) per ordinary share from operations £	**0.09**	(0.31)	(0.35)

* See Note 3 - 'Changes to accounting policies - Adoption of IFRS 15 *Revenue from contracts with customers*.'

Basic earnings / (loss) per ordinary share has been calculated by dividing the profit / (loss) for the year ended January 31, 2019, by the weighted average number of shares in issue during the year ended January 31, 2019. Diluted earnings per ordinary share has been calculated by adjusting the weighted average number of ordinary shares outstanding to assume conversion of all potentially dilutive ordinary shares. Potentially dilutive ordinary shares are the number of shares that could have been acquired at fair value based on the monetary value of the subscription rights attached to share options in-the-money compared with the number of shares that would have been issued assuming the exercise of share options in-the-money.

At January 31, 2019, total outstanding share options were 9,168,396 and total outstanding restricted stock units ('RSUs') were 814,256. Of these equity instruments, 8,094,227 were not included in the calculation of potentially dilutive ordinary shares for the year ended January 31, 2019, as they are not dilutive.

IAS 33 '*Earnings per Share*' requires the presentation of diluted earnings per share where a company could be called upon to issue shares that would decrease net profit or loss per share. As the Group reported net losses for the year ended January 31, 2018, the weighted average number of ordinary shares outstanding used to calculate the diluted earnings / (loss) per ordinary share is the same as that used to calculate the basic earnings / (loss) per ordinary share, as the exercise of share options would have the effect of reducing loss per ordinary share which is not dilutive.

14. Goodwill

	Discuva Limited £000	MuOx Limited £000	Total £000
Cost			
At February 1, 2018	1,814	664	2,478
At January 31, 2019	1,814	664	2,478
Accumulated impairment			
At February 1, 2018	—	—	—
Impairment	—	(664)	(664)
At January 31, 2019	—	(664)	(664)
Net book amount			
At February 1, 2018	1,814	664	2,478
At January 31, 2019	1,814	—	1,814

	Discuva Limited £000	MuOx Limited £000	Total £000
Cost			
At February 1, 2017	—	664	664
Additions	1,814	—	1,814
At January 31, 2018	1,814	664	2,478
Accumulated impairment			
At February 1, 2017	—	—	—
At January 31, 2018	—	—	—
Net book amount			
At February 1, 2017	—	664	664
At January 31, 2018	1,814	664	2,478

Goodwill represents the difference between the fair value of the identifiable assets acquired and liabilities assumed and the amount paid in consideration**.** In accordance with IAS 36 '*Impairment of Assets*', the remaining goodwill has been reviewed for impairment and no further provision is considered necessary. The impairment reviews of goodwill undertaken during the financial year and at the year end are included as part of the intangible assets impairment review in Note 15 'Intangible assets.' Goodwill relating to MuOx Limited formed part of the same cash-generating unit as the utrophin program acquired. Goodwill relating to Discuva Limited forms part of the same cash-generating unit as the Discuva Platform acquired.

On December 23, 2017, the Group acquired 100% of the share capital of Discuva Limited a privately held U.K.-based company, resulting in the recognition of £1.8 million of goodwill. Goodwill recognized in respect of Discuva Limited is attributable to the synergies expected with the Group's ongoing business as a result of the acquisition and the existing Discuva Limited workforce (which cannot be separately valued under IFRS accounting standards).

15. Intangible assets

	Utrophin program acquired £000	Discuva Platform acquired £000	Option over non-financial assets £000	Other patents and licenses £000	Total £000
Cost					
At February 1, 2018	3,321	10,670	668	265	14,924
Additions	—	—	—	6	6
Disposals	—	—	—	(49)	(49)
At January 31, 2019	3,321	10,670	668	222	14,881
Accumulated amortization					
At February 1, 2018	—	(79)	(4)	(56)	(139)
Charge for the year	—	(739)	(45)	(45)	(829)
Impairment	(3,321)	—	—	—	(3,321)
Disposals	—	—	—	12	12
At January 31, 2019	(3,321)	(818)	(49)	(89)	(4,277)
Net book amount					
At February 1, 2018	3,321	10,591	664	209	14,785
At January 31, 2019	—	9,852	619	133	10,604

	Iminosugar related programs acquired £000	Utrophin program acquired £000	Discuva Platform acquired £000	Option over non-financial assets £000	Other patents and licenses £000	Total £000
Cost						
At February 1, 2017	1,380	3,321	—	—	204	4,905
Acquisition of subsidiary	—	—	10,670	668	—	11,338
Additions	—	—	—	—	119	119
Disposals	(1,380)	—	—	—	(58)	(1,438)
At January 31, 2018	—	3,321	10,670	668	265	14,924
Accumulated amortization						
At February 1, 2017	(1,380)	—	—	—	(55)	(1,435)
Charge for the year	—	—	(79)	(4)	(23)	(106)
Disposals	1,380	—	—	—	22	1,402
At January 31, 2018	—	—	(79)	(4)	(56)	(139)
Net book amount						
At February 1, 2017	—	3,321	—	—	149	3,470
At January 31, 2018	—	3,321	10,591	664	209	14,785

Amortization of intangible assets is included in the line 'Research and development' shown on the face of the Consolidated Statement of Comprehensive Income.

In accordance with IAS 36, intangible assets not subject to amortization and the associated goodwill are reviewed for impairment annually or whenever there is an indication that the intangible asset may be impaired. The recoverable amount of an asset or a cash-generating unit is defined as the higher of its fair value and its value in use.

MuOx Limited goodwill and utrophin program acquired cash-generating unit

As discussed in Note 9 '*Impairment of goodwill and intangible assets*', as a result of the Group's decision in June 2018 to discontinue development of ezutromid, an impairment charge of £4.0 million was recognized, representing the full aggregate carrying value of the intangible asset of £3.3 million and goodwill of £0.7 million.

15. Intangible assets (continued)

Discuva Limited goodwill and Discuva Platform acquired cash-generating unit

The Discuva Platform acquired as part of the acquisition of Discuva Limited and the associated goodwill have been reviewed for impairment using a milestone analysis approach, since reliable estimated future cash flows cannot yet be formed to determine the value in use. The milestone analysis approach assesses whether the fair value of these assets, determined upon acquisition of Discuva Limited in December 2017, still remain appropriate. Based on this assessment, the Directors believe that the carrying value of the intangible asset and associated goodwill are supported by the underlying asset.

The key milestone events that were considered as part of the impairment assessment are as follows:

- research and development milestones achieved; and
- external transactions achieved.

The key sensitivity is our ability to meet ongoing milestone events, if these milestone events are not achieved as expected then the related intangible asset would likely be fully impaired.

16. Property, plant and equipment

Cost	Leasehold improvements £000	Laboratory equipment £000	Office and IT equipment £000	Total £000
At February 1, 2018	340	299	486	1,125
Additions	—	62	57	119
Disposals	—	(22)	(52)	(74)
Revaluation	—	—	5	5
At January 31, 2019	**340**	**339**	**496**	**1,175**
Accumulated depreciation				
At February 1, 2018	(31)	(36)	(249)	(316)
Charge for the year	(34)	(156)	(119)	(309)
Disposals	—	21	47	68
Revaluation	—	—	(2)	(2)
At January 31, 2019	**(65)**	**(171)**	**(323)**	**(559)**
Net book value				
At February 1, 2018	309	263	237	809
At January 31, 2019	**275**	**168**	**173**	**616**

Cost	Leasehold improvements £000	Laboratory equipment £000	Office and IT equipment £000	Total £000
At February 1, 2017	9	19	284	312
Acquisition of subsidiary	—	280	49	329
Additions	340	—	173	513
Disposals	**(9)**	—	(14)	(23)
At January 31, 2018	**340**	**299**	**486**	**1,125**
Accumulated depreciation				
At February 1, 2017	(9)	(17)	(170)	(196)
Charge for the year	(31)	(19)	(90)	(140)
Disposals	9	—	10	19
At January 31, 2018	**(31)**	**(36)**	**(249)**	**(316)**
Net book value				
At February 1, 2017	—	2	114	116
At January 31, 2018	**309**	**263**	**237**	**809**

17. Trade and other receivables

	January 31, 2019	January 31, 2018
	£000	£000
Trade receivables	**1,656**	—
Other receivables	**3,847**	3,600
Prepayments	**7,433**	6,498
Accrued income	**611**	1,036
	13,547	11,134

Trade receivables consist of amounts outstanding from Sarepta at January 31, 2019.

Included within prepayments is £6.8 million of prepayments relating to research and development expenditure. These amounts are determined based on the estimated costs to complete each study or activity, the estimation of the current stage of completion and the invoices received. The key sensitivity is the estimated current stage of completion of each study or activity. If the estimated stage of completion increased by 5% then the aggregate increase in accruals and decrease in prepayments would result in an overall increase in total research and development expenses of £1.0 million. If the estimated stage of completion decreased by 5% then the aggregate decrease in accruals and increase in prepayments would result in an overall decrease in total research and development expenses of £1.2 million.

18. Trade and other payables

	January 31, 2019	January 31, 2018
	£000	£000
Trade payables	**4,422**	4,414
Other taxes and social security	**190**	164
Accruals	**4,095**	4,078
Other creditors	**158**	276
	8,865	8,932

Included within accruals is £1.9 million of accruals relating to research and development expenditure. These amounts are determined based on the estimated costs to complete each study or activity, the estimation of the current stage of completion and the invoices received. See Note 17 'Trade and other receivables' for information regarding the sensitivity of this estimate.

19. Deferred revenue and income

	January 31, 2019	January 31, 2018 (Adjusted*)
	£000	£000
Due within one year		
Deferred revenue	**499**	11,478
Deferred other operating income	**2,875**	2,356
	3,374	**13,834**
Due more than one year		
Deferred revenue	**831**	27,270
	831	**27,270**
Total deferred revenue	**1,330**	**38,748**
Total deferred other operating income	**2,875**	**2,356**

* See Note 3 - 'Changes to accounting policies - Adoption of IFRS 15 *Revenue from contracts with customers*.'

19. Deferred revenue and income (continued)

The Group adopted IFRS 15 effective February 1, 2018, as required. For details on the performance obligations identified and judgments exercised by management in the application of IFRS 15 see Note 3 ‘Changes to accounting policies -Adoption of IFRS 15 Revenue from contracts with customers.'

Revenues of £37.4 million included in deferred revenue as at January 31, 2018 (adjusted), were recognized during the year ended January 31, 2019. All revenues recognized during the year ended January 31, 2018, were included in deferred revenue as at January 31, 2017.

See Note 5 'Revenue' for details on the Group's revenue agreements and revenue recognition.

20. Contingent consideration

During the financial year, the Group reassessed the contingent consideration in line with the anticipated settlement of consideration liabilities relating to the acquisition of Discuva Limited ('Discuva') in December 2017. The Group estimated the total expected additional cash outflows to be £0.8 million, which is based on the terms of the share purchase agreement. The additional expected payment is primarily due to research and development tax credits received and receivable by Discuva in respect of financial years prior to the Group's acquisition, of which the sellers are due a specified portion of these amounts. During the year ended January 31, 2019, a payment of £0.2 million was made for the research and development tax credits received, leaving an estimated contingent consideration liability of £0.6 million.

21. Financial liabilities on funding arrangements

The Group entered into charitable funding arrangements with the Wellcome Trust and the U.S. not for profit organizations, the Muscular Dystrophy Association (‘MDA’) and Duchenne Partners Fund (‘DPF’). In exchange for the funding provided, these arrangements required the Group to pay royalties on potential future revenues generated from the CDI and DMD programs respectively or transfer the rights over unexploited intellectual property.

Discount factors used in the financial liability models were calculated using appropriate measures and rates which could have been obtained in the period that the funding agreements were entered into and are in the range of 16% to 18% for the financial liabilities of funding arrangements previously recognized.

Because of the Group's decision in June 2018 to discontinue the development of ezutromid, the financial liabilities attributable to the charitable funding arrangements with MDA and DPF were remeasured during the year ended January 31, 2019, as future royalties on revenues generated from the DMD program are no longer anticipated. This remeasurement resulted in a credit to the Statement of Comprehensive Income. The portion of the credit presented as other operating income during the year ended January 31, 2019, represents the component of the funding received from MDA and DPF not previously credited to the Statement of Comprehensive Income upon initial recognition of the financial liability. The portion of the credit presented as finance income during the year ended January 31, 2019, relates to previous remeasurements and discounting associated with the financial liability which were previously recognized as finance costs.

In October 2017, the Group and the Wellcome Trust entered into an equity and revenue sharing agreement under which the Wellcome Trust agreed to terminate all of its rights pertaining to the exploitation of intellectual property related to the CDI program meaning the arrangement no longer met the definition of a financial liability under IFRS and the financial liability was derecognized.

21. Financial liabilities on funding arrangements (continued)

The value of the estimated financial liabilities for funding arrangements as of January 31, 2019, amounted to £nil (January 31, 2018: £3.1 million).

	January 31, 2019	January 31, 2018
	£000	£000
At February 1	**3,090**	5,919
Unwinding of discount factor	**233**	754
Derecognition of financial liabilities – finance income	**—**	(3,085)
Remeasurement of financial liabilities on funding arrangements - (finance income) / finance cost	**(2,784)**	410
Net finance income on funding arrangements accounting for as financial liabilities	**(2,551)**	(1,921)
Remeasurement or derecognition of financial liabilities – other operating income	**(539)**	(908)
At January 31	**—**	3,090

As the Group is discontinuing the development of ezutromid, there are no sensitivities disclosed in relation to the charitable funding arrangements with MDA and DPF, since there are no reasonably possible changes in assumptions that would result in a different value of the liability as at January 31, 2019.

22. Financial instruments

	Note	**January 31, 2019**	January 31, 2018
		£000	£000
Financial assets at amortized cost			
Trade and other receivables[(1)]	**17**	**5,503**	3,600
Cash and cash equivalents		**26,858**	20,102
		32,361	23,702
Financial liabilities measured at amortized cost			
Trade and other payables	**18**	**8,865**	8,932
Financial liabilities on funding arrangements	**21**	**—**	3,090
		8,865	12,022
Financial liabilities measured at fair value through profit and loss			
Contingent consideration	**20**	**629**	—

(1) Prepayments and accrued income have been excluded as they are not considered to be a financial instrument.

The Group's activities expose it to a variety of financial risks: foreign currency risk; interest rate risk; credit risk; and liquidity risk.

The Group's principal financial instrument comprises cash and cash equivalents, and this is used to finance the Group's operations. Other financial instruments include trade and other receivables and trade and other payables that arise directly from its operations. The category of other receivables all mature within one year.

The Group has compared fair value to book value for each class of financial asset and liability and no differences were identified. The Group has a policy, which has been consistently followed, of not trading in financial instruments.

22. Financial instruments (continued)

Foreign currency risk

Foreign currency risk refers to the risk that the value of a financial commitment or recognized asset or liability will fluctuate due to changes in foreign currency rates. The Group's net income and financial position, as expressed in Pounds Sterling, are exposed to movements in foreign exchange rates against the U.S. Dollar and the Euro. The main trading currencies of the Group are Pounds Sterling, the U.S. Dollar, and the Euro. The Group is exposed to foreign currency risk as a result of trading transactions, including the receipt of potential payments related to the Group's agreements with Sarepta, Eurofarma, BARDA and CARB-X, capital raises in the U.S. and the translation of foreign bank accounts.

The exposure to foreign exchange is monitored by the Group's finance function. Exposures are generally managed through natural hedging *via* the currency denomination of cash balances and any realized impact currently is not material to the Group.

	January 31, 2019	January 31, 2018
	£000	£000
Cash at bank and in hand		
Pounds Sterling	**3,363**	5,535
U.S. Dollar	**23,495**	14,567
	26,858	20,102

Interest rate risk

One of the risks arising from the Group's financial instruments is interest rate risk. The Group holds no derivative instruments to manage interest rate risk; instead the Group placed deposits surplus to short-term working capital requirements with a variety of reputable U.K.-based and U.S.-based banks and building societies. There were no amounts on short term deposits at the year end. These balances are placed at fixed rates of deposit with maturities between one month and three months.

The Group's cash and short-term deposits were as follows:

	January 31, 2019	January 31, 2018
	£000	£000
On current account	**26,858**	20,102
	26,858	20,102

The interest rates for dated deposits were dependent on the rates offered by the Group's borrowers. The interest rate for short-term deposits is variable dependent on the rates offered by the Group's banks. During the year to January 31, 2019, the banking facilities returned an average rate after fees of 0.02% (2018: 0.02%).

The Group's exposure to interest rate risk is illustrated with regard to the opening and closing cash balances and the difference that an increase or decrease of 1% in interest rates would have made based on the average cash balance of £23.5 million (2018: £24.1 million) in the year:

Year ended January 31, 2019	**(1)%**	**Actual**	**1%**
Interest rate	**—**	**0.02**	**1.02**
Interest received (£000)	**—**	**4**	**239**
Year ended January 31, 2018	(1)%	Actual	1%
Interest rate	—	0.02	1.02
Interest received (£000)	—	5	246

Credit risk

The credit risk with respect to customers is limited as the Group has only a small number of customers, being Sarepta and Eurofarma. The Group had £1.7 million trade receivables outstanding at January 31, 2019, from Sarepta.

Financial instruments that potentially expose the Group to concentrations of credit risk consist primarily of short-term cash deposits and trade accounts receivable. Cash is held at a variety of financial institutions with strong credit ratings; these cash deposits typically bore minimal credit risk in the year.

Cash balances maintained during the year have been principally held with reputable U.K.-based and U.S.-based banks and building societies. The Group does not believe that this constituted a major credit risk.

As of January 31, 2019, and January 31, 2018, the majority of cash and cash equivalents were placed with HSBC Bank plc.

22. Financial instruments (continued)

Liquidity risk

Prudent liquidity risk management implies maintaining sufficient cash and the availability of funding through an adequate amount of committed credit facilities.

The Group ordinarily finances its activities through cash generated from operating activities, and private and public offerings of equity securities. The Group's operating cash flows together with available cash and cash equivalents are expected to be sufficient to enable the Group to fund its anticipated needs through January 31, 2020. See Note 1 ‘Going concern’.

All of the financial liability categories at each balance sheet date, excluding the financial liabilities on funding arrangements, have maturity dates of less than 12 months from the year end date. Provisions are amounts contingent upon events taking place and the recognition of deferred taxation is dependent upon future profits arising.

Capital management

The primary aim of the Group’s capital management, defined as its share capital and share premium, is to safeguard the Group’s ability to continue as a going concern, to support its programs and maximize shareholder value.

The Group monitors its capital structure and makes adjustments, as and when it is deemed necessary and appropriate to do so, using such methods as the issuing of new ordinary shares. The capital structure of the Group has come entirely from equity issues.

23. Provisions for other liabilities and charges and contingent liabilities

	Assumed contingent liabilities £000s	Dilapidations £000s	Royalties £000s	Total £000s
At February 1, 2018	1,466	150	25	1,641
Additions	—	—	19	19
Unwinding of the discount factor	191	—	—	191
At January 31, 2019	**1,657**	**150**	**44**	**1,851**

	Assumed contingent liabilities £000s	Dilapidations £000s	Royalties £000s	Total £000s
At February 1, 2017	—	85	—	85
Additions	1,466	150	25	1,641
Used during the year	—	(85)	—	(85)
At January 31, 2018	**1,466**	**150**	**25**	**1,641**

Assumed contingent liability

As part of the acquisition of Discuva Limited ('Discuva') in December 2017, the Group assumed certain contingent liabilities as certain employees, former employees and former directors of Discuva are eligible for payments from Discuva based on specified development and clinical milestones related to proprietary product candidates developed under the Discuva Platform. The timing of these potential payments is uncertain.

On the date of acquisition, the fair value of the assumed contingent liability was estimated using the expected value of the payments. The assumed contingent liabilities are subsequently measured at amortized cost using discounted cash flow models which calculate the risk adjusted net present values of estimated potential future cash flows of the payments. The assumed contingent liabilities are remeasured when there is a specific significant event that provides evidence of a significant change in the probability of successful development and clinical milestones being achieved. The models will be updated for changes in the probability of successful development and clinical milestones being achieved and other associated assumptions with the discount factor to remain unchanged within the model. A discount factor of 13% has been used to discount the contingent liabilities back to net present value. This discount factor has been calculated using appropriate measures and rates which could have been obtained in the period that the contingent liabilities were assumed.

23. Provisions for other liabilities and charges and contingent liabilities (continued)

The estimated fair value of the assumed contingent liability as at January 31, 2019, is £1.7 million (January 31, 2018: £1.5 million). The contingent liability has not been remeasured during the period. The table below describes the value of the assumed contingent liabilities as at January 31, 2019, of £1.7 million compared to what the total value would be following the presented variations to the underlying assumptions in the model:

	January 31, 2019
	£000s
Estimated assumed contingent liabilities	1,658
1% lower discount rate	1,770
1% higher discount rate	1,560
10% lower probability of success	1,366
10% higher probability of success	1,927

Dilapidations

Management has made a provision in respect of the dilapidation costs associated with the reinstatement obligations on their current lease based on best estimates. It is management's intention to utilize the provision at the end of the lease term.

Royalties

The provision in respect of royalties relates to the amounts due to the Wellcome Trust under the terms of the funding arrangement as described below. The provision has been discounted to take account of the effect of the time value of money, applying a discount rate of 0.8%. Further information on the contingent liabilities included in the Wellcome Trust arrangement are detailed below.

In addition to those items provided for above, the Group also has the following contingent liabilities:

The School of Pharmacy, University of London

The Group has agreed to pay The School of Pharmacy, University of London, a low single-digit share of all revenue, pre and post commercialization, received by the Group in respect of ridinilazole up to a maximum of £1.0 million in consideration of their role in the development of the initial compound series from which ridinilazole was later identified. Following the license and commercialization agreement entered into with Eurofarma, an initial payment was made to The School of Pharmacy of £0.04 million.

Wellcome Trust

Under the terms of the funding arrangement entered into in October 2017, the Wellcome Trust is entitled to a share of the cumulative net revenue that the Group or its affiliates receive from exploiting the exploitation IP or award products. If Summit undertakes the commercialization of ridinilazole, the Wellcome Trust would be eligible to receive a low-single digit percentage share of net revenues. If a third party undertakes the commercialization of ridinilazole, the Wellcome Trust would be eligible to receive a mid-single digit percentage share of net revenues received by Summit from sales by the third party and a milestone payment of a low-single digit percentage of any cumulative pre-commercial payments received by Summit from third-party licensees. In both instances outlined above, the Group would also be obligated to pay the Wellcome Trust a milestone of a specified amount if cumulative net revenue exceeds a specified amount. Following the license and commercialization agreement entered into with Eurofarma, an initial payment became due to the Wellcome Trust upon commercialization of ridinilazole. The payment has been provided for by the Group as at the year end date and has been discounted back to net present value relative to the expected timing of commercialization of ridinilazole.

24. Deferred tax liability

The Group's deferred tax liability includes amounts recognized upon acquisition of Discuva Limited, which took place in the year ended January 31, 2018. During the year ended January 31, 2019, amounts recognized upon acquisition of MuOx Limited of £0.6 million were released to the Statement of Comprehensive Income when the related intangible asset was impaired in full, see Note 9 'Impairment of goodwill and intangible assets' for further details.

	Year ended January 31, 2019	Year ended January 31, 2018
	£000	£000
Amounts falling due after more than one year		
At February 1	**2,379**	565
Release of temporary difference relating to the intangible asset	**(704)**	—
Acquisition of subsidiary	—	1,814
At January 31	**1,675**	2,379

There is an unrecognized deferred tax asset in relation to the trading losses carried forward of £12,400,000 (2018: £11,944,000), £26,000 in relation to provisions (2018: £26,000) and £32,000 (2018: £588,000) in relation to future exercisable shares. There is a deferred tax liability of £43,000 (2018: £71,000) in respect of accelerated capital allowances, which has been offset against the deferred tax asset in relation to trading losses carried forward.

The unrecognized deferred tax asset would be recovered against future company taxable profits. In the opinion of the Directors, there is insufficient evidence that the asset will be recovered, and as such the deferred tax asset has not been recognized in the financial statements.

25. Share capital

	January 31, 2019	January 31, 2018
	£000	£000
Allotted, called up and fully paid		
160,389,881 (2018: 73,563,624) Ordinary Shares of 1p each	**1,604**	736

Changes to the number of ordinary shares in issue have been as follows:

	Number of shares	**Total nominal value £000**	**Total share premium £000**	**Total consideration £000**
At February 1, 2017	61,841,566	618	46,420	47,038
New share capital issued (net of transaction costs)	8,389,250	84	13,419	13,503
Issue of ordinary shares as consideration for a business combination (1)	2,934,272	30	—	30
New share capital issued from exercise of warrants	50,000	1	9	10
Share options exercised	348,536	3	389	392
At January 31, 2018	**73,563,624**	**736**	**60,237**	**60,973**
At February 1, 2018	73,563,624	736	60,237	60,973
New share capital issued (net of transaction costs)	86,458,333	864	32,471	33,335
Share options exercised	367,924	4	98	102
At January 31, 2019	**160,389,881**	**1,604**	**92,806**	**94,410**

(1) The difference between the nominal value of the share capital acquired in Discuva Limited and fair value of shares issued in the business combination using the acquisition method of accounting was recognized as part of the Group's merger reserve arising as a result of certain requirements in the United Kingdom.

25. Share capital (continued)

On March 29, 2018, the company completed an equity placing on the AIM market of the London Stock Exchange, issuing 8,333,333 new ordinary shares at a price of 180 pence per share. Total gross proceeds of £15.0 million were raised and directly attributable transaction costs of £0.9 million were incurred and accounted for as a deduction from equity.

On January 9, 2019, the company completed a private placement of 15,625,000 American Depository Shares ('ADS') at a price of $1.60 per ADS. Each ADS represents five ordinary shares of one penny nominal value each in the capital of the company, meaning 78,125,000 new ordinary shares were issued. Total gross proceeds of $25.0 million (£19.6 million) were raised and directly attributable transaction costs of £0.4 million were incurred.

During the year to January 31, 2019, the following exercises of share options and restricted stock units took place:

Date	Number of options exercised
March 16, 2018	4,216
April 18, 2018	38,850
April 23, 2018	48,981
July 18, 2018	136,991
October 24, 2018	138,886
	367,924

The total net proceeds from exercised share options during the year was £0.1 million.

All new ordinary shares rank pari passu with existing ordinary shares.

Following the equity placings and the exercise of the above share options, the number of ordinary shares in issue was 160,389,881.

Dividends

No dividends were paid or declared in the year ended January 31, 2019 (year ended January 31, 2018: £nil).

26. Share option scheme and restricted stock units

At January 31, 2019, the outstanding share options, which include the share options granted to Directors, are shown below:

Date of grant	Exercise price (£)	Number of shares	Date from which exercisable	Expiry date
Approved EMI scheme				
April 7, 2011	0.65	5,873	April 8, 2014	April 7, 2021
May 10, 2012	0.60	150,046	May 10, 2014	May 10, 2022
December 24, 2012	0.85	21,500	December 24, 2015	December 24, 2022
January 31, 2013	0.20	72,973	July 31, 2013	January 31, 2023
July 15, 2014	1.26	100,000	July 15, 2016	July 15, 2024
June 23, 2016	1.05	58,564	June 23, 2017	June 23, 2026
		408,956		
Unapproved scheme				
December 18, 2013	0.20	76,364	June 18, 2014	December 18, 2023
July 15, 2014	1.26	175,000	July 15, 2016	July 15, 2024
July 15, 2014	0.80	100,000	May 30, 2015	May 30, 2023
January 21, 2015	1.23	75,000	January 21, 2017	January 21, 2025
June 23, 2016	0.01	110,576	July 21, 2016	June 23, 2026
June 23, 2016	1.05	43,740	June 23, 2017	June 23, 2026
June 27, 2017	1.80	5,989	June 27, 2017	June 27, 2027
July 18, 2017	1.83	11,825	June 18, 2018	June 18, 2027
October 24, 2017	1.80	12,264	October 24, 2018	October 24, 2027
April 20, 2018	2.05	9,514	April 23, 2019	April 23, 2028
October 19, 2018	0.30	4,324,198	October 19, 2019	October 19, 2028
October 19, 2018	0.30	3,814,970	October 19, 2021	October 19, 2028
		8,759,440		
		9,168,396		

The Group has no legal or constructive obligation to repurchase or settle the options in cash.

The movement in the number of share options is set out below:

	Weighted average exercise price £	Year ended January 31, 2019	Weighted average exercise price £	Year ended January 31, 2018
Outstanding at February 1,	**1.43**	**8,577,236**	1.17	7,383,401
Granted during the year	**0.76**	**13,081,048**	1.83	2,972,903
Lapsed / surrendered during the year	**1.52**	**(12,397,841)**	0.99	(1,430,532)
Exercised during the year	**1.08**	**(92,047)**	1.13	(348,536)
Number of options outstanding at January 31,	**0.35**	**9,168,396**	1.43	8,577,236

During the year ended January 31, 2019, the executive director, key management and employees voluntarily surrendered options to subscribe for a total of 7,172,054 ordinary shares. The share-based payment expense for the year ended January 31, 2019, was £4.7 million (2018: £1.6 million). This increase is primarily due to the surrender of share options, resulting in an accelerated share-based payment expense of the remaining fair value of those awards.

As at January 31, 2019, 1,029,228 share options were capable of being exercised with a weighted average exercise price per option of 82 pence (2018: 2,042,546 with a weighted average exercise price per option of 100 pence). The options outstanding at January 31, 2019, had a weighted average exercise price per option of 35 pence (2018: 143 pence), and a weighted average remaining contractual life of 9.2 years (2018: 7.9 years).

26. Share option scheme and restricted stock units (continued)

The fair value per share option award granted and the assumptions used in the calculations are as follows:

Date of grant	Type of award	Number of shares	Exercise price (£)	Share price at grant date (£)	Fair value per option (£)	Award life (years)	Risk free rate
April 07, 2011	EMI	5,873	0.65	0.65	0.47	5.00	2.70%
May 10, 2012	EMI	150,046	0.60	0.52	0.24	5.00	1.00%
December 24, 2012	EMI	21,500	0.85	0.85	0.59	5.00	0.90%
January 31, 2013	EMI	72,973	0.20	0.94	0.74	5.00	1.00%
December 18, 2013	Unapproved	76,364	0.20	1.85	1.65	5.00	1.00%
July 15, 2014	EMI	100,000	1.26	1.26	0.65	3.00	1.30%
July 15, 2014	Unapproved	175,000	1.26	1.26	0.65	3.00	1.30%
July 15, 2014	Unapproved	100,000	0.80	0.81	0.65	1.90	0.50%
January 21, 2015	Unapproved	75,000	1.23	1.22	0.64	3.00	0.60%
June 23, 2016	EMI	58,564	1.05	1.05	0.25	3.00	0.30%
June 23, 2016	Unapproved	110,576	0.01	1.05	1.04	0.50	0.30%
June 23, 2016	Unapproved	43,740	1.05	1.05	0.25	3.00	0.30%
June 27, 2017	Unapproved	5,989	1.80	1.78	0.64	3.00	0.23%
July 18, 2017	Unapproved	11,825	1.83	1.83	0.66	3.00	0.26%
October 24, 2017	Unapproved	12,264	1.80	1.70	0.57	3.00	0.46%
April 20, 2018	Unapproved	9,514	2.05	2.05	0.69	3.00	0.79%
October 19, 2018	Unapproved	4,324,198	0.30	0.30	0.09	3.00	0.81%
October 19, 2018	Unapproved	3,814,970	0.30	0.30	0.12	3.00	0.90%
		9,168,396					

The key assumptions used in calculating the share-based payments are as follows:

a. Black-Scholes valuation methodology was used for all share options issued since 2016. These options do not have market-based performance related conditions.

b. The majority of share option awards made before 2016 had market-based performance related conditions and have been modeled using the Monte-Carlo methodology. The options granted on January 31, 2013, and December 18, 2013, do not have market-based performance related conditions.

c. Figures in the range of 39%-134% have been used for expected volatility. This has been derived from historic share price performance, weighted to exclude periods of unusually high volatility.

d. Expected dividend yield is nil, consistent with the Directors' view that the Group's business model is to generate value through capital growth rather than the payment of dividends.

e. The risk-free rate is equal to the prevailing U.K. Gilts rate at grant date that most closely matches the expected term of the grant.

f. Share options are assumed to be exercised immediately on vesting.

g. The fair value of share options awarded where there are different vesting installments is the average of the fair values calculated per installment.

26. Share option scheme and restricted stock units (continued)

At January 31, 2019, the outstanding restricted stock units ('RSUs') in the form of nominal-cost options, which have been granted to non-executive directors, are shown below:

Date of grant	Exercise price (£)	Number of shares	Date from which exercisable	Expiry date
April 20, 2018	0.01	121,950	April 20, 2019	December 31, 2019
January 11, 2019	0.01	692,306	January 11, 2020	December 31, 2020
		814,256		

The movement in the number of RSUs is set out below:

	Weighted average exercise price £	Year ended January 31, 2019	Weighted average exercise price £	Year ended January 31, 2018
Outstanding at February 1,	**0.01**	**275,877**	—	—
Granted during the year	**0.01**	**814,256**	0.01	275,877
Exercised during the year	**0.01**	**(275,877)**	—	—
Number of RSUs outstanding at January 31,	**0.01**	**814,256**	0.01	275,877

As at January 31, 2019, nil RSUs were capable of being exercised (2018: nil). The RSUs outstanding at January 31, 2019, had a weighted average exercise price per RSU of 1 penny (2018: 1 penny), and a weighted average remaining contractual life of 1.8 years (2018: 0.9 years).

The fair value per RSU award granted and the assumptions used in the calculations are as follows:

Date of grant	Number of shares	Exercise price (£)	Share price at grant date (£)	Fair value per option (£)	Award life (years)	Risk free rate
April 20, 2018	121,950	0.01	2.05	2.04	1.00	0.70%
January 11, 2019	692,306	0.01	0.26	0.25	1.00	0.79%
	814,256					

The key assumptions used in calculating the share-based payments are as follows:

a. Black-Scholes valuation methodology was used for all RSUs.

b. Figures in the range of 50%-57% have been used for expected volatility. This has been derived from historic share price performance, weighted to exclude periods of unusually high volatility.

c. Expected dividend yield is nil, consistent with the Directors' view that the Group's business model is to generate value through capital growth rather than the payment of dividends.

d. The risk-free rate is equal to the prevailing U.K. Gilts rate at grant date that most closely matches the expected term of the grant.

e. RSUs are assumed to be exercised immediately on vesting.

27. Fixed assets purchase commitments

At January 31, 2019, the Group had no capital commitments (January 31, 2018: nil).

28. Leasing and other commitments

The Group's total commitments under non-cancelable operating leases are as follows:

	Land & Buildings	
	January 31, 2019	January 31, 2018
	£000	£000
Leases which expire		
Not later than one year	**357**	337
Later than one year and not later than five years	**723**	1,143
	1,080	1,480

In addition to land and buildings, the Group enters into contracts in the normal course of business with contract research organizations to assist in the performance of research and development activities and other services and products for operating purposes. These contracts generally provide for termination on notice, and therefore are cancelable contracts and not reflected in the table above.

29. Related party transactions

Professor Stephen Davies, a non-executive director who resigned in September 2018, is a member of the board of directors of Oxford University Innovation Limited. During the year, £nil (2018: £24,000) was charged by Oxford University Innovation Limited in connection with payments due in respect of the strategic alliance between the Group and Oxford University that was entered into in November 2013. Of this amount, £nil was outstanding at the year end (2018: £12,000).

See Note 7 'Directors and employees' for details of key management emoluments.

Confidential Materials omitted and filed separately with the
Securities and Exchange Commission. Double asterisks denote omissions.

Exhibit 4.13

AMENDMENT OF SOLICITATION/MODIFICATION OF CONTRACT		1.CONTRACT ID CODE	PAGE OF PAGES 1 9
2.AMENDMENT/MODIFICATION NO. 0001	3.EFFECTIVE DATE See Block 16C	4.REQUISITION/PURCHASE REQ. NO. N/A	5.PROJECT NO. (If applicable)
6.ISSUED BY CODE	ASPR-BARDA	7.ADMINISTERED BY *(If other than Item 5)* CODE	ASPR-BARDA02
ASPR-BARDA O'NEILL HOUSE OFFICE BUILDING Room 22G13 Washington DC 20515		US DEPT OF HEALTH & HUMAN SERVICES ASPR AMCG O'NEILL HOUSE OFFICE BUILDING Room 22G13 Washington DC 20515	

8.NAME AND ADDRESS OF CONTRACTOR *(No., Street, City, County, State and ZIP Code)*			9A.AMENDMENT OF SOLICITATION NO.
SUMMIT (OXFORD) LIMITED 1510803 SUMMIT (OXFORD) LIMITED 85B PA 85B PARK DRIVE MILTON PARK ABINGDON OXFORDSHIRE OX14 4SB			9B.DATED (SEE ITEM 11)
			10A.MODIFICATION OF CONTRACT/ORDER NO. HHSO100201700014C
			10B.DATED (SEE ITEM 13)
CODE 1510803	FACILITY CODE	x	09/05/2017

11.**THIS ITEM ONLY APPLIES TO AMENDMENTS OF SOLICITATIONS**

The above solicitation is amended as set forth in Item 14. The hour and date specified for receipt of Offers ☐ is extended. ☐ is not extended. Offers must acknowledge receipt of this amendment prior to the hour and date specified in the solicitation or as amended, by one of the following methods: (a) By completing Items 8 and 15, and returning copies of the amendments; (b) By acknowledging receipt of this amendment on each copy of the offer submitted; or (c) By separate letter or telegram which includes a reference to the solicitation and amendment numbers. FAILURE OF YOUR ACKNOWLEDGEMENT TO BE RECEIVED AT THE PLACE DESIGNATED FOR THE RECEIPT OF THE OFFERS PRIOR TO THE HOUR AND DATE SPECIFIED MAY RESULT IN REJECTION OF YOUR OFFER. If by virtue of this amendment you desire to change an offer already submitted, such change may be made by telegram or letter, provided each telegram or letter makes reference to the solicitation and this amendment and is received prior to the opening hour and date specified.

12.ACCOUNTING AND APPROPRIATION DATA (If required)
See Schedule

13. **THIS ITEM ONLY APPLIES TO MODIFICATION OF CONTRACTS/ORDERS. IT MODIFIES THE CONTRACT/ORDER NO. AS DESCRIBED IN ITEM 14.**

CHECK ONE	
	A. THIS CHANGE ORDER IS ISSUED PURSUANT TO: (Specify authority) THE CHANGES SET FORTH IN ITEM 14 ARE MADE IN THE CONTRACT ORDER NO. IN ITEM 10A.
	B. THE ABOVE NUMBERED CONTRACT/ORDER IS MODIFIED TO REFLECT THE ADMINISTRATIVE CHANGES (such as changes in paying office appropriation date, etc.) SET FORTH IN ITEM 14, PURSUANT TO THE AUTHORITY OF FAR 43 103(b).
X	C. THIS SUPPLEMENTAL AGREEMENT IS ENTERED INTO PURSUANT TO AUTHORITY OF: FAR 42.103(a)(3) Mutual Agreement of the Parties
	D. OTHER (Specify type of modification and authority)

E. IMPORTANT: Contractor ☐ is not ☒ is required to sign this document and return 2 copies to the issuing office.

14. DESCRIPTION OF AMENDMENT/MODIFICATION (Organized by UCF section headings including solicitation/contract subject matter where feasible.)
Tax ID Number: CO-0000487
DUNS Number: 733628718
The Purpose of this Modification is to remove the requirement for an Earned Value Management System from the contract and substitute a new Statement of Work to reflect the removal of the EVMS requirement.

See Continuation Sheet
Period of Performance: 09/05/2017 to 09/30/2018

Except as provided herein, all terms and condition of the document referenced in Item 9A or 10A, as heretofore changes, remains unchanged and in full force and effect.

15A.NAME AND TITLE OF SIGNER *(Type or print)*		16A.NAME OF CONTRACTING OFFICER (Type or print)	
ERIK OSTROWSKI, CFO		FRANCINE L. HEMPHILL	
15B.NAME OF CONTRACTOR	15C.DATE SIGNED	16B.UNITED STATES OF AMERICA	16C.DATE SIGNED
BY /s/ Erik Ostrowski, CFO *(Signature of person authorized to sign)*	19 JUNE 2018	BY /s/ Francine L. Hemphill *(Signature of Contracting Officer)*	6/19/18

NSN 7540-01-152-8070
Previous edition is NOT usable

STANDARD FORM 30 (REV. 10-83)
Prescribed by GSA
FAR (48 CFR) 53.214(a)

Beginning with the effective date of this modification, the Government and the Contractor mutually agree as follows:

1. Article C.3 EARNED VALUE MANAGEMENT SYSTEM (EVMS) IMPLEMENTATION REQUIREMENTS is deleted.

2. Article F.2 DELIVERABLES

1. Summary of Contract Deliverables: this summary is deleted and replaced as follows:

TECHNICAL DELIVERABLES

CDRL#	Deliverable	Deliverable Description	Reporting Procedures and Due Dates
01	Kickoff Meeting	The Contractor shall complete a Kickoff meeting after contract award	Due: Within [**] of contact award. Materials: Contractor shall provide itinerary and agenda to CO and COR at least [**] business days in advance of site visit. CO approves and the COR distributes itinerary and agenda within [**] business days. Due out: Contractor provides meeting minutes to CO and COR within 5 business days after the meeting. The CO and COR reviews, comments, and the CO approves minutes within [**] business days.
02	Quarterly Meetings	The Contractor shall hold recurring teleconference or face-to-face Project Review Meetings approximately every third month either in Washington D.C. or at work sites of the Contractor or subcontractors. Face-to-face meetings shall alternate between Washington DC and Contractor, sub-contractor sites, with the first to be held in Washington DC. The meetings will be used to discuss contract progress in relation to, the Program Management deliverables described below as well as study designs, technical, regulatory, and ethical aspects of the program.	Materials: Contractor shall provide itinerary and agenda to CO and COR at least [**] business days in advance of site visit. The COR approves and distributes itinerary and agenda within [**] business days. Due out: Contractor provides meeting minutes to the CO and the COR within [**] business days after the meeting. The CO and COR reviews, comments, and the CO approves minutes within [**] business days.
03	[**] Teleconference Meetings	The Contractor shall participate in teleconferences every [**] with the CO and the COR to discuss the performance of the contract.	Materials: Contractor provides agenda to the CO and COR no later than [**] business days in advance of meeting. The COR approves and distributes agenda prior to meeting. Due out: Contractor provides meeting minutes to the CO and COR within [**] business days following the meeting. The CO and COR reviews, comments, and the COR approves minutes within [**] business days following the meeting.

04 (Monthly) 05 (Annual)	Monthly & Annual Technical Progress Reports	The Monthly and Annual Technical Progress report shall address each of the below items and be cross-referenced to the Work Breakdown Structure (WBS), and the Statement of Work (SOW). 1.An Executive Summary highlighting the progress, issues and relevant manufacturing, non-clinical, clinical and regulatory activities. The Executive Summary should highlight only critical issues for that reporting period and resolution approach; limited to 2-3 pages. 2.Progress in meeting contract milestones - broken out by subtasks within each milestone, overall project assessment, problems encountered and recommended solutions. The reports shall detail the planned and actual progress during the period covered, explaining occurrences of any differences between the two and the corrective steps. 3.The reports shall also include a [**]-month rolling forecast of the key planned activities, referencing the WBS. 4.A tracking log of progress on regulatory submissions with the FDA number, description of submission, date of submission, status of submission and next steps. 5.Estimated and Actual Expenses. 6.This report shall also contain a narrative or table detailing whether there is a significant discrepancy (>10%) at this time between the % of work completed and the cumulative costs incurred to date. Monthly and actual expenses should be broken down to the appropriate WBS level. This section of the report should also contain estimates for the Subcontractors' expenses from the previous month if the Subcontractor did not submit a bill in the previous month. If the subcontractor(s) was not working or did not incur any costs in the previous month, then a statement to this effect should be included in this report for those respective subcontractors.	Due: Monthly Reports shall be submitted on the [**] day of the month after the end of each month with an Annual Report submitted on the [**] calendar day of the final month of each contract year for the previous twelve calendar months. Monthly progress reports are not required for the periods when the Annual Report(s) and Final Report are due. The CO and the COR will review the monthly reports and provide feedback within [**] business days of receiving the report. The CO approves acceptance of monthly and annual reports.

06	Risk Management Plan	The Contractor shall provide a Risk Management Plan that outlines the impacts of each risk in relation to the cost, schedule, and performance objectives. The plan shall include risk mitigation strategies. Each risk mitigation strategy will capture how the corrective action will reduce impacts on cost, schedule and performance.	Due: Within [**] days of contract award. Due out: Contractor provides updated Risk Management Plan to Monthly Progress Report. The COR shall provide Contractor with written comments in response submitted plan. Contractor must address, in writing, all commercially reasonable concerns raised by the COR within [**] business days of Contractor's receipt of COR's concerns for CO approval.
07	Deviation Notification and Mitigation Strategy	Contractor shall notify the CO of significant changes in the schedule defined as increases in cost above 5% or schedule slippage of more than 30 days, which would require a PoP extension. Contractor shall provide a high level management strategy for risk mitigation.	Due: As needed.
08	Go/No-Go Decision Gate Presentation	Contractor shall provide a presentation detailing technical progress made towards completion of Go/No-Go decision gate milestones following a prescribed template provided by the CO prior to the IPR	Materials: Contractor shall provide presentation materials to the CO and COR [**] business days prior to the In-Process Review (IPR). Contractor shall submit written justification of progress towards satisfying Go/No-Go criteria. After reviewing, CO and COR will provide a written response within [**] business days.
09	Incident Report	Contractor shall communicate and document all critical programmatic concerns, risks, or potential risks with the CO and COR.	Due: Within [**] of activity or incident or within [**] for a security activity or incident via email or telephone, with written follow-up to the CO and COR. Additional updates due within [**] of additional developments. Due out Contractor shall submit within [**] business days, a Corrective Action Plan (if deemed necessary by either party) to address any potential issues. If corrective action is deemed necessary, Contractor must address in writing, its consideration of concerns raised by the CO, with [**] business days of receiving such concerns in writing.
10	Draft and Final Reports for Clinical and Non-Clinical Studies	Contractor shall provide Draft and Final Clinical/Non-Clinical Study Reports to the CO and COR for review and comment.	Draft - within [**] calendar days after completion of analysis and at least [**] business days prior to submission to FDA. Subcontractor prepared reports received by the Contractor shall be submitted to the CO and COR for review and comment no later than [**] business days after receipt by Contractor. The CO shall provide written comments to the Draft Final Report for Clinical and Non-Clinical Studies within [**] business days after the submission. Final - due [**] calendar days after receiving comments on the Draft Final Report for Clinical and Non-Clinical Studies. If corrective action is recommended, Contractor must address, in writing, all reasonable concerns raised by the CO in writing Contractor shall consider revising reports to address CO's recommendations prior to FDA submission. Final FDA submissions shall be provided to the CO and COR concurrently or no later than [**] after submission to the FDA.

11	Standard Operating Procedures	The Contractor shall make internal and, to the extent possible, subcontractor Standard Operating Procedures (SOPs) available for review electronically.	Upon request from the CO.
12	Manufacturing Campaign Reports	Contractor shall provide Manufacturing Campaign Reports to the CO and COR for review and comment prior to submission to FDA. The COR and CO reserve the right to request within the PoP a non-proprietary Manufacturing Campaign Report for distribution within the USG.	Due: Contractor will submit Manufacturing Campaign Reports at least [**] business days prior to FDA submission. Due out: If corrective action is recommended, Contractor must address, in writing, all concerns raised by the CO in writing. Contractor shall consider revising reports to address CO and COR's concerns and/or recommendations prior to FDA submission. Final FDA submission shall be submitted to the CO and COR concurrently or no later than [**] after submission to the FDA.
13	FDA Correspondence	The Contractor shall memorialize any correspondence between Contractor and FDA and submit to the CO and COR. All documents shall be duly marked as either "Draft" or "Final".	Due: Contractor shall provide written summary of any FDA correspondence within [**] business days of correspondence.
14	FDA Meetings	The Contractor shall forward the dates and times of any meeting with the FDA to the CO and COR and make arrangements for appropriate government staff to attend the FDA meetings. Government staff shall include up to a maximum of four people (COR, CO and up to 2 subject matter experts).	Contractor shall notify the CO and COR of upcoming FDA meeting within [**] of scheduling Type A, B or C meetings OR within [**] of meeting occurrence for ad hoc meetings. The Contractor shall forward Initial Contractor and FDA-issued draft minutes and final minutes of any meeting with the FDA to the CO and COR within [**] business days of receipt. All documents shall be duly marked as either "Draft" or "Final".
15	FDA Submissions	The Contractor shall provide the CO and COR the opportunity to review and comment upon all draft submissions before submission to the FDA. Contractor shall provide the CO and COR with an electronic copy of the final FDA submission. All documents shall be duly marked as either "Draft" or "Final".	Due: Contractor shall submit draft FDA submissions to the CO and COR at least [**] business days prior to FDA submission. The CO and COR will provide feedback to Contractor within [**] business days of receipt. Due out: if corrective action is recommended, the Contractor must address, in writing, its consideration of all concerns raised by the CO. The Contractor shall consider revising their documents to address CO's concerns and/or recommendations prior to FDA submission. Final FDA submissions shall be submitted to the CO and COR concurrently or no later than [**] of its submission to CDER.

16	FDA Audits	In the event of an FDA inspection which occurs as a result of this contract and for the product, or for any other FDA inspection that has the reasonable potential to impact the performance of this contract, the Contractor shall provide the USG with an exact copy (non-redacted) of the FDA Form 433 and the Establishment Inspection Report (EIR). The Contractor shall provide the COR and CO with copies of the plan for addressing areas of non-conformance to FDA regulations for GLP, GMP, or GCP guidelines as identified in the audit report, status updates during the plans execution and a copy of all final responses to the FDA. The Contractor shall also provide redacted copies of any FDA audits received from subcontractors that occur as a result of this contract or for this product. The Contractor shall make arrangements for CO and BARDA representative(s) to be present during the final debrief by the regulatory inspector.	Contractor shall notify the CO and COR within [**] business days of a scheduled FDA audit or within [**] of an ad hoc site visit/audit if the FDA does not provide advanced notice. Contractor shall provide copies of any FDA audit report received from subcontractors that occur as a result of this contract or for this product within [**] business days of receiving correspondence from the FDA or third-party. Within [**] business days of audit report, Contractor shall provide CO with a plan for addressing areas of nonconformance, if any are identified.
17	QA Audit Reports	The COR reserves the right to participate in QA audits. Upon completion of the audit/site visit the Contractor shall provide a report capturing the findings, results and next steps in proceeding with the subcontractor. If action is requested of the subcontractor, detailed concerns for addressing areas of non-conformance to FDA regulations for GLP, GMP, or GCP guidelines, as identified in the audit report, must be provided to the CO and COR. The Contractor shall provide-responses from the subcontractors to address these concerns and plans for corrective action execution.	Contractor shall notify the CO and COR [**] days in advance of upcoming, ongoing, or recent audits/site visits of subcontractors as part of weekly communications. Contractor shall notify the CO and COR within [**] business days of report completion.
18	Government Audit	Contractor shall accommodate periodic or ad hoc site visits by the CO and COR. If the CO, COR, Contractor, or other parties identifies any issues during an audit, the Contractor shall capture the issues, identify potential solutions, and provide a report to the CO and COR.	If issues are identified during the audit, Contractor shall submit a report to the CO and COR detailing the finding and corrective action(s) within [**] business days of the audit. Due out: The CO and COR will review the report and provide a response to the Contractor with [**] business days. Once corrective action is completed, the Contractor will provide a final report to the CO and COR.

19	Technical Documents	Upon request, Contractor shall provide CO and COR with deliverables from the following contract funded activities: process Development Reports, Assay Qualification Plan/Report, Assay Validation Plan/Report, Assay Technology Transfer Report, Batch Records, SOPs, Master Production Records, Certificate of Analysis, Clinical Studies Data or Reports. The CO and COR reserve the right to "request within the PoP a non-proprietary technical document for distribution within the Government.	Contractor shall provide technical document within [**] business days of COR's request. Contractor can request additional time on an as needed basis. If corrective action is recommended by the COR, the Contractor must address, in writing, concerns raised by the COR to the COR and CO in writing.
20	Animal Model or Other Technology Transfer Package	Contractor shall provide Animal Model or Other Technology Transfer Package relevant data.	Contractor shall provide data within [**] business days of the COR's request to the CO and COR.
21	Raw Data or Data Analysis	Contractor shall provide raw data or data analysis to the CO and COR upon request.	Contractor shall provide data or data analysis to the CO and COR within [**] business days of request.
22	Product Transition Strategy	Contractor shall provide a 2-4 page summary document containing a Product Transition Strategy to support transition of the product(s) prior to end of the base and/or option(s) POP. The Product Transition Strategy should provide a strategic plan for further development and/or stockpiling of the product. The transition strategy shall provide options and/or a specific approach for the transition of MCM product for further development, procurement, approval and/or stockpile.	Contractor shall provide a Product Transition Strategy to support transition of the produces) [**] days prior to the end of the (base/option) POP as addendum to the Quarterly Project Status Report.
23	Publications	Any manuscript or scientific meeting abstract containing data generated under this contract must be submitted to the CO and COR for review prior to submission.	Contractor must submit all manuscript or scientific meeting abstract to the CO and COR within [**] days for manuscripts and [**] days for abstracts. Contractor must address in writing all concerns raised by the CO and COR in writing. Final submissions shall be submitted to the CO and COR concurrently or no later than [**] after its submission.
24	Press Releases	Contractor agrees to accurately and factually represent the work conducted under this contract in all press releases.	With the exception of ad-hoc press releases required by applicable law or regulations, Contractor shall ensure that the CO and COR has received and approved an advanced copy of any draft press release to this contract not less than [**] business days prior to the issuance of the press release. The CO shall revert with comments within [**] of receipt of the draft press release. Should no comments be forthcoming from the CO by end of the [**], Summit will be permitted to issue the press release If corrective action is required, the Contractor agrees to accurately and factually represent the work conducted under this contract in all press releases. Any final press releases shall be submitted to the CO and COR no later than [**] prior to its release.

25	Draft and Final Technical Progress Report	A Draft Final Technical Progress Report containing a summation of the work performed and the results obtained for the entire contract PoP. The draft report shall be duly marked as 'Draft'. The Final Technical Progress Report incorporating feedback received from the CO and COR and containing a summation of the work performed and the results obtained for the entire contract PoP. The final report shall document the results of the entire contract. This report shall be in sufficient detail to fully describe the progress achieved under all milestones. The final report shall be duly marked as "Final".	Due: Contractor shall provide a draft Technical Progress Report [**] calendar days before the end of the Pop and the Final Technical Progress Report on or before the completion date of the PoP. Subcontractor prepared reports received by the Contractor shall be submitted to the CO and COR for review and comment no later than [**] business days after receipt by the Contractor. Due out: the CO shall provide feedback on draft report within [**] calendar days of receipt, which the Contractor shall consider incorporating into the Final Report. Contractor shall submit, with the Final Technical Progress Report, a summary (not to exceed 200 words) of salient results achieved during the performance of the contract.
26	Draft and Final Study Protocols	Contractor shall provide all Draft and Final Study Protocols to the COR for evaluation. (The CO and COR reserves the right to request within the period of performance a non-proprietary Study Protocol for distribution within the United States Government (USG))	The Contractor will submit all proposed protocols to the CO and COR at least [**] business days prior to study start. If corrective action is required, the Contractor must address in writing all concerns raised by the CO and COR to the satisfaction of the COR before study execution and provide the CO and COR a revised draft protocol that addresses the CO's comments and requested changes. After receiving the revised Study Protocol that satisfies the COR, the CO will approve the revised Study Protocol and will provide a written approval to the Contractor that provides authorization to the Contractor to execute the specific study. Contractor shall not proceed with any study protocol until the COR gives its approval and the Contractor has provided the CO and COR with a final and approved Study Protocol.
27	Clinical Study Status Update	Contractor shall provide COR with a status update of clinical studies that are actively enrolling patients to include by study site: cumulative enrollment; new enrollments; screen failures; patients dropped from study; AE and SAEs; activation or inactivation of study sites; investigator appointments or changes; and status of IRB/IEC review/approval/renewal. Contractor will provide proposed format for the COR's review and approval	Update will be submitted by e-mail or other electronic format to be provided by the COR by the end of the [**] business day of each new month. Updates, to the extent they are available, will be presented during biweekly teleconferences. If no changes have occurred since the prior update only a simple statement that there is no new data is required.

3. Under Section F.2 DELIVERABLES: Subparagraph 2.A.i (Monthly Progress Report).

a. SECTION IV: This Section is deleted.

4. Under Section F.2 DELIVERABLES Subparagraph 2.A.ii (Annual Progress Report)

a. SECTION IV: This Section is deleted.

5. Under Section F.2 DELIVERABLES Subparagraph 2.C (EARNED VALUE MANAGEMENT (EVM) DELIVERABLES):

This Section is deleted except for **iv. Risk Management Plan** and **v. Requirement for Notification of Deviation and Mitigation Strategy** which is changed to read as follows:

"Contractor shall notify the Government of significant changes in the schedule defined as increases in cost above [**]% or schedule slippage of more than 30 days, which would require an extension to the period of performance. Contractor shall provide a high level management strategy for risk mitigation. Notice due as needed."

6. Under SECTION J (LIST OF ATTACHMENTS),

a. Delete ATTACHMENT 1, Statement of Work dated June 2, 2017 (4 pages) and replace with Statement of Work dated April 2, 2018 (4 pages).

b. Delete ATTACHMENT 8. 7 Principles of Earned Value Management Implementation Guide (Tier 2),

(30 pages)

END OF MODIFICATION 0001 TO HHSO100201700014C

HHSO100201700014C

Contractual Statement of Work

CLINICAL DEVELOPMENT OF DRUG

Topic Area of Interest No. 3

April 2, 2018

PREAMBLE

Independently and not as an agency of the Government, Summit (Oxford) Limited (hereafter the "Contractor") shall be required to furnish all the necessary services, qualified personnel, material, equipment, and facilities, not otherwise provided by the Government, as needed to perform the Statement of Work submitted in response to the BARDA Broad Agency Announcement (BAA) BARDA CBRN BAA-16-100-SOL-00001.

The Government reserves the right to modify the milestones, progress, schedule, budget, or deliverables to add or delete deliverables, process, or schedules if the need arises. Because of the nature of this research and development (R&D) contract and the complexities inherit in this and prior programs, at designated milestones the Government will evaluate whether work should be redirected, removed, or whether schedule or budget adjustments should be made. The Government reserves the right to change the product, process, schedule, or events to add or delete part or all of these elements as the need arises.

Overall Objectives and Scope

The overall objective of this contract is to advance the development of ridinilazole, a novel therapy for the treatment of *Clostridium difficile* Infections (CDI) and reducing the recurrence of CDI. The scope of work for this contract includes clinical and manufacturing development activities that fall into the following areas: non-clinical toxicology studies; clinical activities; manufacturing activities; and all associated regulatory, quality assurance, management, and administrative activities. The Research and Development (R&D) effort for ridinilazole will progress in specific stages that cover the base performance (I) segment and option segment (II) as specified herein. The Contractor must complete specific tasks required in each of the two discrete work segments. The statement of work has been broken into the following phases which are discrete work segments:

1. CLIN 1: [**]
2. CLIN 2: [**]
3. CLIN 3: [**]
4. CLIN 4: [**]

1. CLIN 1 [**]

The overall objective of CLIN 1 will be to [**].

1.1 **Program Management (WBS 1.1)**

[**]

2. CLIN 2: [**]
The overall objective of CLIN2 is to [**]

2.1 **Program Management (WBS 1.1)**
[**]

3. CLIN 3: [**]
The overall objective of CLIN3 is to [**].

3.1 **Program Management (WBS 1.1)**
[**]

4. CLIN 4: [**]
4.1 **Program Management (WBS 1.1)**
[**]

5. OTHER ITEMS
5.1 **Facilities, Equipment and Other Resources. (Contract: Section J)**
[**].

END

STATEMENT OF WORK

HHSO100201700014C

Confidential Materials omitted and filed separately with the
Securities and Exchange Commission. Double asterisks denote omissions.

Exhibit 4.14

AMENDMENT OF SOLICITATION/MODIFICATION OF CONTRACT		CONTRACT ID CODE	PAGE OF PAGES 1 6
2.AMENDMENT/MODIFICATION NO. 0002	3.EFFECTIVE DATE See Block 16C	4.REQUISITION/PURCHASE REQ. NO. OS222399	5.PROJECT NO. (If applicable)
6.ISSUED BY CODE	ASPR-BARDA	7.ADMINISTERED BY *(If other than Item 6)* CODE	ASPR-BARDA02
ASPR-BARDA O'NEILL HOUSE OFFICE BUILDING Room 22G13 Washington DC 20515		US DEPT OF HEALTH & HUMAN SERVICES ASPR AMCG O'NEILL HOUSE OFFICE BUILDING Room 22G13 Washington DC 20515	

8.NAME AND ADDRESS OF CONTRACTOR *(No., Street, City, County, State and ZIP Code)*		(x)	9A.AMENDMENT OF SOLICITATION NO.
			9B.DATED (SEE ITEM 11)
SUMMIT (OXFORD) LIMITED 1510803 SUMMIT (OXFORD) LIMITED85B PA 85B PARK DRIVE MILTON PARK ABINGDON OXFORDSHIRE OX14 4SB			10A.MODIFICATION OF CONTRACT/ORDER NO. HHSO100201700014C
			10B.DATED (SEE ITEM 13) 09/05/2017
CODE 1510803	FACILITY CODE	x	

11. THIS ITEM ONLY APPLIES TO AMENDMENTS OF SOLICITATIONS

The above solicitation is amended as set forth in Item 14. The hour and date specified for receipt of Offers ☐ is extended. ☐ is not extended. Offers must acknowledge receipt of this amendment prior to the hour and date specified in the solicitation or as amended, by one of the following methods: (a) By completing Items 8 and 15, and returning copies of the amendments; (b) By acknowledging receipt of this amendment on each copy of the offer submitted; or (c) By separate letter or telegram which includes a reference to the solicitation and amendment numbers. FAILURE OF YOUR ACKNOWLEDGEMENT TO BE RECEIVED AT THE PLACE DESIGNATED FOR THE RECEIPT OF THE OFFERS PRIOR TO THE HOUR AND DATE SPECIFIED MAY RESULT IN REJECTION OF YOUR OFFER. If by virtue of this amendment you desire to change an offer already submitted, such change may be made by telegram or letter, provided each telegram or letter makes reference to the solicitation and this amendment and is received prior to the opening hour and date specified.

12.ACCOUNTING AND APPROPRIATION DATA (If required) Net Increase: $12,000,000.00
2018.1992018.25106

13.THIS ITEM ONLY APPLIES TO MODIFICATION OF CONTRACTS/ORDERS. IT MODIFIES THE CONTRACT/ORDER NO. AS DESCRIBED IN ITEM 14.

CHECK ONE	
X	A. THIS CHANGE ORDER IS ISSUED PURSUANT TO: (Specify authority) THE CHANGES SET FORTH IN ITEM 14 ARE MADE IN THE CONTRACT ORDER NO. IN ITEM 10A. FAR 52.243-2 ALT V
	B. THE ABOVE NUMBERED CONTRACT/ORDER IS MODIFIED TO REFLECT THE ADMINISTRATIVE CHANGES (such as changes in paying office appropriation date, etc.) SET FORTH IN ITEM 14, PURSUANT TO THE AUTHORITY OF FAR 43 103(b).
X	C. THIS SUPPLEMENTAL AGREEMENT IS ENTERED INTO PURSUANT TO AUTHORITY OF: FAR 52.217-9 Option to Extend the Term of the Contract
	D. OTHER (Specify type of modification and authority)

E. IMPORTANT: Contractor ☐ is not ☒ is required to sign this document and return 2 copies to the issuing office.

14. DESCRIPTION OF AMENDMENT/MODIFICATION (Organized by UCF section headings including solicitation/contract subject matter where feasible.)
Tax ID Number: CO-0000487
DUNS Number:733628718
The Purpose of this Modification is to 1) exercise CLIN 3 (Option 2), 2) extend the period of performance of the Base Period to end on 6/30/2019, 3) change the U.S. Government's and the Contractor's contribution for CLIN 3, 4) revise the SOW and 5) designate a new Contracting Officer's Representative (COR)
FUNDS ALLOTTED PRIOR TO THIS MODIFICATION $31,967,000.00
FUNDS ALLOTTED WITH THIS MODIFICATION: $12,000,000.00
FUNDS ALLOTTED TO DATE: $43,967,000.00
PERIOD OF PERFORMANCE: SEPTEMBER 5, 2017 TO APRIL 30, 2022

Continued…
Except as provided herein, all terms and condition of the document referenced in Item 9A or 10A, as heretofore changes, remains unchanged and in full force and effect.

15A.NAME AND TITLE OF SIGNER *(Type or print)*		16A.NAME OF CONTRACTING OFFICER (Type or print)	
GLYN EDWARDS, CEO		FRANCINE L. HEMPHILL	
15B.NAME OF CONTRACTOR SUMMIT (OXFORD) LIMITED	15C.DATE SIGNED	16B.UNITED STATES OF AMERICA	16C.DATE SIGNED
BY /s/Glyn Edwards *(Signature of person authorized to sign)*	14 AUG 2018	BY /s/ Francine L. Hemphill *(Signature of Contracting Officer)*	14 AUG 2018

NSN 7540-01-152-8070
Previous edition is NOT usable

STANDARD FORM 30 (REV. 10-83)
Prescribed by GSA
FAR (48 CFR) 53.214(a)

NAME OF OFFEROR OR CONTRACTOR

SUMMIT (OXFORD) LIMITED 1510803

ITEM NO.	SUPPLIES/SERVICES	QUANTITY	UNIT	UNIT PRICE	AMOUNT
(A)	(B)	(C)	(D)	(E)	(F)
5					

	See Continuation Sheet Delivery: 06/23/2018 Delivery Location Code: HHS/OS/ASPR HHS/OS/ASPR 200 C St SW WASHINGTON DC 20201 US Appr. Yr.: 2018 CAN: 1992018 Object Class: 25106 FOB: Destination Period of Performance: 09/05/2017 to 04/30/2022 Add Item 5 as follows: ASPR-18-03011 - - Exercise CLIN 3 under Summit Therapeutics contract HHSO100201700014C Obligated Amount: $12,000,000.00				12,000,000.00

OPTIONAL FORM 336 (4-86)

Sponsored by GSA

FAR (48 CFR) 53.110

NSN 7540-01-152-8067

Beginning with the effective date of this modification, the Government and the Contractor mutually agree to exercise Option 2 (CLIN 3) as follows:

A. In accordance with the changes that come into effect due to the exercising of option two (2) the following sections are changed:

1. ARTICLE B.2 ESTIMATED COST,

2. The Governmental shall provide monies for the base period segment (CLIN 001) in an amount not to exceed $31,967,000. The Contractor's share of the Base Period is estimated at $[**]. The Government will provide monies for the Option 2 period segment (CLIN 0003) in an amount not to exceed $12,000,000. The Government will not be responsible for any Contractor incurred costs that exceed these amounts unless a modification to the contract is signed by the Contracting Officer which expressly increases the amount. The Contractor's share of the Option 2 period segment (CLIN 0003) is estimated at $[**].

5. It is estimated that the amount currently allotted will cover performance of the Base period through June 30, 2019 and of Option 2 through [**]

CLIN	Period of Performance	Supplies/Services	Government Share	Contractor Share	Total Cost	Status
Base/ CLIN 0001	Sept 5, 2017 Through June 30, 2019	[**]	$31,967,000	$[**]	$[**]	Executed

2. ARTICLE B.3. OPTION PRICES

a. Unless the Government exercises its option pursuant to FAR Clause 52.217-9 (Option to Extend the Term of the Contract), contained in ARTICLE 1.2, the contract consists only of the base period (CLIN 0001) and Option 2 (CLIN 0003) specified in the Statement of Work as defined in SECTIONS C and F, for the price set forth in ARTICLE B.2 of the contract.

b. Pursuant to FAR Clause 52.217-9 (Option to Extend the Term of the Contract), the Government may, by unilateral contract modification, require the contractor to perform the remaining Option Work Segments specified in the Statement of Work as defined in SECTIONS C and F of this contract. If the Government decides to exercise an option(s), the Government will provide the Contractor a preliminary written notice of its intent to exercise the option at least [**] days before the contract expires. If option 1 CLIN 0002 and Option 3 CLIN 0004 are exercised, the estimated cost of the contract will be increased as set forth in the table below:

CLIN	Period of Performance	Supplies/Services	Government Share	Contractor Share	Total Cost	Status
Option 1/CLIN 0002	[**], 2019 Through [**]	[**]	$31,967,000	$[**]	$[**]	Executed
Option 2/CLIN 0003	[**], 2018 Through [**]	[**]	$12,000,000	$[**]	$[**]	Executed
Option 3/CLIN 0004	[**] through [**], 2022	[**]	$[**]	$[**]	$[**]	Not Executed
	TOTAL		$61,461,899	$[**]	$[**]	

B. Under SECTION B (SUPPLIES OR SERVICES and PRICES/COSTS), ARTICLE B.4 (Provisions Applicable to Direct Costs), paragraph b (Travel Costs), is deleted and replaces as follows:

b. Travel Costs

1. Total expenditures for travel (transportation, lodging, substance, and incidental expenses) incurred in direct performance of this contract of the base period segment (CLIN 0001) shall not exceed $[**] without the prior written approval of the Contracting Officer. The Government is not responsible for the travel portion of the Option 2 period (CLIN 003). The Contractor shall notify the Contracting Officer in writing when travel expenditures have exceeded [**]% ($[**]) of the base period expenses. Costs must be consistent with Federal Acquisition Regulations (FAR) 52.247-63 - Preference for U.S. Air Flag carriers whenever relevant.

C. Under SECTION F, ARTICLE F.2, DELIVERABLES the first paragraph is deleted and replaced as follows:

Successful performance of the final contract shall be deemed to occur upon completion of performance of the work set for in the Statement of Work dated June 29, 2018 set forth in SECTION J - List of Attachments of this contract and upon delivery and acceptance, as required by the Statement of Work, by the Contracting Officer, of each of the deliverables described in SECTION C, SECTION F, and SECTION J.

D. Under SECTION F, ARTICLE F.2 DELIVERABLES, Subparagraph a. Summary of Contract Deliverables: the COR's address is deleted and replace as follows:

HHS/ASPR/BARDA
ATTN: [**]
Contracting Officer's Representative
Room [**] - O'Neill House Office Building
Washington, DC 20515
Email: [**]

E. Under ARTICLE G.2 CONTRACTING OFFICER'S REPRESENTATIVE (COR) the COR's name, title and address is deleted and replaced as follows:

[**]
Division of CBRN Countermeasures
Biomedical Advanced Research & Development Authority (BARDA)
Department of Health and Human Services
Mailing Address:
Contracting Officer's Representative
Room [**] - O'Neill House Office Building
Washington, DC 20515
Email: [**]

F. Under ARTICLE G.5 INVOICE/FINANCING REQUEST AND CONTRACT FINANCIAL REPORTING the address chart is deleted and replaced as follows:

PSC_Invoices@psc.hhs.gov	[**] Contracting Officer DHHS/OS/ASPR/BARDA Room [**] O'Neill House Office Building Washington, DC 20515 Email [**]	[**] Contracting Specialist DHHS/OS/ASPR/BARDA Room [**] O'Neill House Office Building Washington, DC 20515 Email: [**]	[**] Contracting Officer Representative DHHS/ASPR/BARDA Room [**] O'Neill House Office Building Washington, DC 20515 Email: [**]

G. Under SECTION J - LIST OF ATTACHMENTS, delete ATTACHMENT 1, Statement of Work dated April 2, 2018 (4 pages) and replace with Statement of Work dated June 29, 2018 (5 pages).

END OF MODIFICATION 002 TO HHSO100201700014C

Modification 2
Attachment 1
HHSO100201700014C
Statement of Work
CLINICAL DEVELOPMENT OF DRUG
Topic Area of Interest No. 3
June 29, 2018

PREAMBLE

Independently and not as an agency of the Government, Summit (Oxford) Limited (hereafter the "Contractor") shall be required to furnish all the necessary services, qualified , material, equipment, and facilities, not otherwise provided by the Government, as needed to perform the Statement of Work submitted in response to the BARDA Broad Agency Announcement (BAA) BARDA CBRN BAA-16-100-SOL-00001.
The Government reserves the right to modify the milestones, progress, schedule, budget, or deliverables to add or delete deliverables, process, or schedules if the need arises. Because of the nature of this research and development (R&D) contract and the complexities inherit in this and prior programs, at designated milestones the Government will evaluate whether work should be redirected, removed, or whether schedule or budget adjustments should be made. The Government reserves the right to change the product, process, schedule, or events to add or delete part or all of these elements as the need arises.

Overall Objectives and Scope

The overall objective of this contract is to advance the development of ridinilazole, a novel therapy for the treatment of *Clostridium difficile* Infections (CDI) and reducing the recurrence of CDI. The scope of work for this contract includes clinical and manufacturing development activities that fall into the following areas: non-clinical toxicology studies; clinical activities; manufacturing activities; and all associated regulatory, quality assurance, management, and administrative activities. The Research and Development (R&D) effort for ridinilazole will progress in specific stages that cover the base performance (I) segment and option segment (II) as work segments. The statement of work has been broken into the following phases which are discrete work segments:

1. CLIN 1: [**]
2. CLIN 2: [**]
3. CLIN 3: [**]
4. CLIN 4: [**]

1. CLIN 1 [**] The overall objective of CLIN 1 will be to [**].

1.1. Program Management (WBS 1.1)

[**].

2. CLIN 2: [**]

The overall objective of CLIN2 is to [**]

2.1 Program Management (WBS 1.1)

[**].

3. CLIN 3: [**]

The overall objective of CLIN3 is to [**].

3.1 Program Management (WBS 1.1)

[**].

4. CLIN 4: [**]

4.1 Program Management (WBS 1.1)

[**]

5. OTHER ITEMS

5.1 Facilities, Equipment and Other Resources. (Contract: Section J)

[**].

END

STATEMENT OF WORK

HHSO100201700014C

Confidential Materials omitted and filed separately with the
Securities and Exchange Commission. Double asterisks denote omissions.

Exhibit 4.15

AMENDMENT OF SOLICITATION/MODIFICATION OF CONTRACT			CONTRACT ID CODE	PAGE OF PAGES 1 2
2. AMENDMENT/MODIFICATION NO. 0003	3.EFFECTIVE DATE See Block 16C	4.REQUISITION/PURCHASE REQ. NO. N/A		5.PROJECT NO. (If applicable)
6. ISSUED BY CODE	ASPR-BARDA	7.ADMINISTERED BY *(If other than Item 5)* CODE		ASPR-BARDA02
ASPR-BARDA O'NEILL HOUSE OFFICE BUILDING Room 21B05 Washington DC 20515		US DEPT OF HEALTH & HUMAN SERVICES ASPR AMCG O'NEILL HOUSE OFFICE BUILDING Room 21B05 Washington DC 20515		
8.NAME AND ADDRESS OF CONTRACTOR *(No., Street, City, County, State and ZIP Code)* SUMMIT (OXFORD) LIMITED 1510803 Attn: [**] SUMMIT (OXFORD) LIMITED 136A EASTERN AVENUE MILTON PARK ABINGDON OXFORDSHIRE OX14 4SB			(x)	9A.AMENDMENT OF SOLICITATION NO.
				9B.DATED (SEE ITEM 11)
				10A.MODIFICATION OF CONTRACT/ORDER NO. HHSO100201700014C
				10B.DATED (SEE ITEM 13)
CODE 1510803	FACILITY CODE		x	09/05/2017

11. THIS ITEM ONLY APPLIES TO AMENDMENTS OF SOLICITATIONS

The above solicitation is amended as set forth in Item 14. The hour and date specified for receipt of Offers ☐ is extended. ☐ is not extended. Offers must acknowledge receipt of this amendment prior to the hour and date specified in the solicitation or as amended, by one of the following methods: (a) By completing Items 8 and 15, and returning copies of the amendments; (b) By acknowledging receipt of this amendment on each copy of the offer submitted; or (c) By separate letter or telegram which includes a reference to the solicitation and amendment numbers. FAILURE OF YOUR ACKNOWLEDGEMENT TO BE RECEIVED AT THE PLACE DESIGNATED FOR THE RECEIPT OF THE OFFERS PRIOR TO THE HOUR AND DATE SPECIFIED MAY RESULT IN REJECTION OF YOUR OFFER. If by virtue of this amendment you desire to change an offer already submitted, such change may be made by telegram or letter, provided each telegram or letter makes reference to the solicitation and this amendment and is received prior to the opening hour and date specified.

12.ACCOUNTING AND APPROPRIATION DATA (If required)

13.THIS ITEM ONLY APPLIES TO MODIFICATION OF CONTRACTS/ORDERS. IT MODIFIES THE CONTRACT/ORDER NO. AS DESCRIBED IN ITEM 14.

CHECK ONE	
	A. THIS CHANGE ORDER IS ISSUED PURSUANT TO: (Specify authority) THE CHANGES SET FORTH IN ITEM 14 ARE MADE IN THE CONTRACT ORDER NO. IN ITEM 10A.
X	B. THE ABOVE NUMBERED CONTRACT/ORDER IS MODIFIED TO REFLECT THE ADMINISTRATIVE CHANGES (such as changes in paying office appropriation date, etc.) SET FORTH IN ITEM 14, PURSUANT TO THE AUTHORITY OF FAR 43 103(b).
X	C. THIS SUPPLEMENTAL AGREEMENT IS ENTERED INTO PURSUANT TO AUTHORITY OF: FAR 43.103(a)(3) Mutual Agreement of the Parties
	D. OTHER (Specify type of modification and authority)

E. IMPORTANT: Contractor ☐ is not ☒ is required to sign this document and return 2 copies to the issuing office.

14. DESCRIPTION OF AMENDMENT/MODIFICATION (Organized by UCF section headings including solicitation/contract subject matter where feasible.)
Tax ID Number: CO-0000487
DUNS Number: 733628718
The Purpose of this Modification is to (1) designate a new Contracting Officer (CO) and a new Contracting Officer's Representative (COR) and to (2) change the Statement of Work (SOW).

No funding is affected by this modification.

See Continuation Sheet
Period of Performance: 09/05/2017 to 04/30/2022

Except as provided herein, all terms and condition of the document referenced in Item 9A or 10A, as heretofore changes, remains unchanged and in full force and effect.

15A.NAME AND TITLE OF SIGNER *(Type or print)*		16A.NAME OF CONTRACTING OFFICER (Type or print)	
MELISSA STRANGE VP, FINANCE		JAMES P. BOWERS	
15B.NAME OF CONTRACTOR	15C.DATE SIGNED	16B.UNITED STATES OF AMERICA	16C.DATE SIGNED
BY /s/ Melissa Strange *(Signature of person authorized to sign)*	13 FEB 19	BY /s/ JAMES P. BOWERS *(Signature of Contracting Officer)*	2/14/2019

NSN 7540-01-152-8070
Previous edition is NOT usable

STANDARD FORM 30 (REV. 10-83)
Prescribed by GSA
FAR (48 CFR) 53.214(a)

1. Beginning with the effective date of this modification, the Government and the Contractor mutually agree as follows:

2. Under SECTION F, ARTICLE F.2 DELIVERABLES, Subparagraph a. Summary of Contract Deliverables: The CO's name and address is deleted and replaced as follows:

HHS/ASPR/BARDA

[**]

Contracting Officer

Room [**] O'Neill House Office Building

Washington, DC 20515

[**] Email: [**]

And the COR's name and address is deleted and replaced as follows:

HHS/ASPR/BARDA

ATTN: [**]

Contracting Officer's Representative

Room [**] - O'Neill House Office Building

Washington, DC 20515

[**]

Email: [**]

3. Under ARTICLE G.2 CONTRACTING OFFICER'S REPRESENTATIVE (COR) the COR's name and address is deleted and replaced as follows:

[**]

Biomedical Advanced Research & Development Authority (BARDA)

Office of Secretary for Preparedness & Response (ASPR)

Department of Health and Human Services

Mailing Address:

Contracting Officer's Representative

Room [**] -O'Neill House Office Building Washington, DC 20515

Email: [**]

4. Under ARTICLE G.5 INVOICE/ FINANCING REQUEST AND CONTRACT FINANCIAL REPORTING the address chart is deleted and replaced as follows:

PSC_Invoices@psc.hhs.gov	[**] Contracting Officer DHHS/OS/ASPR/BARDA Room [**] O'Neill House Office Building Washington, DC 20515 Email: [**]	[**] Contracting Officer Representative DHHS/ASPR/BARDA Room [**] O'Neill House Office Building Washington, DC 20515 Email: [**]

5. Under SECTION J - LIST OF ATTACHMENTS, delete ATTACHMENT 1, Statement of Work dated June 29, 2018 (5 pages) and replace with Statement of Work dated February 4, 2019 (5 pages).

END OF MODIFICATION 0003 TO HHS0100201700014C

HHSO100201700014C

Contractual Statement of Work

CLINICAL DEVELOPMENT OF DRUG

Topic Area of Interest No. 3

4 February 4, 2019

PREAMBLE

Independently and not as an agency of the Government, Summit (Oxford) Limited (hereafter the "Contractor") shall be required to furnish all the necessary services, qualified personnel, material, equipment, and facilities, not otherwise provided by the Government, as needed to perform the Statement of Work submitted in response to the BARDA Broad Agency Announcement (BAA) BARDA CBRN BAA-16-100-SOL-00001.

The Government reserves the right to modify the milestones, progress, schedule, budget, or deliverables to add or delete deliverables, process, or schedules if the need arises. Because of the nature of this research and development (R&D) contract and the complexities inherit in this and prior programs, at designated milestones the Government will evaluate whether work should be redirected, removed, or whether schedule or budget adjustments should be made. The Government reserves the right to change the product, process, schedule, or events to add or delete part or all of these elements as the need arises.

Overall Objectives and Scope

The overall objective of this contract is to advance the development of ridinilazole, a novel therapy for the treatment of *Clostridium difficile* Infections (CDI) and reducing the recurrence of CDI. The scope of work for this contract includes clinical and manufacturing development activities that fall into the following areas: non-clinical toxicology studies; clinical activities; manufacturing activities; and all associated regulatory, quality assurance, management, and administrative activities. The Research and Development (R&D) effort for ridinilazole will progress in specific stages that cover the base performance (I) segment and option segment (II) as specified herein. The Contractor must complete specific tasks required in each of the two discrete work segments. The statement of work has been broken into the following phases which are discrete work segments:

1. CLIN 1: [**]
2. CLIN 2: [**]
3. CLIN 3: [**]
4. CLIN 4: [**]

1. CLIN 1: [**]

The overall objective of CLIN 1 will be to [**].

1.1 Program Management (WBS 1.1)

[**]

.

2. CLIN 2: [**]

The overall objective of CLIN2 is to [**]

2.1 Program Management (WBS 1.1)

[**]

3. CLIN 3: [**]

The overall objective of CLIN3 is to [**].

3.1 Program Management (WBS 1.1)

[**].

4. CLIN 4: [**]

4.1 Program Management (WBS 1.1)

[**]

5. OTHER ITEMS

5.1 Facilities, Equipment and Other Resources. (Contract: Section J)

[**].

END

STATEMENT OF WORK

HHSO100201700014C

Exhibit 8.1

SUBSIDIARIES OF THE REGISTRANT

Name of Subsidiary	Jurisdiction of incorporation or organization
Summit (Oxford) Limited	England and Wales
Discuva Limited	England and Wales
Summit Therapeutics Inc.	Delaware, USA
Summit Corporation Limited	England and Wales
Summit (Wales) Limited	England and Wales
Summit (Cambridge) Limited	England and Wales
Summit Discovery 1 Limited	England and Wales
Summit Corporation Employee Benefit Trust Company Limited	England and Wales
MuOx Limited	England and Wales
Summit Infectious Diseases Limited	England and Wales

Certification by the Chief Executive Officer

Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Glyn Edwards, certify that:

1. I have reviewed this annual report on Form 20-F of Summit Therapeutics plc (the "Company");

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the Company as of, and for, the periods presented in this report;

4. The Company's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the Company and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the Company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with 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 and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the Company's auditors and the audit committee of the Company's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the Company's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the Company's internal control over financial reporting.

Date: March 29, 2019

By: /S/ Glyn Edwards

Name: Glyn Edwards

Title: Chief Executive Officer

(*Principal Executive Officer*)

Certification by the Principal Financial Officer

Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Melissa Strange, certify that:

1. I have reviewed this annual report on Form 20-F of Summit Therapeutics plc (the "Company");

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the Company as of, and for, the periods presented in this report;

4. The Company's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the Company and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the Company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with 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 and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the Company's auditors and the audit committee of the Company's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the Company's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the Company's internal control over financial reporting.

Date: March 29, 2019

By: /s/ Melissa Strange

Name: Melissa Strange

Title: Vice President of Finance

(*Principal Financial Officer*)

Certification by the Chief Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

In connection with the Annual Report on Form 20-F of Summit Therapeutics plc (the "Company") for the year ended January 31, 2019, as filed with the U.S. Securities and Exchange Commission on the date hereof (the "Report"), the undersigned Glyn Edwards, as Chief Executive Officer of the Company, and Melissa Strange, as Vice President of Finance and Principal Financial Officer of the Company, each hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of his or her knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 29, 2019

By: /s/ Glyn Edwards
Name: Glyn Edwards
Title: *Chief Executive Officer*

By: /s/ Melissa Strange
Name: Melissa Strange
Title: *Vice President of Finance*

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statement on Form F-3 (No. 333-224938) of Summit Therapeutics plc of our report dated March 27, 2019 relating to the consolidated financial statements, which appears in this Form 20-F.

/s/ PricewaterhouseCoopers LLP

PricewaterhouseCoopers LLP
Reading, UK
March 29, 2019