

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

Amendment No. 1
 to
Form F-1
 REGISTRATION STATEMENT
 UNDER
 THE SECURITIES ACT OF 1933

MEREO BIOPHARMA GROUP PLC
 (EXACT NAME OF REGISTRANT AS SPECIFIED IN ITS CHARTER)

Not Applicable
 (Translation of Registrant's Name into English)

United Kingdom
 (State or other Jurisdiction of
 Incorporation or Organization)

2834
 (Primary Standard Industrial
 Classification Code Number)

Not Applicable
 (I.R.S. Employer
 Identification Number)

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Approximate date of commencement of proposed sale to the public:
As soon as practicable after this Registration Statement becomes effective.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. ☐

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933.

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 7(a)(2)(B) of the Securities Act. ☐

CALCULATION OF REGISTRATION FEE

TITLE OF EACH CLASS OF SECURITIES TO BE REGISTERED	PROPOSED MAXIMUM AGGREGATE OFFERING PRICE(2)(3)	AMOUNT OF REGISTRATION FEE(4)(5)
Ordinary shares, nominal value £0.003 per ordinary share(1)	\$80,500,000	\$10,022

- (1) In the U.S. offering, all ordinary shares are in the form of American Depositary Shares, or ADSs, with each ADS representing four ordinary shares. ADSs issuable upon deposit of the ordinary shares registered hereby are being registered pursuant to a separate registration statement on Form F-6 (File No. 333- 223890).
- (2) Estimated solely for the purpose of calculating the amount of the registration fee pursuant to Rule 457(o) of the Securities Act of 1933, as amended.
- (3) Includes the aggregate offering price of (a) additional ordinary shares which the underwriters have the option to purchase and (b) ordinary shares which are being offered in a private placement in Europe and other countries outside of the United States and Canada but which may be resold from time to time in the United States in transactions requiring registration under the Securities Act or exemption therefrom. The total number of ordinary shares in the U.S. offering and the European private placement is subject to reallocation between them. All or part of the ordinary shares may be in the form of ADSs in the U.S. offering.
- (4) Calculated pursuant to Rule 457(o) based on an estimate of the proposed maximum aggregate offering price.
- (5) Previously paid.

The Registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

The information in this preliminary prospectus is not complete and may be changed. This preliminary prospectus is not an offer to sell these securities and is not soliciting an offer to buy these securities in any state or jurisdiction where the offer or sale is not permitted.

PRELIMINARY PROSPECTUS (Subject to Completion)

Dated April
9, 2018

15,892,917 Ordinary Shares
(including Ordinary Shares in the form of American Depositary Shares)



£ per Ordinary Share
\$ per American Depositary Share

We are offering an aggregate of 15,892,917 of our ordinary shares, including ordinary shares in the form of American Depositary Shares, or ADSs, in a global offering.

We are offering 2,838,021 ADSs through the underwriters named in this prospectus in the United States, or the U.S. offering. Each ADS represents four ordinary shares. This is our initial public offering of our ADSs, and no public market currently exists for our ADSs. We have applied to list our ADSs on The Nasdaq Global Market under the symbol "MREO."

We are offering 4,540,833 ordinary shares through the underwriters named in this prospectus in Europe and countries outside of the United States and Canada in a concurrent private placement, or the European private placement.

The closing of each of the U.S. offering and the European private placement, together referred to as the global offering, will be conditioned upon the other. The total number of ordinary shares in the U.S. offering and the European private placement is subject to reallocation between them.

Our ordinary shares trade on AIM, a market of the London Stock Exchange, under the symbol "MPH." On April 4, 2018, the last reported sale price of our ordinary shares on AIM was £3.14 per ordinary share (equivalent to \$17.62 per ADS based on an exchange rate of £1.00 to \$1.4027). For a discussion of the factors considered in determining the initial public offering price of our ADSs in the U.S. offering and the offering price of our ordinary shares in the European private placement, see "Underwriting".

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012 and, as such, will be subject to reduced public company disclosure requirements. Please see "Prospectus Summary—Implications of Being an Emerging Growth Company and a Foreign Private Issuer" for additional information.

Our business and an investment in our ordinary shares and ADSs involve significant risks. See "[Risk Factors](#)" beginning on page 14 of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed on the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

	PER ORDINARY SHARE	PER ADS	TOTAL
Offering price	£	\$	\$
Underwriting discounts and commissions(1)	£	\$	\$
Proceeds, before expenses, to Mereo BioPharma Group plc	£	\$	\$

(1) See "Underwriting" for additional information regarding underwriting compensation.

The underwriters may also purchase up to an additional 425,703 ADSs from us in the U.S. offering at the initial public offering price, less underwriting discounts and commissions, within 30 days from the date of this prospectus to cover overallocments.

The underwriters expect to deliver ADSs in the U.S. offering and ordinary shares in the European private placement against payment in New York, New York and London, United Kingdom, respectively, on or about , 2018.

Cowen

BMO Capital Markets

RBC Capital Markets

JMP Securities

Cantor Fitzgerald Europe

Prospectus dated , 2018

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We are responsible for the information contained in this prospectus and any free-writing prospectus we prepare or authorize. We have not, and the underwriters have not, authorized anyone to provide you with different information, and we and the underwriters take no responsibility for any other information others may give you. We are not, and the underwriters are not, making an offer to sell our ADSs or ordinary shares in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained in this prospectus is accurate as of any date other than the date on the front cover of this prospectus, regardless of the time of delivery of this prospectus or the sale of any ADSs or ordinary shares.

For investors outside the United States, neither we nor the underwriters have done anything that would permit the global offering or possession or distribution of this prospectus in any jurisdiction, other than the United States, where action for that purpose is required. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the global offering and the distribution of this prospectus outside the United States.

We are a public limited company incorporated under the laws of England and Wales and a majority of our outstanding securities are owned by non-U.S. residents. Under the rules of the U.S. Securities and Exchange Commission, or SEC, we are currently eligible for treatment as a "foreign private issuer." As a foreign private issuer, we will not be required to file periodic reports and financial statements with the SEC as frequently or as promptly as domestic registrants whose securities are registered under the Securities Exchange Act of 1934, as amended.

ABOUT THIS PROSPECTUS

Unless otherwise indicated or the context otherwise requires, all references in this prospectus to the terms “Mereo,” the “Company,” “we,” “us,” and “our” refer to Mereo BioPharma Group plc and our wholly owned subsidiaries Mereo BioPharma 1 Limited, Mereo BioPharma 2 Limited, Mereo BioPharma 3 Limited, and Mereo BioPharma 4 Limited.

PRESENTATION OF FINANCIAL INFORMATION

This prospectus includes our audited consolidated financial statements as of and for the years ended December 31, 2016 and 2017 prepared in accordance with International Financial Reporting Standards, or IFRS, as issued by the International Accounting Standards Board, or IASB. None of our financial statements were prepared in accordance with U.S. GAAP.

Our financial information is presented in pounds sterling. For the convenience of the reader, in this prospectus, unless otherwise indicated, translations from pounds sterling into U.S. dollars were made at the rate of £1.00 to \$1.4027, which was the noon buying rate of the Federal Reserve Bank of New York on March 30, 2018. Such U.S. dollar amounts are not necessarily indicative of the amounts of U.S. dollars that could actually have been purchased upon exchange of pounds sterling at the dates indicated. All references in this prospectus to “\$” mean U.S. dollars and all references to “£” and “GBP” mean pounds sterling.

We have made rounding adjustments to some of the figures included in this prospectus. Accordingly, numerical figures shown as totals in some tables may not be an arithmetic aggregation of the figures that preceded them.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus. This summary may not contain all the information that may be important to you, and we urge you to read this entire prospectus carefully, including "Risk Factors," "Business," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements, including the notes thereto, before deciding to invest in our ADSs or ordinary shares.

Overview

We are a multi-asset biopharmaceutical company focused on the acquisition, development, and commercialization of innovative therapeutics that aim to improve outcomes for patients with rare and specialty diseases. Our portfolio consists of four clinical-stage product candidates, each of which we acquired from large pharmaceutical companies. We are developing BPS-804 for the treatment of osteogenesis imperfecta, or OI, AZD-9668 for the treatment of severe alpha-1 antitrypsin deficiency, or AATD, BCT-197 for the treatment of acute exacerbations of chronic obstructive pulmonary disease, or AECOPD, and BGS-649 for the treatment of hypogonadotropic hypogonadism, or HH, in obese men. Each of our product candidates has generated positive clinical data for our target indication or for a related indication. We believe our portfolio is well diversified because each of our product candidates employs a different mechanism of action and targets a separate indication. We intend to develop and directly commercialize our rare disease product candidates. For our specialty disease product candidates, we intend to develop them through late-stage clinical milestones and then seek strategic relationships for further clinical development and/or commercialization.

Our strategy is to selectively acquire product candidates that have already received significant investment from pharmaceutical companies and that have substantial pre-clinical, clinical, and manufacturing data packages. Since our inception in March 2015, we have successfully executed on this strategy by acquiring our current product candidates from Novartis Pharma AG, or Novartis, and AstraZeneca AB, or AstraZeneca. We have commenced or completed large, randomized, placebo-controlled Phase 2 clinical trials for three of our product candidates. In December 2017, we reported top-line data from our completed Phase 2 dose-ranging clinical trial for BCT-197, and in March 2018, we reported top-line data from our Phase 2b dose-ranging clinical trial for BGS-649. We intend to commence additional late-stage clinical trials in 2018.

The following table summarizes our pipeline. We have global commercial rights to all of our product candidates.

Product Candidate Indication	Phase 1	Phase 2a	Phase 2b	Phase 3	Last Milestone	Next Anticipated Milestone
BPS-804 (setrusumab) Osteogenesis Imperfecta					Phase 2b initiated	Commence pediatric Phase 2b/3 study in Europe and Canada in the second half of 2018
AZD-9668 (alvelestat) Severe Alpha-1 Antitrypsin Deficiency					Positive Phase 2 data in bronchiectasis	Initiate Phase 2 trial in AATD in the second half of 2018
BCT-197 (acumapimod) Acute Exacerbations of COPD					Positive Phase 2 data	Enter into strategic relationship for further clinical development
BGS-649 (leflutrolole) Hypogonadotropic Hypogonadism in Obese Men					Positive Phase 2b data	Phase 2b extension study data in 4Q 2018

Our team has extensive experience in the pharmaceutical and biotechnology sector in the identification, acquisition, development, manufacturing, and commercialization of product candidates in multiple therapeutic areas. Our senior management team has long-standing relationships with senior executives of large pharmaceutical companies, which we believe enhances our ability to identify and acquire additional product candidates. Since June 9, 2016, our ordinary shares have traded on AIM, a market of the London Stock Exchange, under the symbol "MPH." Since our inception in March 2015, we have raised a total of £102.8 million in gross proceeds from private and public placements of our ordinary shares to institutional investors.

BPS-804 for the Treatment of Osteogenesis Imperfecta

BPS-804, or setrusumab, is a novel antibody we are developing as a treatment for OI, a rare genetic disease that results in bones that can break easily and is commonly known as brittle bone disease. OI is a debilitating orphan disease for which there are no treatments approved by the U.S. Food and Drug Administration, or FDA, or European Medicines Agency, or EMA. It is estimated that OI affects a minimum of 20,000 people in the United States and approximately 32,000 people in Germany, Spain, France, Italy, and the United Kingdom. BPS-804 is designed to inhibit sclerostin, a protein that inhibits the activity of bone-forming cells. We believe BPS-804's mechanism of action is well suited for the treatment of OI and has the potential to become a novel treatment option for patients that could reduce fractures and improve patient quality of life.

Prior to our acquisition of BPS-804, Novartis conducted four clinical trials in 106 subjects. One of these trials was a Phase 2 randomized, open-label, intra-patient dose-escalating proof-of-concept trial in the United States, Canada, and Europe in adults with OI. Treatment with BPS-804 showed a statistically significant increase in lumbar spine bone mineral density from baseline, which was sustained at day 141 of the trial, 16 weeks after the last dose of BPS-804. Treatment with BPS-804 also showed a statistically significant improvement in all measured bone formation biomarkers and a clinically relevant reduction in a bone resorption biomarker at day 43 of the trial. We believe that the observed increase in lumbar spine bone mineral density in patients treated with BPS-804, along with the biomarker data, support the potential of BPS-804 for the treatment of OI.

In 2016, we obtained orphan drug designation in OI for BPS-804 in the United States and the European Union, or EU, and in February 2017, BPS-804 was accepted into the adaptive pathways program in the EU. In addition, BPS-804 was admitted to the PRIME scheme of the EMA in November 2017. In May 2017, we initiated a randomized, double-blind, placebo-controlled Phase 2b clinical trial of BPS-804 in adults in the United States, Europe and Canada. We intend to enroll approximately 120 patients for this trial. We expect the results from this trial, if favorable, along with validation of our use of high resolution peripheral quantitative computerized tomography, or HRPqCT, as a biomarker for fracture, may be sufficient to support the submission of a Conditional Marketing Authorisation, or CMA, to the EMA for BPS-804 for the treatment of adults with OI in the EU. We also intend to commence a Phase 2b/3 clinical trial of BPS-804 in children with OI in 2018 in Europe and Canada. We intend to enroll approximately 150 patients for this trial, with fracture rate as the primary endpoint. We expect the results from this trial, if favorable, may be sufficient to validate our use of HRPqCT and support the submission of a CMA to the EMA for BPS-804 for the treatment of children with severe OI in the EU.

In the United States, the FDA has denied our request for a Type C meeting to discuss the initiation of a pediatric Phase 2b study for BPS-804 for the treatment of patients with severe OI. The FDA has cited that a serious cardiovascular safety concern exists in adults treated with sclerostin inhibitors that has yet to be resolved. We do not believe the FDA's concern is related to BPS-804. Given the undetermined risk/benefit assessment in adults, the FDA believes it is premature to conduct a study of sclerostin inhibitors in children. If this safety issue is resolved, we plan on submitting our proposed

Phase 2b/3 study for BPS-804 in children with severe OI to the FDA to expand the proposed trial into the United States. We believe the FDA's position does not impact our ability to conduct our clinical development activities of BPS-804 in Europe and Canada for children with severe OI and our clinical development activities of BPS-804 in Europe, the United States and Canada for adults with OI.

AZD-9668 for the Treatment of Severe Alpha-1-Antitrypsin Deficiency

AZD-9668, or alvelestat, is a novel, oral small molecule we are developing for the treatment of severe AATD, a potentially life-threatening rare, genetic condition. There are an estimated 50,000 patients in North America and 60,000 patients in Europe with severe AATD. Treatment of AATD involves bronchodilators and inhaled corticosteroid medications or surgical options such as lung volume reduction surgery and lung transplantation. Intravenous augmentation therapy is available for AATD using a partially purified plasma preparation highly enriched for AATD. However, this therapy was approved by the FDA based on its biochemical efficacy but not based on clinical outcome data.

AATD is caused by a lack of alpha-1 antitrypsin, or AAT, a protein that protects the lungs from enzymatic degradation. This degradation leads to severe debilitating diseases, including early-onset pulmonary emphysema, a disease that irreversibly destroys the tissues that support lung function. AZD-9668 is designed to inhibit neutrophil elastase, or NE, a neutrophil protease and a key enzyme involved in the destruction of lung tissue. We believe the inhibition of NE has the potential to protect AATD patients from further lung damage.

Prior to our license of AZD-9668, AstraZeneca conducted 12 clinical trials involving 1,776 subjects. Although these trials were conducted in other indications, we believe the data demonstrated potential clinical benefit and biomarker evidence of treatment effect for AATD patients. In particular, we believe the results from two Phase 2 clinical trials conducted for the treatment of bronchiectasis and cystic fibrosis, or CF, are most relevant in assessing AZD-9668's potential to treat severe AATD. AstraZeneca conducted a double-blind, placebo-controlled Phase 2 clinical trial in bronchiectasis in a total of 38 patients, 22 of whom were treated with AZD-9668. The results of this four-week trial showed a statistically significant improvement in the amount of air that can be forcibly exhaled in one second, or FEV1, a standard measure of exhalation, and a clinically meaningful improvement of slow vital capacity, which measures the volume of air on a slow exhale. We believe that bronchiectasis and AATD share common pathological features that support the potential for AZD-9668 to treat severe AATD. Additionally, we believe that data from the Phase 2 CF trial provides proof of concept for mechanistic effect and the use of a biomarker of lung degradation in diseases of high or unopposed NE, such as severe AATD.

We intend to initiate a Phase 2 proof-of-concept clinical trial in patients with severe AATD in the second half of 2018. We intend to enroll approximately 150 patients. If the results are favorable, we intend to seek regulatory advice on the design of, and commence, a pivotal trial.

BCT-197 for the Treatment of AECOPD

BCT-197, or acumapimod, is a p38 MAP kinase inhibitor we are developing as an oral first-line acute therapy for patients with AECOPD. Chronic obstructive pulmonary disease, or COPD, is a non-fully-reversible, progressive lung disease in which inflammation plays a central role. There are an estimated 16 million people in the United States and 13 million people in Europe diagnosed with COPD. Of all hospital admissions in the United States related to COPD, approximately 63% are for AECOPD patients. We believe BCT-197 offers a potential new treatment for controlling inflammation by targeting pathways that drive the pathological mechanism behind AECOPD. Since there are

currently no approved therapies in the United States or the EU to treat AECOPD, we believe that there is significant medical need for a drug which is disease-modifying. We believe BCT-197 could potentially prevent AECOPD instead of just treating the symptoms and improve quality of life, slow the progression of the disease, and significantly reduce direct healthcare costs.

Prior to our acquisition of BCT-197, Novartis conducted five clinical trials in 459 subjects, including a double-blind, Phase 2 clinical trial in AECOPD in Europe comparing BCT-197 to the steroid prednisolone and a placebo control. AECOPD patients receiving BCT-197 showed a statistically significant improvement in lung function at the highest dose.

In December 2017, we reported top-line data from our completed Phase 2 dose-ranging clinical trial for BCT-197. The trial was conducted in 282 patients with AECOPD to explore two different dosing regimens on top of standard of care, which included steroids, antibiotics, and bronchodilators. Both dosing regimens showed a statistically significant change in FEV1 from baseline to Day 7, meeting the trial's primary endpoint on an intent-to-treat patient population basis. Treatment with BCT-197 also showed a statistically significant reduction in the number of COPD exacerbations that required hospitalization. In addition, BCT-197 was observed to be well tolerated. Based on these results, we plan to enter into one or more strategic relationships with third parties for further clinical development and, if approved, commercialization, of BCT-197.

BGS-649 for the Treatment of Hypogonadotropic Hypogonadism

BGS-649, or leflutrolole, is a once-weekly oral therapy we are developing for the treatment of HH in obese men. HH is a clinical syndrome that results from inadequate levels of testosterone. Based on World Health Organization estimates and scientific data, we estimate there are approximately seven million cases of HH in obese men in the United States and approximately five million cases of HH in obese men in Europe. In these men, a decline in testosterone is exacerbated by high levels of the aromatase enzyme, which is present in fat tissue and leads to a reduction in testosterone. BGS-649 is designed to inhibit the aromatase enzyme and is being developed to restore normal levels of testosterone without causing excessively high testosterone levels or reducing the levels of luteinizing hormone, or LH, or follicular stimulating hormone, or FSH. Both FSH and LH play key roles in sperm formation and LH plays a key role in endogenous testosterone formation. In contrast to current therapies for HH, which involve the exogenous administration of testosterone and lead to further down regulation of LH and FSH, we believe that BGS-649, by preserving sperm formation through LH and FSH production, may present a benefit to patients.

Prior to our acquisition of BGS-649, Novartis conducted seven clinical trials in 131 subjects, including a two-part Phase 2 proof-of-concept trial for HH in obese men in North America. The first part was open-label to evaluate the pharmacokinetics and pharmacodynamics of a range of doses of BGS-649 administered orally once a week in obese men. Consistent with the goal of the trial, BGS-649 treatment increased testosterone into the normal range in all patients. The second part was two-arm, randomized, placebo-controlled, double-blind and lasted 12-weeks, with a three-month follow-up. Testosterone increase was statistically significant in the BGS-649 group with no evidence of increased total testosterone levels beyond the upper limit of the normal range in any patient exposed to BGS-649. Both FSH and LH levels also increased in the BGS-649 group.

In March 2018, we reported top-line data from our Phase 2b dose-ranging clinical trial of BGS-649 for the treatment of HH in obese men. The trial enrolled 271 patients who were administered placebo or one of three doses of BGS-649. The trial met its primary endpoint of normalizing testosterone levels in at least 75% of subjects after 24 weeks of treatment and all of the secondary endpoints, including normalizing testosterone in at least 90% of patients after 24 weeks of treatment at the two highest

doses and improvement in LH and FSH levels at all three doses. BGS-649 was observed to be well tolerated in the trial. A subset of patients have entered into a six month safety extension study, and we expect data from the extension study in the fourth quarter of 2018. We intend to commence additional late stage clinical developmental studies of BGS-649 in 2019.

Our Strategy

- ***Rapidly develop and directly commercialize our rare disease product candidates.*** We have commenced a Phase 2b clinical trial of BPS-804 for the treatment of OI in adults in the United States, Europe and Canada. If the results from this trial are favorable and our use of HRPqCT as a biomarker for fracture is validated, we intend to submit a CMA to the EMA for the treatment of OI in adults in the EU. We also intend to commence a Phase 2b/3 clinical trial of BPS-804 for the treatment of OI in children in the second half of 2018 in Europe and Canada. We expect that the results from this trial, if favorable, will be sufficient to validate our use of HRPqCT and support the submission of a CMA to the EMA for BPS-804 for the treatment of children with severe OI in the EU. We intend to initiate a Phase 2 clinical trial of AZD-9668 for the treatment of severe AATD in the second half of 2018 and, if the results are favorable and pending regulatory feedback, continue to develop AZD-9668 toward approval and commercialization. We plan to establish our own sales and marketing organization in the United States and Europe for BPS-804 and AZD-9668 and any future rare disease product candidates.
- ***Efficiently advance our specialty disease product candidates and explore strategic relationships with third parties for further clinical development and/or commercialization.*** Based on the top-line results from our Phase 2 clinical trial of BCT-197, we plan to enter into one or more strategic relationships with third parties for BCT-197 to undertake the next phase of clinical development and, if approved, commercialization. In March 2018, we also reported top-line Phase 2b data for BGS-649 for the treatment of HH. We intend to continue the clinical development of BGS-649 and plan to enter into strategic relationships with third parties for commercialization, if approved. We may also enter into strategic relationships with third parties to complete the clinical development of BGS-649.
- ***Leverage our expertise in business development to expand our pipeline of product candidates.*** Our senior management team has extensive relationships with large pharmaceutical and biotechnology companies, as evidenced by the acquisition of our four clinical-stage product candidates. We intend to leverage these relationships to grow our pipeline with a focus on rare diseases. We intend to continue to identify, acquire, develop, and ultimately commercialize novel product candidates that have received significant investment from large pharmaceutical companies. We will continue to focus on acquiring product candidates with either proof-of-concept clinical data in our target indication or with clinical data in a related indication and a strong scientific rationale that supports development in our target indication. Using a disciplined approach, we intend to continue building a diverse portfolio of product candidates that we believe have compelling market potential, robust pre-clinical, clinical, and manufacturing data packages, and a clear regulatory pathway.
- ***Continue to be a partner of choice for large pharmaceutical and biotechnology companies.*** We believe that we are a preferred partner for large pharmaceutical and biotechnology companies as they seek to unlock the potential in their development pipelines and deliver therapeutics to patients in areas of high unmet medical need. We have strong relationships with these companies, as evidenced by our agreements with Novartis and AstraZeneca, and a track record of structuring transactions that enable us to leverage our core capabilities while creating value for all stakeholders. We intend to continue to enter into strategic relationships that align our interests with those of large pharmaceutical and biotechnology companies and that we believe to be mutually beneficial.

Corporate Information

We were incorporated as a private limited company with the legal name Mereo BioPharma Group Limited under the laws of England and Wales on March 10, 2015 with the company number 09481161. On June 3, 2016, we were re-registered as a public limited company with the legal name Mereo BioPharma Group plc. Since June 9, 2016, our ordinary shares have traded on AIM under the symbol “MPH.” Our registered office address is Fourth Floor, One Cavendish Place, London, W1G 0QF, United Kingdom and our telephone number is +44 (0) 33 3023 7300. Our website address is www.mereobiopharma.com. The information contained on, or that can be accessed from, our website does not form part of this prospectus. Our agent for service of process in the United States is Cogeny Global Inc.

Risks Associated with Our Business

Our business is subject to a number of risks of which you should be aware before making an investment decision. You should carefully consider all of the information set forth in this prospectus and, in particular, should evaluate the specific factors set forth under “Risk Factors” in deciding whether to invest in our ADSs or ordinary shares. Among these important risks are the following:

- We have a limited operating history, have never generated any product revenue, have incurred significant operating losses since our inception, expect to incur significant operating losses for the foreseeable future, and may never achieve or maintain profitability.
- We may not be successful in our efforts to identify and acquire additional product candidates.
- We will need additional funding to complete the development and commercialization of our product candidates, if approved, and to acquire additional product candidates, and if we are unable to raise capital when needed, we could be forced to delay, reduce, or eliminate our product development programs or future commercialization efforts.
- We depend heavily on the success of our product candidates, and we cannot give any assurance that our product candidates will receive regulatory approval for any indication, which is necessary before they can be commercialized.
- We are, and will continue to be, dependent on pre-clinical and clinical trials conducted prior to our acquisition of a product candidate having been conducted in compliance with all applicable regulatory requirements and clinical standards and the results having been accurately reported, including for trials conducted by Novartis and AstraZeneca for our current product candidates.
- Undesirable side effects that may be caused by BPS-804, AZD-9668, BCT-197, and BGS-649 could cause us or regulatory authorities to interrupt, delay or halt clinical trials, and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, the EMA, or other comparable foreign authorities.
- We rely, and expect to continue to rely, on third parties to conduct our clinical trials and to manufacture our product candidates for pre-clinical and clinical testing, and those third parties may not perform satisfactorily, which could delay our product development activities.
- If we are unable to adequately protect our technology, or to secure and maintain freedom to operate or issued patents protecting our product candidates, others could preclude us from commercializing our technology and products or compete against us more directly.
- We face significant competition from other biotechnology and pharmaceutical companies.
- We will likely be classified as a passive foreign investment company in the current taxable year and may be classified as a passive foreign investment company in any future taxable year, which may result in adverse U.S. federal income tax consequences to U.S. holders of our ADSs or ordinary shares.

- As a foreign private issuer, we are exempt from a number of rules under the U.S. securities laws and Nasdaq corporate governance rules and are permitted to file less information with the SEC than U.S. companies, which may limit the information available to holders of our ADSs and ordinary shares.

Implications of Being an Emerging Growth Company and a Foreign Private Issuer

Emerging Growth Company

We are an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. As an emerging growth company we may take advantage of certain exemptions from various reporting requirements that are applicable to other publicly traded entities that are not emerging growth companies. These exemptions include:

- the option to present only two years of audited financial statements and only two years of related Management's Discussion and Analysis of Financial Condition and Results of Operations in this prospectus;
- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002;
- 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 (i.e., an auditor discussion and analysis);
- not being required to submit certain executive compensation matters to stockholder advisory votes, such as “say-on-pay,” “say-on-frequency,” and “say-on-golden parachutes;” and
- not being required to disclose certain executive compensation related items such as the correlation between executive compensation and performance and comparisons of the chief executive officer's compensation to median employee compensation.

We may take advantage of these provisions until the earliest of: (i) the last day of the first fiscal year in which our annual gross revenues exceed \$1.07 billion; (ii) the last day of 2023; (iii) the date that we become a “large accelerated filer” as defined in Rule 12b-2 under the Exchange Act, which would occur if the market value of our common equity held by non-affiliates exceeds \$700 million as of the last business day of our most recently completed second fiscal quarter; or (iv) the date on which we have issued more than \$1.0 billion in non-convertible debt securities during any three-year period.

As a result, we do not know if some investors will find our ADSs or ordinary shares less attractive. The result may be a less active trading market for our ADSs or ordinary shares, and the price of our ADSs or ordinary shares may become more volatile.

Section 107 of the JOBS Act also provides that an emerging growth company can take advantage of the extended transition period provided in Section 13(a) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, for complying with new or revised accounting standards. In other words, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We are choosing to irrevocably opt out of this extended transition period and, as a result, we will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies. Under federal securities laws, our decision to opt out of the extended transition period is irrevocable.

Foreign Private Issuer

Upon the completion of the U.S. offering, we will report under the Exchange Act as a non-U.S. company with foreign private issuer status. Even after we no longer qualify as an emerging growth company, as long as we qualify as a foreign private issuer under the Exchange Act we will be exempt from certain provisions of the Exchange Act that are applicable to U.S. domestic public companies, including:

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

Both foreign private issuers and emerging growth companies also are exempt from certain more stringent executive compensation disclosure rules. Thus, even if we no longer qualify as an emerging growth company, but remain a foreign private issuer, we will continue to be exempt from the more stringent compensation disclosures required of companies that are neither an emerging growth company nor a foreign private issuer.

The Offering	
Global offering	15,892,917 ordinary shares offered by us, consisting of 11,352,084 ordinary shares in the form of ADSs offered in the U.S. offering and 4,540,833 ordinary shares offered in the European private placement. The closing of each of the U.S. offering and the European private placement is conditioned upon the other. The total number of ordinary shares in the U.S. offering and European private placement is subject to reallocation between these offerings as permitted under applicable laws and regulations.
U.S. offering	2,838,021 ADSs
European private placement	4,540,833 ordinary shares
Ordinary shares to be outstanding immediately after the global offering	86,987,891 ordinary shares (or 88,690,703 ordinary shares if the underwriters exercise in full their option to purchase an additional 425,703 ADSs), including ordinary shares in the form of ADSs
Underwriters' option to purchase additional ADSs in the U.S. offering	425,703 ADSs
Offering price	On April 4, 2018, the last reported sale price of our ordinary shares on AIM was £3.14 per ordinary share (equivalent to \$17.62 per ADS). For a discussion of the factors considered in determining the initial public offering price of our ADSs in the U.S. offering and the price of our ordinary shares in the European private placement, see "Underwriting".
American Depositary Shares	Each ADS represents four ordinary shares, nominal value £0.003 per ordinary share. As an ADS holder, you will not be treated as one of our shareholders and you will not have shareholder rights. You will have the rights of an ADS holder or beneficial owner of ADSs as provided in the deposit agreement among us, the depositary, and holders and beneficial owners of ADSs from time to time. To better understand the terms of our ADSs, see "Description of American Depositary Shares." We also encourage you to read the deposit agreement, the form of which is filed as an exhibit to the registration statement of which this prospectus forms a part.
Depositary	Citibank, N.A.

Use of proceeds	We estimate that the net proceeds to us from the global offering will be approximately \$62.0 million (or approximately \$69.0 million if the underwriters exercise in full their option to purchase additional ADSs), based on an assumed initial public offering price of \$17.62 per ADS in the U.S. offering and an assumed offering price of £3.14 per ordinary share in the European private placement, which reflect the last reported sale price of our ordinary shares on AIM on April 4, 2018, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds from the global offering, together with our existing cash resources, to advance the clinical development of BPS-804, AZD-9668, and BGS-649, and the remainder to fund general research and development activities, working capital and other general corporate purposes. See “Use of Proceeds.”
Risk factors	See “Risk Factors” and the other information included in this prospectus for a discussion of factors you should consider before deciding to invest in our ADSs or ordinary shares.
Proposed Nasdaq trading symbol	“MREO”
AIM trading symbol	“MPH”
<p>The number of our ordinary shares to be outstanding after the global offering is based on 71,094,974 ordinary shares outstanding as of March 31, 2018 and excludes:</p> <ul style="list-style-type: none"> ▪ 11,916,424 ordinary shares issuable upon the exercise of share options outstanding as of March 31, 2018 at a weighted average exercise price of £1.42 per ordinary share; ▪ 100,820 ordinary shares that may be issued upon exercise of share options issued under our Deferred Bonus Share Plan, as described in “Management—Equity Compensation Arrangements,” as of March 31, 2018; ▪ 1,891,179 ordinary shares that may be issued upon conversion of certain convertible notes issued to Novartis, as described in “Related Parties—Other Transactions with Novartis—Novartis Notes,” or the Novartis Notes, as of April 9, 2018; ▪ 696,490 ordinary shares issuable upon the exercise of warrants to purchase ordinary shares outstanding as of March 31, 2018 at a weighted average exercise price of £3.16 per ordinary share; and ▪ 1,430,000 ordinary shares issuable upon exercise of share options to be granted to our directors under our Share Option Plan for Non-Executive Directors and to our executive officers under our Share Option Scheme, upon the effectiveness of the registration statement of which this prospectus forms a part, at an exercise price per share equal to the offering price per ordinary share in the European private placement, as more fully described in “Management—Incentive Award Arrangements.” 	

Unless otherwise indicated, all information contained in this prospectus assumes or gives effect to:

- no exercise of the outstanding share options after March 31, 2018;
- no conversion of the Novartis Notes after March 31, 2018;
- no exercise of the warrants to purchase ordinary shares after March 31, 2018; and
- no exercise by the underwriters of their option to purchase additional ADSs.

Summary Consolidated Financial Data

The following tables set forth our summary consolidated financial data for the period indicated. We have derived the consolidated statement of comprehensive loss data for the years ended December 31, 2016 and 2017 and the consolidated balance sheet data as of December 31, 2017 from our audited consolidated financial statements included elsewhere in this prospectus. Our historical results are not necessarily indicative of the results that should be expected for any future period. You should read the following summary consolidated financial data together with the audited consolidated financial statements included elsewhere in this prospectus and the sections titled "Exchange Rate Information" and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

We maintain our books and records in pounds sterling, and we prepare our financial statements in accordance with IFRS as issued by the IASB. We report our financial results in pounds sterling. For the convenience of the reader and except as otherwise indicated, we have translated pound sterling amounts in the tables below as of December 31, 2017 and for the years ended December 31, 2016 and 2017 into U.S. dollars at the noon buying rate of the Federal Reserve Bank of New York on December 29, 2017, which was £1.00 to \$1.3529. 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.

	Year Ended December 31,			
	2016		2017	
	(£)	(\$)	(£)	(\$)
	(in thousands, except per ordinary share data)			
Consolidated Statement of Comprehensive Loss Data:				
Research and development expenses	(24,563)	(33,231)	(34,607)	(46,819)
General and administrative expenses	(11,617)	(15,716)	(10,697)	(14,472)
Operating loss	(36,179)	(48,947)	(45,304)	(61,292)
Finance income	375	507	827	1,119
Finance charge	(180)	(243)	(1,090)	(1,475)
Net foreign exchange gain/(loss)	2,263	3,061	(1,384)	(1,873)
Net loss before tax	(33,722)	(45,622)	(46,951)	(63,520)
Income tax benefit	5,331	7,213	8,152	11,029
Loss attributable to equity holders of the Company	(28,390)	(38,409)	(38,799)	(52,491)
Total comprehensive loss attributable to equity holders of the Company	(28,390)	(38,409)	(38,799)	(52,491)
Basic and diluted loss per share	(0.63)	(0.85)	(0.56)	(0.76)

	As of December 31, 2017,			
	Actual		As Adjusted(1)(2)	
	(£)	(\$)	(£)	(\$)
	(in thousands)			
Consolidated Balance Sheet Data:				
Cash and short-term deposits and short-term investments	52,545	71,088	96,745	133,088
Total assets	96,335	130,332	140,526	192,319
Issued capital	213	289	261	355
Share premium	118,227	159,949	162,380	221,882
Accumulated loss	(79,316)	(107,307)	(79,316)	(107,307)
Total equity	62,483	84,534	106,684	146,532
Total liabilities(3)	33,852	45,798	33,852	45,798

- (1) The as adjusted balance sheet data give effect to the sale by us of 15,892,917 ordinary shares (including 11,352,084 ordinary shares in the form of ADSs) in the global offering at an assumed initial public offering price of \$17.62 per ADS in the U.S. offering and an assumed offering price of £3.14 per ordinary share in the European private placement, which reflect the last reported sale price of our ordinary shares on AIM on April 4, 2018 and, for the price per ADS, the exchange rate on March 30, 2018, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.
- (2) This as adjusted information is illustrative only and will depend on the actual offering prices and other terms of the global offering determined at pricing. Each £0.1 (\$0.14) increase or decrease in the assumed offering price of £3.14 (\$4.40) per ordinary share, which reflects the last reported sale price of our ordinary shares on AIM on April 4, 2018, would increase or decrease the as adjusted amount of each of cash and short-term deposits and short-term investments, total assets, and total equity by £1.5 million (\$2.1 million), assuming that the number of ordinary shares (including ordinary shares in the form of ADSs) offered by us in the global offering, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. An increase or decrease of 1,000,000 in the number of ordinary shares (including ordinary shares in the form of ADSs) offered by us in the global offering, as set forth on the cover page of this prospectus, would increase or decrease the as adjusted amount of each of cash and short-term deposits and short-term investments, total assets, and total equity by £2.9 million (\$4.1 million), assuming no change in the assumed initial public offering price per ADS or in the assumed offering price per ordinary share and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. U.S. dollar translations in this footnote were made at the exchange rate on March 30, 2018.
- (3) Includes £2.0 million (\$2.7 million) aggregate principal amount of, and accrued interest on, the Novartis Notes. See “Related Party Transactions—Other Transactions with Novartis—Novartis Notes.”

RISK FACTORS

You should carefully consider the risks and uncertainties described below and the other information in this prospectus before making an investment in our ADSs or ordinary shares. Our business, financial condition, results of operations, or prospects could be materially and adversely affected if any of these risks occurs, and as a result, the market price of our ADSs or ordinary shares could decline and you could lose all or part of your investment. This prospectus also contains forward-looking statements that involve risks and uncertainties. See "Cautionary Statement Regarding Forward-Looking Statements." Our actual results could differ materially and adversely from those anticipated in these forward-looking statements as a result of certain factors, including those set forth below.

Risks Related to Our Business and Industry

We have a limited operating history and have never generated any product revenue.

We are a multi-asset, clinical-stage biopharmaceutical company with a limited operating history, and have incurred significant operating losses since our inception. We had net losses of £28.4 million and £38.8 million in the years ended December 31, 2016 and 2017, respectively. As of December 31, 2016 and 2017, we had an accumulated loss of £40.6 million and £79.3 million, respectively. Our losses have resulted principally from expenses incurred from the research and development of our product candidates and from general and administrative costs that we have incurred while building our business infrastructure. We expect to continue to incur significant operating losses for the foreseeable future as we seek to acquire new product candidates, expand our research and development efforts, and seek to obtain regulatory approval and potentially commercialize our product candidates. We anticipate that our expenses will increase substantially as we:

- continue to conduct our ongoing Phase 2b clinical trial of BPS-804 for the treatment of OI in adults, and our ongoing safety extension study of BGS-649 for the treatment of HH;
- commence our planned pediatric Phase 2b/3 clinical trial of BPS-804 for the treatment of OI in Europe and Canada, our planned Phase 2 clinical trial of AZD-9668 for the treatment of severe AATD, and late-stage clinical program of BGS-649 for the treatment of HH;
- seek to acquire additional novel product candidates to treat rare and specialty diseases;
- seek regulatory approvals for our product candidates;
- potentially establish a commercial infrastructure and work with CMOs to scale up manufacturing processes to commercialize selected product candidates, if approved;
- maintain, expand, and protect our intellectual property portfolio;
- secure, maintain, or obtain freedom to operate for our technologies and products;
- add clinical, scientific, operational, financial, and management personnel, including personnel to support the development of our product candidates and potential future commercialization efforts; and
- expand our operations in the United Kingdom and potentially hire employees in the United States.

Our expenses may also increase substantially if we experience any delays or encounter any issues with any of the above, including, but not limited to, failed clinical trials, complex results, safety issues, or unforeseen regulatory challenges.

We have devoted substantially all of our financial resources and efforts to the acquisition and clinical development of BPS-804, AZD-9668, BCT-197, and BGS-649. We have not completed the clinical development of any product candidate through approval.

To become and remain profitable, we must succeed in developing and commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing clinical trials of our current or any future product candidates, obtaining regulatory approval for our product candidates that successfully complete clinical trials, establishing manufacturing supplies and marketing capabilities, and ultimately commercializing or entering into strategic relationships for our current and future product candidates, if approved. We are only in the preliminary stages of many of these activities. We may never succeed in these activities and, even if we do, we may never generate revenue that is significant enough to achieve profitability.

Because of the numerous risks and uncertainties associated with biopharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. We may be subject to different or contradictory regulatory requirements in different countries, and different regulatory authorities may not be aligned on the clinical trials necessary to support approval of our product candidates. If we are required by the FDA, the EMA, or other regulatory authorities to perform studies in addition to those we currently anticipate, or if there are any delays in completing our clinical trials or the development of our current product candidates, our expenses could increase and our ability to generate revenue could be further delayed. In addition, we may not be able to acquire new product candidates or may encounter unexpected difficulties or delays in such acquisitions, which would impair our business.

Even if we do generate product royalties or product sales, we may never achieve or sustain profitability. Our failure to sustain profitability would depress the market price of our ADSs and ordinary shares and could impair our ability to raise capital, acquire new product candidates, expand our business, or continue our operations. A decline in the market price of our ADSs or ordinary shares also could cause you to lose all or a 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.

Since our inception, we have devoted substantially all of our resources to acquiring and developing BPS-804, AZD-9668, BCT-197, and BGS-649; building our intellectual property portfolio; developing our supply chain; planning our business; raising capital; and providing general and administrative support for these operations. We have not yet demonstrated our ability to successfully complete any Phase 3 or other pivotal clinical trials, obtain regulatory approval, arrange for third parties to manufacture commercial-scale products, or conduct or partner with others to conduct sales and marketing activities necessary for successful product commercialization. Additionally, although we have acquired product candidates from two large pharmaceutical companies, we have not demonstrated the sustainability of our business model of acquiring and developing product candidates for rare and specialty diseases from, and becoming a partner of choice for, large pharmaceutical companies, nor have we demonstrated our ability to obtain approvals for or to commercialize these product candidates. 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.

We may not be successful in our efforts to identify and acquire additional product candidates.

Part of our strategy involves identifying and acquiring novel product candidates that have received significant investment from large pharmaceutical companies and that have substantial pre-clinical, clinical, and manufacturing data packages. The process by which we identify product candidates may fail to yield product candidates for clinical development for a number of reasons, including those discussed in these risk factors and also:

- any product candidates we acquire that have generated positive clinical data for our target indication or in diseases other than our target indications may not prove to be effective in treating our target indications;

- potential product candidates may, with further studies, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance;
- the regulatory pathway for a potential product candidate may be too complex and difficult to navigate successfully or economically; or
- there may be competitive bids for potential product candidates which we do not seek to or are unable to match.

In addition, we may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful. Further, time and resources spent searching for, identifying, acquiring, and developing potential product candidates may distract our management's attention from our primary business or other development programs. If we are unable to identify and acquire additional suitable product candidates for clinical development, this would adversely impact our business strategy and our financial position and share price.

We will need additional funding to complete the development of our current product candidates; to license, acquire, and develop future product candidates; and to commercialize our product candidates, if approved. If we are unable to raise capital when needed, we could be forced to delay, reduce, or eliminate our product development programs or any future commercialization efforts.

We expect our expenses to increase in connection with our ongoing activities, particularly as we conduct our ongoing Phase 2b clinical trial for BPS-804 and our ongoing safety extension study of BGS-649, our planned pediatric Phase 2b/3 study for BPS-804, our planned Phase 2 clinical trial for AZD-9668 and late-stage clinical development for BGS-649. We also expect our expenses to rise as we seek to acquire and develop new product candidates. In addition, if we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales, and distribution for any products we commercialize directly. Furthermore, upon the closing of the global offering, we expect to incur additional costs associated with operating as a public company in the United Kingdom and the United States and maintaining listings on both AIM and The Nasdaq Global Market, or Nasdaq. 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, any future commercialization efforts, or acquisitions of potential product candidates.

We expect that our existing cash resources, together with anticipated net proceeds from the global offering, will enable us to fund our operating expenses and capital expenditure requirements into the first quarter of 2020. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect, or our operating plan may change as a result of many factors unknown to us. These factors, among others, may necessitate that we seek additional capital sooner than currently planned. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans.

Our future capital requirements will depend on many factors, including:

- the costs, timing, and results of our ongoing Phase 2b clinical trial for BPS-804 and our ongoing safety extension study of BGS-649; our planned pediatric Phase 2b/3 study for BPS-804; our planned Phase 2 clinical trial for AZD-9668; and late-stage clinical development for BGS-649;
- the costs and timing of manufacturing clinical supplies of our product candidates;

- the costs, timing, and outcome of regulatory review of our product candidates, including post-marketing studies that could be required by regulatory authorities;
- the costs, timing, and outcome of potential future commercialization activities, including manufacturing, marketing, sales, and distribution, for our product candidates that we commercialize directly;
- the timing and amount of revenue, if any, received from commercial sales of our product candidates;
- the costs and timing of preparing, filing, and prosecuting patent applications; maintaining and enforcing our intellectual property rights; and defending any intellectual property-related claims, including any claims by third parties that we are infringing upon their intellectual property rights;
- the sales price and availability of adequate third-party coverage and reimbursement for our product candidates;
- the effect of competitors and market developments; and
- the extent to which we are able to acquire new product candidates or enter into licensing or collaboration arrangements for our product candidates, although we currently have no commitments or agreements to complete any such transactions.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect our business, the holdings or the rights of our shareholders, or the value of our ADSs or ordinary shares.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay, or discontinue our research and development programs or any commercialization efforts; be unable to expand our operations or acquire product candidates; or be unable to otherwise capitalize on our business opportunities, as desired, which could harm our business and potentially force us to discontinue operations.

Raising additional capital may cause dilution to, or adversely affect the rights of, our security holders, including purchasers of our ADSs or ordinary shares in the global offering; 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 may finance our cash needs through securities offerings, debt financings, license and collaboration agreements, or other capital raising transactions. If we raise capital through securities offerings, your ownership interest will be diluted, and the terms of the securities we issue in such transaction may include liquidation or other preferences that adversely affect your rights as a holder of our ADSs or ordinary shares. Debt financing, if available, could result in fixed payment obligations, and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, to acquire, sell or license intellectual property rights, to make capital expenditures, to declare dividends, or other operating restrictions. For example, our credit facility with Silicon Valley Bank and Kreos Capital V (UK) Limited, or the credit facility, requires us to seek consent for certain corporate transactions, dispositions, or incurrences of certain debt. If we raise additional funds through collaboration or licensing agreements, we may have to relinquish valuable rights to our technologies, future revenue streams, or product candidates or grant licenses on terms that may not be favorable to us. In addition, we could also be required to seek funds through arrangements with collaborators or others at an earlier stage than otherwise would be desirable. Raising additional capital through any of these or other means could adversely affect our business and the holdings or rights of our security holders, and may cause the market price of our ADSs or ordinary shares to decline.

We depend heavily on the success of BPS-804, AZD-9668, BCT-197, and BGS-649. We cannot give any assurance that any of these product candidates will receive regulatory approval, which is necessary before they can be commercialized. If we are unable to commercialize, whether on our own or through agreements with third parties, BPS-804, AZD-9668, BCT-197, or BGS-649, or experience significant delays in doing so, our ability to generate revenue and our financial condition will be adversely affected.

We do not currently generate any revenue from sales of any products, and we may never be able to develop or commercialize a marketable product. We have invested substantially all of our efforts and financial resources in the acquisition and development of BPS-804, AZD-9668, BCT-197, and BGS-649, and we do not have any other product candidates currently under development. Our ability to generate royalty and product revenues, which we do not expect will occur for at least the next several years, if ever, will depend heavily on the successful development and eventual commercialization of our current product candidates, if approved, which may never occur. Our current product candidates will require additional clinical development, management of clinical and manufacturing activities, regulatory approval in multiple jurisdictions, procurement of manufacturing supply, commercialization, substantial additional investment, and significant marketing efforts before we generate any revenue from product sales. For example, we intend to commence a Phase 2b/3 clinical trial of BPS-804, our most advanced product candidate, in children with OI in 2018. We are currently in communication with the EMA regarding the endpoints for the trial, and the EMA has not approved the pediatric investigation plan, or PIP, for this trial. While we anticipate approval of the PIP from the EMA, we may not receive such approval. In addition, the FDA may not approve our pediatric trial for BPS-804 in the future. Either of these occurrences would adversely affect the clinical development of BPS-804, which would adversely affect our commercialization plans.

We are not permitted to market or promote any product candidates in the United States, Europe, or other countries before we receive regulatory approval from the FDA, the EMA, or comparable foreign regulatory authorities, and we may never receive such regulatory approval for our current product candidates. We have not submitted a Biologics License application, or BLA, or a New Drug Application, or NDA, to the FDA; a Marketing Authorization Application, or MAA, to the EMA; or comparable applications to other regulatory authorities, and do not expect to be in a position to do so in the foreseeable future. The success of our current product candidates will depend on many factors, including the following:

- we may not be able to demonstrate that any of our current product candidates is safe and effective as a treatment for the targeted indications to the satisfaction of the applicable regulatory authorities;
- the applicable regulatory authorities may require additional clinical trials of our current product candidates, which would increase our costs and prolong development;
- the results of clinical trials of our current product candidates may not meet the level of statistical or clinical significance required by the applicable regulatory authorities for marketing approval;
- the applicable regulatory authorities may disagree with the number, design, size, conduct, or implementation of our planned and future clinical trials for our current product candidates;
- the contract research organizations, or CROs, that we retain to conduct clinical trials may take actions outside of our control that materially adversely impact clinical trials for our current product candidates;
- the applicable regulatory authorities may not find the data from clinical trials sufficient to demonstrate that the clinical and other benefits of our current product candidates outweigh their safety risks;
- the applicable regulatory authorities may disagree with our interpretation of data from our clinical trials or may require that we conduct additional trials;

- the applicable regulatory authorities may not accept data generated at our clinical trial sites;
- if we submit a BLA or NDA to the FDA, and it is reviewed by an advisory committee, the FDA may have difficulties scheduling an advisory committee meeting in a timely manner or the advisory committee may recommend against approval of our application or may recommend that the FDA require, as a condition of approval, additional pre-clinical studies or clinical trials, limitations on approved labeling, or distribution and use restrictions;
- the applicable regulatory authorities may require development of a risk evaluation and mitigation strategy, or REMS, as a condition of approval;
- the applicable regulatory authorities may identify deficiencies in the manufacturing processes or facilities of our third-party manufacturers;
- the applicable regulatory authorities may change its approval policies or adopt new regulations;
- through our clinical trials, we may discover factors that limit the commercial viability of our current product candidates or make the commercialization of any of our current product candidates unfeasible;
- if approved, acceptance of our current product candidates by patients, the medical community, and third-party payors; our ability to compete with other therapies to treat OI, AATD, AECOPD, or HH; continued acceptable safety profiles following approval of our current product candidates; and our ability to qualify for, maintain, enforce, and defend our intellectual property rights and claims.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or may not be able to successfully commercialize our current product candidates.

We cannot be certain that our current product candidates will be successful in clinical trials or receive regulatory approval. Further, our current product candidates may not receive regulatory approval even if they are successful in clinical trials. If we do not receive regulatory approvals for our current product candidates, we may not be able to continue our operations. Even if we successfully obtain regulatory approvals to manufacture and market our current product candidates, our revenues will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval and have commercial rights. If the markets for patient subsets that we are targeting are not as significant as we estimate, we may not generate significant revenues from sales of such products, if approved.

We plan to seek regulatory approval to commercialize our current product candidates both in the United States and the EU, and potentially in additional foreign countries. While the scope of regulatory approval is similar in many countries, to obtain separate regulatory approval in multiple countries requires us to comply with the numerous and varying regulatory requirements of such countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing and distribution, and we cannot predict success in these jurisdictions.

Our business may become subject to economic, political, regulatory and other risks associated with international operations.

Our business is subject to risks associated with conducting business internationally. We source research and development, manufacturing, consulting, and other services from companies based throughout the United States, the EU, and Switzerland, and we conduct our clinical trials in the United States, Canada, certain European countries, and other countries. Accordingly, our future results could be harmed by a variety of factors, including:

- economic weakness, including inflation, or political instability in particular non-U.K. economies and markets;
- differing regulatory requirements for drug approvals in non-U.K. countries;

- differing jurisdictions could present different issues for securing, maintaining, or obtaining freedom to operate for our intellectual property in such jurisdictions;
- potentially reduced protection for intellectual property rights;
- difficulties in compliance with non-U.K. laws and regulations;
- changes in non-U.K. regulations and customs, tariffs, and trade barriers;
- changes in non-U.K. currency exchange rates of the pound sterling and currency controls;
- changes in a specific country's or region's political or economic environment, including the implications of the United Kingdom's withdrawal from the EU;
- trade protection measures, import or export licensing requirements or other restrictive actions by U.K. or non-U.K. governments;
- differing reimbursement regimes and price controls in certain non-U.K. markets;
- negative consequences from changes in tax laws;
- compliance with tax, employment, immigration, and labor laws for employees living or traveling outside of the United Kingdom;
- workforce uncertainty in countries where labor unrest is more common than in the United Kingdom;
- difficulties associated with staffing and managing international operations, including differing labor relations;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters including earthquakes, typhoons, hurricanes, floods, and fires.

Exchange rate fluctuations may materially affect our results of operations and financial condition.

Owing to the international scope of our operations, fluctuations in exchange rates, particularly between the pound sterling and the U.S. dollar, the euro, or the Swiss Franc, may adversely affect us. Further, potential future revenue may be derived from multiple jurisdictions and in multiple currencies. As a result, our business and the price of our ADSs and ordinary shares may be affected by fluctuations in foreign exchange rates not only between the pound sterling and the U.S. dollar, but also the currencies of other countries, which may have a significant impact on our results of operations and cash flows from period to period. Currently, we do not have any exchange rate hedging arrangements in place.

The United Kingdom's withdrawal from the EU may have a negative effect on global economic conditions, financial markets and our business, which could reduce the price of our ADSs and ordinary shares.

Following the vote of a majority of the eligible members of the electorate in the United Kingdom to withdraw from the EU in a national referendum held on June 23, 2016, the U.K. government served notice under Article 50 of the Treaty of the European Union on March 29, 2017 to formally initiate a withdrawal process. The United Kingdom and the EU have a two-year period under Article 50 to negotiate the terms for withdrawal. Any extension of the negotiation period for withdrawal will require the consent of all of the remaining 27 member states.

The referendum and withdrawal have created significant uncertainty about the future relationship between the United Kingdom and the EU. Lack of clarity about future U.K. laws and regulations as the United Kingdom determines which EU-derived laws and regulations to replace or replicate as part of a withdrawal, including healthcare and pharmaceutical regulations; 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 decrease foreign direct investment in the United Kingdom, increase costs, depress economic activity, and restrict our access to capital. If the United Kingdom and the EU are unable to negotiate acceptable withdrawal terms or if other EU member states pursue withdrawal, barrier-free access between the United Kingdom and other EU member states or among the European economic area overall could be diminished or eliminated. These developments, or the perception that any of them could occur, have had and may continue to have a significant adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. Asset valuations, currency exchange rates, and credit ratings may be especially subject to increased market volatility. In addition, changes to U.K. border and immigration policy could occur as a result of the United Kingdom's withdrawal from the EU, affecting our ability to recruit and retain employees from outside the United Kingdom. Any of these factors could have a significant adverse effect on our business, financial condition, results of operations, and prospects.

Risks Related to Development, Clinical Testing, Manufacturing and Regulatory Approval

BPS-804, AZD-9668, BCT-197, and BGS-649 are in clinical development. Clinical drug development is a lengthy and expensive process with uncertain timelines and uncertain outcomes, and results of earlier studies and trials may not be predictive of future results. If clinical trials of our product candidates are prolonged or delayed, or if our product candidates fail to show the desired safety and efficacy in later stage clinical trials, we may be unable to obtain required regulatory approvals and be unable to commercialize our product candidates on a timely basis, or at all.

To obtain the requisite regulatory approvals to market and sell any of our product candidates, we must demonstrate through extensive clinical trials that such product candidates are safe and effective in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of pre-clinical studies and early-stage clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through pre-clinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Our future clinical trial results may not be successful.

We may experience delays in our ongoing clinical trials and we do not know whether planned clinical trials will begin on time, need to be redesigned, enroll patients on time or be completed on schedule, if at all. Our clinical trials can be delayed, suspended, or terminated for a variety of reasons, including the following:

- delays in or failure to obtain regulatory or ethics committee approval to commence a trial, for example, if we fail to obtain approval by the EMA for the PIP for BPS-804 or if we are unable to submit our proposed protocol to the FDA for a pediatric clinical trial for BPS-804;
- delays in or failure to reach agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- failure of our CROs to execute our trials in accordance with the clinical trial protocol; good laboratory, clinical, and manufacturing practices, or GxP; or other regulatory or contractual obligations;
- delays in or failure to obtain institutional review board, or IRB, approval, centrally or at each site;

- delays in or failure to recruit suitable patients to participate in a trial;
- failure to have patients complete a trial or return for post-treatment follow-up;
- for our rare disease product candidates, failure to enroll a sufficient number of patients with the rare disease and clinical trial design challenges such as, but not limited to, the off-label use of drugs to treat rare disease or where the most common treatment method has not been clinically tested or has been approved on the basis of a different endpoint and not directly tied to a clinical outcome study, for example, augmentation therapy for AATD;
- clinical sites deviating from trial protocol or dropping out of a trial or committing gross misconduct or fraud;
- adding new clinical trial sites;
- unexpected technical issues during manufacture, storage, or transport of our product candidates and the corresponding drug product;
- inability to manufacture sufficient quantities of our product candidates for use in clinical trials;
- third-party actions claiming infringement by our product candidates in clinical trials inside or outside of the United States and obtaining injunctions interfering with our progress;
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters including earthquakes, typhoons, hurricanes, floods, and fires;
- safety or tolerability concerns causing us or our collaborators, as applicable, to suspend or terminate a trial if we or our collaborators find that the participants are being exposed to unacceptable health risks;
- changes in regulatory requirements, policies, and guidelines;
- lower than anticipated retention rates of patients and healthy volunteers in clinical trials;
- unexpected technical issues with the equipment used to conduct clinical trials or analyze the results;
- our third-party research contractors failing to comply with regulatory requirements or to meet their contractual obligations to us in a timely manner, or at all;
- delays in establishing the appropriate dosage levels or frequency of dosing or treatment in clinical trials;
- difficulty in identifying the populations that we are trying to treat in a particular trial, which may delay enrollment and reduce the power of a clinical trial to detect statistically significant results;
- the quality or stability of our product candidates falling below acceptable standards for either safety or efficacy; and
- discoveries that may reduce the commercial viability of our product candidates.

We could encounter delays if a clinical trial is suspended or terminated by us, by the IRBs, centrally or at the institutions in which such trials are being conducted, by the Data Monitoring Committee or Data Safety Monitoring Board for such trial or by the FDA, the EMA, or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols; inspection of the clinical trial operations or trial site by the FDA, the EMA, or other regulatory authorities resulting in the imposition of a clinical hold; unforeseen safety issues or adverse side effects; failure to demonstrate a benefit from using a drug; failure of our clinical trials to demonstrate adequate efficacy and safety; changes in governmental regulations or administrative actions; or lack of adequate funding to continue the clinical trial.

A number of academic institutions are currently conducting and sponsoring clinical trials relating to our product candidate AZD-9668, including a clinical trial in patients with Type 2 diabetes and a clinical trial in patients with bronchiolitis obliterans. We do not control the design or administration of investigator-sponsored trials, and the investigator-sponsored trials could identify significant concerns

with respect to AZD-9668 that could impact our findings from our clinical trials, and adversely affect our ability to obtain marketing approval from the FDA or other applicable authorities. To the extent the results of these or other investigator-sponsored trials are inconsistent with, or different from, the results of our company-sponsored trials or raise concerns regarding AZD-9668, the FDA or a foreign regulatory authority may question the results of the company-sponsored trial, or subject such results to greater scrutiny than it otherwise would. In these circumstances, the FDA or such foreign regulatory authorities may require us to conduct additional clinical studies or submit additional clinical data, which could delay clinical development or marketing approval of AZD-9668.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA, the EMA, or another regulatory authority. The FDA, the EMA, or the other regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA, the EMA, or the other regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA, the EMA, or the other regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of our product candidates.

If we experience delays in the completion of any clinical trial of our product candidates or any clinical trial of our product candidates is terminated, the commercial prospects of our product candidates may be harmed, and our ability to generate product revenues from our product candidates, if any, will be delayed. Moreover, any delays in completing our clinical trials will increase our costs, slow down the development and approval process of our product candidates, and jeopardize our ability to commence product sales and generate revenue, if any. Significant clinical trial delays could also allow our competitors to bring products to market before we do or shorten any periods during which we have the exclusive right to commercialize our product candidates and could impair our ability to commercialize our product candidates. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

Clinical trials must be conducted in accordance with the laws and regulations of the FDA, EU rules and regulations and other applicable regulatory authorities' legal requirements, regulations or guidelines, and are subject to oversight by these governmental agencies and IRBs, centrally or at the institutions where the clinical trials are conducted. In addition, clinical trials must be conducted with supplies of our product candidates produced in compliance with the requirements of current good manufacturing practice, or cGMP, and other regulations. Furthermore, we rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials and while we have agreements governing their committed activities, we have limited influence over their actual performance. We depend on our collaborators and on medical institutions and CROs to conduct our clinical trials in compliance with good clinical practice, or GCP, requirements. To the extent our collaborators or the CROs fail to enroll participants for our clinical trials, fail to conduct the study to GCP standards, or are delayed for a significant time in the execution of trials, including achieving full enrollment, we may be affected by increased costs, program delays, or both. In addition, clinical trials that are conducted in countries outside the EU and the United States may subject us to further delays and expenses as a result of increased shipment costs, additional regulatory requirements, and the engagement of non-EU and non-U.S. CROs, as well as expose us to risks associated with clinical investigators who are unknown to the FDA or the EMA, and different standards of diagnosis, screening, and medical care.

Prior to our acquisition of BPS-804, AZD-9668, BCT-197, and BGS-649, we were not involved in the development of these product candidates and, as a result, we are dependent on Novartis and AstraZeneca having accurately reported the results and correctly collected and interpreted the data from all clinical trials conducted prior to our acquisition.

We were not involved in the development of our current product candidates prior to our acquisition of them. We licensed AZD-9668 from AstraZeneca only in October 2017, and we may experience difficulties in the transition of this product candidate from AstraZeneca to us, which may result in delays in our clinical trial, including regulatory approval of the trial, for AZD-9668, particularly if we do not receive all of the necessary clinical trial materials, information, reports, and data in a timely manner. For all of our current product candidates, we have had no involvement with or control over their pre-clinical and clinical development prior to our acquisition of them. We are dependent on Novartis and AstraZeneca having conducted their research and development in accordance with the applicable protocols and legal, regulatory, and scientific standards; having accurately reported the results of all clinical trials conducted prior to our acquisition; and having correctly collected and interpreted the data from these trials. To the extent Novartis or AstraZeneca have not complied, the clinical development, regulatory approval, or commercialization of our product candidates may be adversely affected.

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

From time to time, we may publish interim “top-line” or preliminary data from our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or “top-line” data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects.

Our product candidates may have serious adverse, undesirable, or unacceptable side effects which may delay or prevent marketing approval or lead to the withdrawal of approval after it has been granted. If such side effects are identified during the development of these product candidates or following approval, if any, we may need to abandon our development of these product candidates, the commercial profile of any approved label may be limited, or we may be subject to other significant negative consequences following marketing approval, if any.

Undesirable side effects that may be caused by BPS-804, AZD-9668, BCT-197, and BGS-649 could cause us or regulatory authorities to interrupt, delay or halt clinical trials, and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, the EMA, or other comparable foreign authorities. Each of our product candidates has completed one or more Phase 2 clinical trials. In the trials conducted prior to our ownership, the most common adverse events observed have been the following:

- for BPS-804, headache, influenza, arthralgia, and fatigue;
- for AZD-9668, headache, nasopharyngitis, and elevated levels of the liver enzymes aspartate aminotransferase and alanine aminotransferase;
- for BCT-197, a mild acne-like rash, dizziness, and headache; and
- for BGS-649, headache, nasal congestion, somnolence, and spontaneous penile erection.

Clinical development for all of these product candidates is ongoing. Results of our ongoing and future clinical trials, or results from clinical trials for other similar product candidates, could reveal a high and unacceptable severity and prevalence of adverse side effects. In such an event, our trials

could be suspended or terminated and the FDA, EMA, or other comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications.

For example, in the United States, the FDA has denied our request for a Type C meeting to discuss the initiation of a pediatric Phase 2b study for BPS-804 for the treatment of patients with severe OI. The FDA has cited that a serious cardiovascular safety concern exists in adults treated with sclerostin inhibitors that has yet to be resolved. We do not believe the FDA's concern is related to BPS-804. Given the undetermined risk/benefit assessment in adults, the FDA believes it is premature to conduct a study of sclerostin inhibitors in children. If this safety issue is resolved, we plan on submitting our proposed Phase 2b/3 study for BPS-804 in children with severe OI to the FDA to expand the proposed trial into the United States. We believe the FDA's position does not impact our ability to conduct our clinical development activities of BPS-804 in Europe and Canada for children with severe OI and our clinical development activities of BPS-804 in Europe, the United States and Canada for adults with OI.

Drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete a trial or result in potential product liability claims. Additionally, if any of our product candidates receives marketing approval and we or others later identify undesirable or unacceptable side effects caused by these product candidates, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of any such product and require us to take it off the market;
- regulatory authorities may require the addition of labeling statements, specific warnings, a contraindication, or field alerts to physicians and pharmacies;
- regulatory authorities may require a medication guide outlining the risks of such side effects for distribution to patients, or that we implement a REMS plan to ensure that the benefits of the product outweigh its risks;
- we may be required to change the way a product is administered, conduct additional clinical trials, or change the labeling of a product;
- we may be subject to limitations on how we may promote the product;
- sales of the product may decrease significantly;
- we may be subject to litigation or product liability claims; and
- our reputation may suffer.

Any of these events could prevent us or any collaborators from achieving or maintaining market acceptance of our product candidates or could substantially increase commercialization costs and expenses, which in turn could delay or prevent us from generating significant revenue from the sale of our product candidates.

We depend on enrollment of patients in our clinical trials for our product candidates. If we are unable to enroll patients in our clinical trials, or enrollment is slower than anticipated, in particular for our product candidates with rare disease indications, our research and development efforts could be adversely affected.

Successful and timely completion of clinical trials for our product candidates will require that we enroll a sufficient number of patient candidates. Trials may be subject to delays as a result of the limited number of patients with the diseases that these product candidates target, patient enrollment taking longer than anticipated, or patient withdrawal. Due to the small number of patients for any rare disease, it may be difficult for us to enroll a sufficient number of patients in our clinical trials for our

product candidates with indications in rare diseases or enrollment for these product candidates may take significantly longer than we anticipate. In addition, we will compete with other companies in enrolling the same limited population of patients, which may further challenge our ability to timely enroll patients in our clinical trials. It is estimated that OI, the target indication for BPS-804, affects a minimum of 20,000 people in the United States and approximately 32,000 people in Germany, Spain, France, Italy, and the United Kingdom, respectively. There are an estimated 50,000 and 60,000 persons in North America and Europe, respectively, with the genotypes that we intend to enroll in our clinical trials for AATD, the target indication for AZD-9668. Patient enrollment depends on many factors, including the size and nature of the patient population, eligibility criteria for the trial, the proximity of patients to clinical sites, the design of the clinical protocol, the availability of competing clinical trials, the availability of new drugs or biologics approved for the indication the clinical trial is investigating, and clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies. These factors may make it difficult for us to enroll enough patients to complete our clinical trials in a timely and cost-effective manner. Delays in the completion of any clinical trial of our product candidates will increase our costs, slow down our development and approval of our product candidates, and delay or potentially jeopardize our ability to commence product sales and generate revenue. In addition, some of the factors that cause or lead to a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

We may become exposed to costly and damaging liability claims, either when testing our product candidates in the clinic or at the commercial stage, and our product liability insurance may not cover all damages from such claims.

We are exposed to potential product liability and professional indemnity risks that are inherent in the development, manufacturing, marketing, and use of pharmaceutical products. Currently, we have no products that have been approved for commercial sale; however, the current and future use of our product candidates by us and any collaborators, in clinical trials, and the sale of these product candidates, if approved, in the future, may expose us to liability claims. These claims might be made by patients that use the product, healthcare providers, pharmaceutical companies, our collaborators, or others selling these product candidates. Any claims against us, regardless of their merit, could be difficult and costly to defend and could adversely affect the market for our product candidates or any prospects for commercialization of our product candidates. In addition, regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our product candidates;
- injury to our reputation;
- withdrawal of clinical trial participants;
- costs to defend related litigation;
- diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- regulatory investigation, product recalls or withdrawals, or labeling, marketing or promotional restrictions;
- loss of revenue; and
- the inability to commercialize or promote our product candidates.

Although the clinical trial process is designed to identify and assess potential side effects, it is always possible that a drug, even after regulatory approval, may exhibit unforeseen side effects. If our product candidates were to cause adverse side effects during clinical trials or after approval, we may be exposed to substantial liabilities. Physicians and patients may not comply with any warnings that identify known potential adverse effects and patients who should not use our product candidates.

Although we maintain product liability insurance for our product candidates, it is possible that our liabilities could exceed our insurance coverage. We intend to expand our insurance coverage to include the sale of commercial products if we obtain marketing approval for any of our product candidates. However, we may not be able to maintain insurance coverage at a reasonable cost or obtain insurance coverage that will be adequate to satisfy any liability that may arise. If a successful product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

The regulatory approval processes of the FDA, the EMA, and comparable foreign authorities are lengthy, time consuming, and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

The time required to obtain approval by the FDA, the EMA, and comparable foreign authorities is unpredictable, but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any of our product candidates and it is possible that none of our product candidates will obtain regulatory approval.

Our product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA, the EMA, or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA, the EMA, or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA, the EMA, or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA, the EMA, or comparable foreign regulatory authorities may disagree with our interpretation of data from pre-clinical studies or clinical trials or may find the data to be unacceptable;
- the data collected from clinical trials may not be sufficient to support the submission of a BLA or NDA in the United States, an MAA in the EU, or other comparable submission to obtain regulatory approval in other countries;
- the FDA, the EMA, or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA, the EMA, or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market any product candidates. The FDA, the EMA, and other regulatory authorities have substantial discretion in the approval process, and determining when or whether regulatory approval will be obtained for a product candidate. Even if we believe the data

collected from clinical trials are promising, such data may not be sufficient to support approval by the FDA, the EMA, or any other regulatory authority.

In addition, even if we were to obtain approval for any jurisdiction, regulatory authorities may approve our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our product candidates, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of such product candidate. Any of the foregoing scenarios could materially harm our commercial prospects and business.

Even if any of our product candidates obtains regulatory approval, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense. Additionally, any of our product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with such product candidate.

If the FDA, the EMA, or a comparable foreign regulatory authority approves any of our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, and recordkeeping for such product candidate will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, facility registration, and drug listing, as well as continued compliance with cGMP requirements for manufacturing, GDP, or good distribution practice, requirements for product distribution, and GCP requirements for any clinical trials that we conduct post-approval, all of which may result in significant expense and limit our ability to commercialize a product candidate. We and our contract manufacturers will also be subject to user fees and periodic inspection by the FDA, the EMA, and other regulatory authorities to monitor compliance with these requirements and the terms of any product approval we may obtain. In addition, any regulatory approvals that we receive for a product candidate may also be subject to limitations on the approved indicated uses for which such product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of such product.

If there are changes in the application of legislation or regulatory policies, or if problems are discovered with a product or the manufacture of a product, or if we or one of our distributors, licensees, or co-marketers fails to comply with regulatory requirements, the regulatory authorities could take various actions. These include imposing fines on us, imposing restrictions on our product or its manufacture, and requiring us to recall or remove a product from the market. The regulatory authorities could also suspend or withdraw our marketing authorizations, or require us to conduct additional clinical trials, change our product labeling, or submit additional MAAs. If any of these events occurs, our ability to sell our product may be impaired, and we may incur substantial additional expense to comply with regulatory requirements.

The policies of the FDA, the EMA, and other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit, or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature, or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States, the United Kingdom, Europe, or other jurisdictions. For example, the current U.S. presidential 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 oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. Notably, in January 2017, an Executive

Order was issued directing all executive agencies, including the FDA, that, for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency 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 in February 2017, the administration indicated that the “two-for-one” provisions may apply not only to agency regulations, but also to significant agency guidance documents, and in September 2017, the FDA published notices in the Federal Register soliciting broad public comment to identify regulations that could be modified in compliance with these Executive Orders. 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 restrictions on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted. In addition, if we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

Even if we obtain marketing approval of any of our product candidates in a major pharmaceutical market such as the United States or the EU, we may not be able to obtain approval or commercialize that product candidate in other markets, which would limit our ability to realize its full market potential.

In order to market any products in a country or territory, we must establish and comply with numerous and varying regulatory requirements of such country or territory regarding safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking regulatory approvals in multiple markets may require additional pre-clinical studies or clinical trials, which would be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our product candidates in those countries. Satisfying these and other regulatory requirements is costly, time consuming, uncertain, and subject to unanticipated delays. In addition, our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. We currently do not have any product candidates approved for sale in the United States, the EU, or any other markets, and our management team does not have experience in obtaining regulatory approval in markets outside of the United States and the EU. If we seek regulatory approval in other markets and fail to obtain marketing approval in those markets or, if our product candidates are approved in such markets but we fail to maintain such approvals, our ability to realize the full market potential of our product candidates will be compromised.

Our employees and independent contractors, including principal investigators, CROs, CMOs, consultants, vendors, and any other third parties we may engage in connection with the development and commercialization of our product candidates may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could adversely affect our business.

Misconduct by our employees and independent contractors, including principal investigators, CROs, CMOs, consultants, vendors, and any other third parties we may engage in connection with the development and commercialization of our product candidates, could include intentional, reckless, or negligent conduct or unauthorized activities that violate: (i) the laws and regulations of the FDA, the EMA

and other similar regulatory authorities, including those laws that require the reporting of true, complete and accurate information to such authorities; (ii) manufacturing standards; (iii) data privacy, security, fraud and abuse, and other healthcare laws and regulations; or (iv) laws that require the reporting of true, complete, and accurate financial information and data. Specifically, sales, marketing, and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing, and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements. Activities subject to these laws could also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creation of fraudulent data in pre-clinical studies or clinical trials, or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with such laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. 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 civil, criminal and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid, other U.S. federal healthcare programs or healthcare programs in other jurisdictions, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

Risks Related to Healthcare Laws and Other Legal Compliance Matters

Enacted and future healthcare legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and may affect the prices we may set.

In the United States, EU and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA, those of greatest importance to the pharmaceutical and biotechnology industries include the following:

- an annual, non-deductible fee payable by any entity that manufactures or imports certain branded prescription drugs and biologic agents (other than those designated as orphan drugs), which is apportioned among these entities according to their market share in certain government healthcare programs;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- new requirements to report certain financial arrangements with physicians and teaching hospitals, including reporting "transfers of value" made or distributed to prescribers and other healthcare providers and reporting investment interests held by physicians and their immediate family members;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and

generic drugs, respectively, and capped the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price, or AMP;

- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs and biologics, including our product candidates, that are inhaled, infused, instilled, implanted, or injected;
- extension of a manufacturer's Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- 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;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- creation of the Independent Payment Advisory Board, which, once empaneled, will have the authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs and those recommendations could have the effect of law unless overruled by a supermajority vote of Congress;
- establishment of a Center for Medicare Innovation at the Centers for Medicare & Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending;
- expansion of the entities eligible for discounts under the Public Health Service program; and
- a licensure framework for follow on biologic products.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of any certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. The Trump administration has also announced that it will discontinue the payment of cost-sharing reduction, or CSR, payments to insurance companies until Congress approves the appropriation of funds for the CSR payments. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. A bipartisan bill to appropriate funds for CSR payments has been introduced in the Senate, but the future of that bill is uncertain. 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, each chamber of Congress have put forth multiple bills this year designed to repeal or repeal and replace portions of the ACA. Although none of these measures have been enacted by Congress to date, Congress may consider other legislation to repeal and replace elements of the ACA. Congress will likely consider other legislation to replace elements of the ACA. We continue to evaluate the effect that the ACA and its possible repeal and replacement has on our business. It is uncertain the extent to which any such changes may impact our business or financial condition.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2025 unless additional action is taken by Congress. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which,

among other things, further reduced Medicare payments to several types of 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. These new laws or any other similar laws introduced in the future may result in additional reductions in Medicare and other health care funding, which could negatively affect our customers and accordingly, our financial operations.

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Individual states in the United States have also become 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. Legally-mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition, and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates or put pressure on our product pricing.

In the EU, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize our product candidates, if approved.

In markets outside of the United States and EU, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

We cannot predict the likelihood, nature, or extent of government regulation that may arise from future legislation or administrative action in the United States, the EU, or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain

regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations, and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations, and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell, and distribute our product candidates, if approved. Such laws include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving, or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order, or recommendation of, any good, facility, item, or service, for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. The U.S. federal Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers on the other hand;
- the U.S. federal false claims and civil monetary penalties laws, including the civil False Claims Act, or FCA, which, among other things, impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes “any request or demand” for money or property presented to the federal government. In addition, manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims;
- the U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services; similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose, among other things, specified requirements relating to the privacy, security and transmission of

individually identifiable health information without appropriate authorization by covered entities subject to the rule, such as health plans, healthcare clearinghouses and healthcare providers as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions;

- the U.S. federal Food, Drug and Cosmetic Act, or FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics, and medical devices;
- the U.S. Public Health Service Act, which prohibits, among other things, the introduction into interstate commerce of a biological product unless a biologics license is in effect for that product;
- the U.S. federal legislation commonly referred to as the Physician Payments Sunshine Act, enacted as part of the ACA, and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics, and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to the government information related to certain payments and other transfers of value to physicians and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members;
- analogous U.S. state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales, and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and
- similar healthcare laws and regulations in the EU and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available under such laws, it is possible that some of our business activities could be subject to challenge under one or more of such laws. The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Ensuring that our current and future internal operations and business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance 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 the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to the imposition of civil, criminal and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, individual imprisonment,

contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment, which could affect our ability to operate our business. Further, defending against any such actions can be costly, time-consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

Due to our international operations, 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.

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 by, or providing prohibited payments or anything else of value 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 any of our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We also are subject to other laws and regulations governing any international operations, including regulations administered by the governments of the United Kingdom and the United States, and authorities in the EU, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, or, collectively, 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. 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, even if it is ultimately determined that we did not violate such laws, could be costly and time-consuming, require significant personnel resources, and harm our reputation.

We will seek to build and continuously improve our systems of internal controls and to remedy any weaknesses identified. There can be no assurance, however, that the policies and procedures will be followed at all times or effectively detect and prevent violations of the applicable laws by one or more of our employees, consultants, agents, or collaborators and, as a result, we could be subject to fines, penalties, or prosecution.

Risks Related to Commercialization

We operate in a highly competitive and rapidly changing industry, which may result in others acquiring, developing, or commercializing competing products before or more successfully than we do.

The biopharmaceutical and pharmaceutical industries are highly competitive and subject to significant and rapid technological change. Our success is highly dependent on our ability to acquire, develop, and obtain marketing approval for new products on a cost-effective basis and to market them successfully. If BPS-804, AZD-9668, BCT-197, or BGS-649 is approved, we will face intense competition from a variety of businesses, including large, fully integrated pharmaceutical companies, specialty pharmaceutical companies, and biopharmaceutical companies in the United States, Europe, and other jurisdictions. These organizations may have significantly greater resources than we do and conduct similar research; seek patent protection; and establish collaborative arrangements for research, development, manufacturing, and marketing of products that may compete with our product candidates.

We expect to face competition for each of our current product candidates, including specifically:

- We consider BPS-804's current closest potential competitors in development for the treatment of OI to be denosumab (Prolia) from Amgen Inc., or Amgen, an anti-resorptive agent, and UCB S.A., or UCB, and Amgen's anti-sclerostin antibody, romosozumab. Blosozumab, an anti-sclerostin antibody, was in Phase 1 development for osteoporosis by Eli Lilly and Company, or Eli Lilly; however, we are not aware of any ongoing clinical trials for this product candidate and we do not believe this product candidate remains under active development. Additionally, Bone Therapeutics SA, or Bone Therapeutics, is developing osteoblastic cell therapy products. Baylor College of Medicine is also conducting a Phase 1 open label trial of fresolimumab, a TGF- β inhibitor, in adult OI patients.
- We consider AZD-9668's current closest potential competitors for the treatment of severe AATD to be alpha1-proteinase inhibitors that are administered intravenously in AAT augmentation therapy. Currently, there are four inhibitors on the market in the United States: Prolastin-C from Grifols, S.A., or Grifols, Aralast from Shire plc, or Shire, Zemaira from CSL Limited, or CSL, and Glassia from Kamada Ltd., or Kamada. Kamada is also investigating an inhaled version of augmentation therapy and Apic Bio, Inc., or Apic Bio and Adverum Biotechnologies, Inc., or Adverum, are in the early stages of developing gene-therapy approaches for AATD. Santhera Pharmaceuticals, or Santhera, has in-licensed an inhaled neutrophil elastase inhibitor and is planning a multiple ascending dose study, with the initial indication targeted being cystic fibrosis.
- For BCT-197, although we are not aware of any approved therapies for the treatment of AECOPD, there are a wide range of established therapies available for COPD as well as a number of products in development, with Verona Pharma plc, or Verona Pharma, GlaxoSmithKline plc, or GlaxoSmithKline, and AstraZeneca each conducting Phase 2 trials on drugs for the treatment of COPD.
- We consider BGS-649's current closest potential competitors for the treatment of HH to be testosterone replacement therapies, or TRT. These include Androgel from AbbVie Inc., or Abbvie, and Eli Lilly's Axiron, both administered transdermally by applying a gel formulation, which are approved in the United States and Europe, and Andriol from Merck & Co., Inc., or Merck, an oral testosterone therapy, which is approved in Europe but not in the United States. There are also other approved TRT products that are administered via injection and other oral TRTs that are still in the development or registration stages, such as JATENZO from Clarus Therapeutics, Inc., or Clarus, and TLANDO from Lipocine, Inc., or Lipocine. The FDA held Advisory Committee meetings in January 2018 for JATENZO and TLANDO. Lipocine has a Prescription Drug User Fee Act, or PDUFA, date of May 8, 2018. In addition, Repros

Therapeutics, Inc., or Repros, is developing a selective estrogen receptor modulator and the EMA's Committee for Medicinal Products for Human Use, or CHMP, adopted a negative opinion recommending the refusal of its marketing authorization. In December 2017, Allergan announced the acquisition of Repros.

We also anticipate that new companies will enter these markets in the future. If we successfully develop and commercialize any of BPS-804, AZD-9668, BCT-197, or BGS-649, they will compete with existing therapies and new therapies that may become available in the future. The highly competitive nature of and rapid technological changes in the biopharmaceutical and pharmaceutical industries could render our product candidates obsolete, less competitive, or uneconomical. Our competitors may, among other things:

- have significantly greater name recognition, financial, manufacturing, marketing, drug development, technical, and human resources than we do, and future mergers and acquisitions in the biopharmaceutical and pharmaceutical industries may result in even more resources being concentrated in our competitors;
- develop and commercialize products that are safer, more effective, less expensive, more convenient, or easier to administer, or have fewer or less severe effects, or in certain cases could be curative for the condition;
- obtain quicker regulatory approval;
- establish superior proprietary positions covering our products and technologies;
- implement more effective approaches to sales and marketing; or
- form more advantageous strategic alliances.

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; and in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer or less severe side effects, are more convenient or are less expensive than our product candidates. Our competitors may also obtain FDA, EMA, or other regulatory approval for their product candidates more rapidly than we may obtain approval for ours, which could result in our competitors establishing or strengthening their market position before we are able to enter the market.

We have obtained orphan drug designation for BPS-804 for the treatment of OI in the United States and EU, but we may be unable to obtain orphan drug designation for AZD-9668 or any future product candidates, and we may be unable to obtain or maintain the benefits associated with orphan drug designation, including the potential for orphan drug exclusivity, for BPS-804 or any other product candidate for which we obtain orphan drug designation.

Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, defined as one occurring in a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the EU, the EMA's Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the EU. Additionally, designation is granted for products intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating, or serious and chronic condition when, without incentives, it is unlikely that sales of the drug in the EU would be sufficient to justify the necessary investment in developing the drug or biological product or where there is no satisfactory

method of diagnosis, prevention, or treatment, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition.

In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax credits for qualified clinical testing, and user-fee waivers. In addition, if a product receives the first FDA approval of that drug for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the rare disease or condition. Under the FDA's regulations, the FDA will deny orphan drug exclusivity to a designated drug upon approval if the FDA has already approved another drug with the same active ingredient for the same indication, unless the drug is demonstrated to be clinically superior to the previously approved drug. In the EU, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity following approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the drug is sufficiently profitable not to justify maintenance of market exclusivity. In the EU, a marketing authorization for an orphan designated product will not be granted if a similar drug has been approved in the EU for the same therapeutic indication, unless the applicant can establish that its product is safer, more effective or otherwise clinically superior. A similar drug is a product containing a similar active substance or substances as those contained in an already authorized product. Similar active substance is defined as an identical active substance, or an active substance with the same principal molecular structural features (but not necessarily all of the same molecular features) and which acts via the same mechanism.

We have obtained orphan drug designation from the FDA and EMA for BPS-804 for the treatment of OI, and we plan to seek orphan drug designation for AZD-9668 and future product candidates. Even with orphan drug designation, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products, which could prevent us from marketing our product candidates if another company is able to obtain orphan drug exclusivity before we do. In addition, exclusive marketing rights in the United States may be unavailable if we seek approval for an indication broader than the orphan-designated indication or may be lost in the United States if the FDA later determines that the request for designation was materially defective or if we are unable to assure sufficient quantities of the drug to meet the needs of patients with the rare disease or condition following approval. Further, even if we obtain orphan drug exclusivity, that exclusivity may not effectively protect our product candidates from competition because different drugs with different active moieties can be approved for the same condition. In addition, the FDA and the EMA can subsequently approve products with the same active moiety for the same condition if the FDA or the EMA concludes that the later drug is safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. In addition, while we intend to seek orphan drug designation for other existing and future product candidates, including AZD-9668, we may never receive such designations.

There have been legal challenges to aspects of the FDA's regulations and policies concerning the exclusivity provisions of the Orphan Drug Act, and future challenges could lead to changes that affect the protections afforded our product candidates in ways that are difficult to predict. In 2014, a U.S. district court invalidated the FDA's denial of orphan exclusivity to an orphan designated drug, which the FDA had based on its determination that the drug was not proven to be clinically superior to a

previously approved “same drug.” In response to the decision, the FDA released a policy statement stating that the court’s decision is limited to the facts of that particular case and that the FDA will continue to deny orphan drug exclusivity to a designated drug upon approval if the drug is the “same” as a previously approved drug, unless the drug is demonstrated to be clinically superior to that previously approved drug. Since then, similar legal challenges have been initiated against the FDA for its denial of orphan drug exclusivity to other designated drugs, and in 2017, Congress amended the Orphan Drug Act to require a demonstration of clinical superiority upon approval as a condition of receiving orphan drug exclusivity when another “same drug” has already been approved for the same indication. In the future, there is the potential for additional legal challenges to the FDA’s orphan drug regulations and policies, and it is uncertain how ongoing and future challenges might affect our business.

We may seek and fail to obtain breakthrough therapy designation by the FDA for BPS-804 or AZD-9668, or any future product candidates or access to the PRIME scheme by the EMA for AZD-9668 or any future product candidates. Even if we obtain such designation or access, the designation or access may not lead to faster development or regulatory review or approval, and it does not increase the likelihood that our product candidates will receive marketing approval.

In 2012, the FDA established a breakthrough therapy designation which is intended to expedite the development and review of product candidates that treat serious or life-threatening diseases where preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement over existing therapies on one or more clinically-significant endpoints, such as substantial treatment effects observed early in clinical development. The designation of a product candidate as a breakthrough therapy provides potential benefits that include but are not limited to more frequent meetings with the FDA to discuss the development plan for the product candidate and ensure collection of appropriate data needed to support approval; more frequent written correspondence from the FDA about such things as the design of the proposed clinical trials and use of biomarkers; intensive guidance on an efficient drug development program, beginning as early as Phase 1; organizational commitment involving senior managers; and eligibility for rolling review and priority review. Drugs and biologics designated as breakthrough therapies by the FDA are also eligible for accelerated approval. Similarly, the EMA has established the PRIME scheme to expedite the development and review of product candidates that show a potential to address to a significant extent an unmet medical need, based on early clinical data. In November 2017, BPS-804 was admitted to the PRIME scheme of the EMA.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. We cannot be sure that our evaluation of our product candidates as qualifying for breakthrough therapy designation will meet the FDA’s expectations. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review, or approval compared to product candidates considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. Similarly, access to the PRIME scheme is at the discretion of the EMA, and we cannot be sure that AZD-9668 or any future product candidates will be granted access to the scheme; that participation in the scheme will result in expedited regulatory review or approval of our product candidates; or that access to the scheme, once granted, will not be revoked.

The successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish adequate coverage, reimbursement levels, and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

The availability and adequacy of coverage and reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers, and other third-party payors are essential for most patients to be able to afford prescription medications such as our product candidates, assuming approval. Our ability to achieve acceptable levels of coverage and reimbursement for products by governmental authorities, private health insurers, and other organizations will have an effect on our ability to successfully commercialize our product candidates. Assuming we obtain coverage for our product candidates by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the United States, the EU, or elsewhere will be available for our product candidates or any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future.

Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs or biologics when an equivalent generic drug, biosimilar, or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidates as substitutable and only offer to reimburse patients for the less expensive product. Even if we show improved efficacy or improved convenience of administration with our product candidates, pricing of existing drugs may limit the amount we will be able to charge for our product candidates. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in our product candidates. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates, and may not be able to obtain a satisfactory financial return on our product candidates.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered. The Medicare and Medicaid programs increasingly are used as models in the United States for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs and biologics. Some third-party payors may require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases at short notice, and we believe that changes in these rules and regulations are likely.

Our operations are also subject to extensive governmental price controls and other market regulations in the United Kingdom and other countries outside of the United States, and we believe the increasing emphasis on cost-containment initiatives in European and other countries have and will

continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our product candidates may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of our product candidates due to the trend toward managed health care, the increasing influence of health maintenance organizations, and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and biologics and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products.

Our existing and future product candidates may not gain market acceptance, in which case our ability to generate product revenues will be compromised.

Even if the FDA, the EMA, or any other regulatory authority approves the marketing of our product candidates, whether developed on our own or with a collaborator, physicians, healthcare providers, patients, or the medical community may not accept or use our product candidates. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenue or any profits from operations. The degree of market acceptance of our product candidates will depend on a variety of factors, including:

- the timing of market introduction;
- the number and clinical profile of competing products;
- the clinical indications for which our product candidates are approved;
- our ability to provide acceptable evidence of safety and efficacy;
- the prevalence and severity of any side effects;
- relative convenience and ease of administration;
- cost-effectiveness;
- marketing and distribution support;
- availability of adequate coverage, reimbursement, and adequate payment from health maintenance organizations and other insurers, both public and private; and
- other potential advantages over alternative treatment methods.

If our product candidates fail to gain market acceptance, our ability to generate revenues will be adversely affected. Even if our product candidates achieve market acceptance, the market may prove not to be large enough to allow us to generate significant revenues.

We intend to directly commercialize our product candidates for rare diseases and to seek strategic relationships with third parties for the commercialization of our product candidates for specialty diseases. If we are unable to develop our own sales, marketing, and distribution capabilities or enter into business arrangements, we may not be successful in commercializing our product candidates.

We have no marketing, sales, or distribution capabilities and we have no experience with marketing, selling or distributing pharmaceutical products. We also have no strategic relationships in

place for the commercialization of our product candidates. For BPS-804 and AZD-9668, if approved, and for any future product candidates for rare diseases, we intend either to establish a sales and marketing organization with technical expertise and supporting distribution capabilities to commercialize these product candidates in major markets or potentially to outsource aspects of these functions to third parties. We may not be able to hire a sales force that is sufficient in size or has adequate expertise in OI, AATD, or other relevant rare diseases. Any failure or delay in the development of our internal sales, marketing, and distribution capabilities would adversely impact the commercialization of these product candidates.

For BCT-197 and BGS-649, and for any future product candidates for specialty diseases, we intend to enter into strategic relationships for the commercialization of these product candidates. These arrangements may also include the late-stage clinical development of a product candidate. As a result, our revenue from product sales may be lower than if we directly marketed or sold these product candidates. In addition, any revenue we receive will depend upon the terms of such arrangement, which may not be as favorable to us as possible, and the efforts of the other party, which may not be adequate or successful and are likely to be beyond our control. If we are unable to enter into these arrangements on acceptable terms or at all, we may not be able to successfully commercialize these product candidates.

These commercialization approaches are expensive and time consuming, and some or all of the costs associated with such efforts may be incurred in advance of any approval of our product candidates. If we are not successful in commercializing our product candidates, either on our own or through strategic relationships with third parties, our future product revenue will suffer and we may incur significant losses.

Any product candidates for which we intend to seek approval as biologic products in the United States may face competition sooner than anticipated.

In the United States, the Biologics Price Competition and Innovation Act of 2009, or BPCIA, created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own pre-clinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity, and potency of their product. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when processes intended to implement the BPCIA may be fully adopted by the FDA, any such processes could adversely affect the future commercial prospects for any biological products.

We believe that if any product candidate is approved as a biological product under a BLA, it should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. Moreover, the extent to which a biosimilar, once approved, will be substituted for a reference product in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

In the EU, MAAs for products that are biosimilar to an already authorized biological product, the so-called reference product, can rely on the safety and efficacy data contained in the dossier of the reference product. To qualify as a biosimilar product the marketing authorization applicant must demonstrate, through comprehensive comparability studies with the reference product, that its product is: (i) highly similar to the reference product notwithstanding the natural variability inherent to all biological medicines, and (ii) that there are no clinically meaningful differences between the biosimilar and the reference product in terms of safety, quality, and efficacy. Biosimilars can only be authorized for use after the period of exclusivity of the reference biological medicine has expired. In general, this means that the biological reference product must have been authorized for at least 10 years before a biosimilar can be made available by another company.

Risks Related to Our Dependence on Third Parties

We rely, and expect to continue to rely, on third parties, including independent investigators and CROs, to conduct our clinical trials. If these CROs do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates, or such approval or commercialization may be delayed, and our business could be substantially harmed.

We have relied upon and plan to continue to rely upon independent clinical investigators and CROs to conduct our clinical trials and to monitor and manage data for our ongoing clinical programs. We rely on these parties for the execution of our clinical trials and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies and trials is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities. We and our independent investigators and CROs are required to comply with GxP requirements, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area, and comparable foreign regulatory authorities for all of our product candidates in clinical development. Regulatory authorities enforce these GxP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we fail to exercise adequate oversight over any of our independent investigators or CROs or if we or any of our independent investigators or CROs fail to comply with applicable GxP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the EMA, or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon a regulatory inspection of us or our independent investigators or CROs, such regulatory authority will determine that any of our clinical trials complies with GxP requirements. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

Further, these independent investigators and CROs are not our employees and we are not able to control, other than by contract, the amount of resources, including time, which they devote to our clinical trials. If our independent investigators or CROs fail to devote sufficient resources to the development of our product candidates, or if their performance is substandard, it may delay or compromise the prospects for approval and commercialization of our product candidates. In addition, the use of third-party service providers requires us to disclose our proprietary information to these parties, which could increase the risk that this information is misappropriated.

If any of our relationships with our independent investigators or CROs terminate, we may not be able to enter into arrangements with alternative independent investigators or CROs or to do so on commercially reasonable terms. Switching or adding additional investigators or CROs involves additional cost and potential delays and requires our management's time and focus. In addition, there is a natural transition period when a new independent investigator or CRO commences work. As a

result, delays could occur, which could materially impact our ability to meet our desired clinical development timelines.

If our independent investigators or CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to a failure to adhere to our clinical protocols, regulatory requirements, or for other reasons, our clinical trials may be extended, delayed, or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

We currently rely on third-party contract manufacturing organizations, or CMOs, for the production of clinical supply of our product candidates and intend to rely on CMOs for the production of commercial supply of our product candidates, if approved. Our dependence on CMOs may impair the development of our product candidates and may impair the commercialization of our product candidates, which would adversely impact our business and financial position.

We have limited personnel with experience in manufacturing, and we do not own facilities for manufacturing our product candidates. Instead, we rely on and expect to continue to rely on CMOs for the supply of cGMP grade clinical trial materials and commercial quantities of our product candidates, if approved. Reliance on CMOs may expose us to more risk than if we were to manufacture our product candidates ourselves. Novartis previously provided clinical supplies for BPS-804, BCT-197, and BGS-649 and certain transitional services. We have moved the clinical supply manufacture for these product candidates to CMOs. We also intend to contract with CMOs for the clinical supply of AZD-9668.

The facilities used to manufacture our product candidates must be approved by the FDA, the EMA, and comparable foreign authorities pursuant to inspections. While we provide oversight of manufacturing activities, we do not and will not control the execution of our manufacturing activities by, and are or will be essentially dependent on, our CMOs for compliance with cGMP requirements for the manufacture of our product candidates. As a result, we are subject to the risk that our product candidates may have manufacturing defects that we have limited ability to prevent. If a CMO cannot successfully manufacture material that conforms to our specifications and the regulatory requirements, we will not be able to secure or maintain regulatory approval for the use of our investigational medicinal products in clinical trials, or for commercial distribution of our product candidates, if approved. In addition, we have limited control over the ability of our CMOs to maintain adequate quality control, quality assurance and qualified personnel. If the FDA, the EMA or comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would delay our development program and significantly impact our ability to develop, obtain regulatory approval for or commercialize our product candidates, if approved. In addition, any failure to achieve and maintain compliance with these laws, regulations and standards could subject us to the risk that we may have to suspend the manufacturing of our product candidates or that obtained approvals could be revoked. Furthermore, CMOs may breach existing agreements they have with us because of factors beyond our control. They may also terminate or refuse to renew their agreement at a time that is costly or otherwise inconvenient for us. In addition, the manufacture of biologics involves expensive and complex processes and worldwide capacity at CMOs for the manufacture of biologics is currently limited. In addition, Novartis has a contractual right to approve or reject any additional CMO we wish to engage for the manufacture of BPS-804. If we were unable to find an adequate CMO or another acceptable solution in time, our clinical trials could be delayed or our commercial activities could be harmed.

We rely on and will continue to rely on CMOs to purchase from third-party suppliers the raw materials necessary to produce our product candidates. We do not and will not have control over the process or timing of the acquisition of these raw materials by our CMOs. Moreover, we currently do not have any agreements for the production of these raw materials. Supplies of raw material could be interrupted from time to time and we cannot be certain that alternative supplies could be obtained within a reasonable timeframe, at an acceptable cost, or at all. In addition, a disruption in the supply of raw materials could delay the commercial launch of our product candidates, if approved, or result in a shortage in supply, which would impair our ability to generate revenues from the sale of our product candidates. Growth in the costs and expenses of raw materials may also impair our ability to cost effectively manufacture our product candidates. There are a limited number of suppliers for the raw materials that we may use to manufacture our product candidates and we may need to assess alternate suppliers to prevent a possible disruption of the manufacture of our product candidates.

Finding new CMOs or third-party suppliers involves additional cost and requires our management's time and focus. In addition, there is typically a transition period when a new CMO commences work. Although we generally do not begin a clinical trial unless we believe we have on hand, or will be able to obtain, a sufficient supply of our product candidates to complete the clinical trial, any significant delay in the supply of our product candidates or the raw materials needed to produce our product candidates, could considerably delay conducting our clinical trials and potential regulatory approval of our product candidates.

As part of their manufacture of our product candidates, our CMOs and third-party suppliers are expected to comply with and respect the proprietary rights of others. If a CMO or third-party supplier fails to acquire the proper licenses or otherwise infringes the proprietary rights of others in the course of providing services to us, we may have to find alternative CMOs or third-party suppliers or defend against claims of infringement, either of which would significantly impact our ability to develop, obtain regulatory approval for or commercialize our product candidates, if approved.

We intend to enter into strategic relationships with third parties, based on a product-by-product assessment, for the development of some of our product candidates. If we fail to enter into these arrangements, our business, development and commercialization prospects could be adversely affected.

Our development program for our product candidates, particularly as we enter late-stage development, will require substantial additional funds. We currently intend to enter into a strategic relationship with a pharmaceutical or biopharmaceutical company for the continued development of BCT-197 and potentially for BGS-649, and we may take the same approach for other product candidates.

These types of development arrangements are complex and time-consuming to negotiate and document, and we may not be able to enter into these arrangements on favorable terms or at all. In addition, we face significant competition from other companies in seeking out these types of development arrangements. If we are successful in entering into such an arrangement, we will be subject to other risks, including our inability to control the amount of time and resources the third party will dedicate to our product candidates, financial or other difficulties experienced by such third party, relinquishing important rights to such third party, and the arrangement failing to be profitable to us.

If we are unable to enter into an appropriate arrangement for the development of BCT-197 and potentially for BGS-649 or other product candidates, we may have to reduce, delay, or terminate the development of such product candidates. If we, instead, decide to increase our expenditures to fund development activities on our own, we will need to obtain additional capital, which may not be available to us on acceptable terms or at all. As a result, our business may be substantially harmed.

Risks Related to Intellectual Property and Data Protection

We rely on patents and other intellectual property rights to protect our product candidates, the obtainment, enforcement, defense and maintenance of which may be challenging and costly. Failure to enforce or protect these rights adequately could harm our ability to compete and impair our business.

Our commercial success depends in part on obtaining and maintaining patents and other forms of intellectual property protection, for example, for compositions-of-matter of our product candidates, formulations of our product candidates, polymorphs, salts and analogs of our product candidates, methods used to manufacture our product candidates, methods for manufacturing of the final drug products, and methods of using our product candidates for the treatment of the indications we are developing or plan to develop, or on in-licensing such rights. Our patent portfolio comprises patents and patent applications which cover our BPS-804, BCT-197, and BGS-649 product candidates acquired or exclusively licensed from Novartis, and patents and patent applications which cover our AZD-9668 product candidate exclusively licensed (with the option to purchase) from AstraZeneca. The assignments of those patents and patent applications which we acquired from Novartis have been registered with the relevant authorities in key territories and the exclusive licenses from AstraZeneca are in the process of being registered with the relevant authorities in key territories. There is no assurance that our pending patent applications will result in issued patents, or if issued as patents, will include claims with sufficient scope of coverage to protect our product candidates, or that any pending patent applications will be issued as patents in a timely manner. Failure to obtain, maintain or extend adequate patent and other intellectual property rights could adversely affect our ability to develop and market our product candidates, resulting in harm to our business.

The patent prosecution process is expensive and time-consuming. We or our licensors may not be able to prepare, file and prosecute all necessary or desirable patent applications for a commercially reasonable cost or in a timely manner or in all jurisdictions. It is also possible that we or our licensors may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Moreover, depending on the terms of any future in-licenses to which we may become a party, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology in-licensed from third parties. Therefore, these patents and patent applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

Further, the issuance, scope, validity, enforceability, and commercial value of our and our current or future licensors' patent rights are highly uncertain. Our and our licensors' pending and future patent applications may not result in issued patents that protect our technology or product candidates, in whole or in part, or that effectively prevent others from commercializing competitive technologies and products. The patent examination process may require us or our licensors to narrow the scope of the claims of our or our licensors' pending and future patent applications, which may limit the scope of patent protection that may be obtained. We cannot assure that all of the potentially relevant prior art relating to our patents and patent applications has been found. If such prior art exists, it can invalidate a patent or prevent a patent application from being issued as a patent. Even if patent applications do successfully issue as patents and even if such patents cover our product candidates, third parties may initiate an opposition, interference, reexamination, post grant review, inter partes review, nullification or derivation action in courts or before patent offices, or similar proceedings challenging the validity, enforceability, or scope of such patents, which may result in the patent claims being narrowed or invalidated. Our and our licensors' patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such patent applications, and then only to the extent the issued claims cover the technology.

Because patent applications are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we or our licensors were the first to file any patent application related to our product candidates. Furthermore, in the United States, if third parties have filed such patent applications on or before March 15, 2013, the date on which the United States changed from a first to invent to a first to file patent system, an interference proceeding can be initiated by such third parties to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. If third parties have filed such applications after March 15, 2013, a derivation proceeding can be initiated by such third parties to determine whether our invention was derived from theirs. Even where we have a valid and enforceable patent, we may not be able to exclude others from practicing our invention where the other party can show that they used the invention in commerce before our filing date or the other party benefits from a compulsory license.

We enjoy only limited geographical protection with respect to certain patents and we may not be able to protect our intellectual property rights throughout the world.

Filing and prosecuting patent applications and defending patents covering our product candidates in all countries throughout the world would be prohibitively expensive. Competitors may use our and our licensors' technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we and our licensors have patent protection, but enforcement rights are not as strong as that in the United States or Europe. These products may compete with our product candidates, and our and our licensors' patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

In addition, we may decide to abandon national and regional patent applications before grant. The examination of each national or regional patent application is an independent proceeding. As a result, patent applications in the same family may issue as patents in some jurisdictions, such as in the United States, but may issue as patents with claims of different scope or may even be refused in other jurisdictions, such as in China, which has different requirements for patentability, including a stringent requirement for a detailed description of medical uses of a claimed drug. It is also quite common that depending on the country, the scope of patent protection may vary for the same product candidate or technology.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws or rules and regulations in the United States and Europe, and many companies have encountered significant difficulties in protecting and defending such rights in such jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in other jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing as patents, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets. If we or our licensors encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our

business in such jurisdictions, the value of these rights may be diminished and we may face additional competition from others in those jurisdictions.

Some countries also have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In those countries, the patent owner may have limited remedies, which could materially diminish the value of such patents. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired.

Our patents and other proprietary rights may not adequately protect our technologies and product candidates, and may not necessarily address all potential threats to our competitive advantage.

The degree of protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- others may be able to make compounds that are the same as or similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed;
- the patents of third parties may impair our ability to develop or commercialize our product candidates;
- the patents of third parties may be extended beyond the expected patent term and thus may impair our ability to develop or commercialize our product candidates;
- we or our licensors or any future strategic collaborators might not have been the first to conceive or reduce to practice the inventions covered by the issued patents or pending patent applications that we own or have exclusively licensed;
- we or our licensors or any future strategic collaborators might not have been the first to file patent applications covering our inventions, our product candidates, or uses of the product candidates in the indications under our development or to be developed;
- it is possible that the pending patent applications that we own or have exclusively licensed may not lead to issued patents;
- issued patents that we own or have exclusively licensed may not provide us with any competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- issued patents that we own or have exclusively licensed may not provide coverage for all aspects of our product candidates in all countries, such as for uses of our product candidates in the indications under our development or to be developed;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- others performing manufacturing or testing for us using our products or technologies could use the intellectual property of others without obtaining a proper license;
- our or our licensors' inventions or technologies may be found to be not patentable; and
- we may not develop additional technologies that are patentable.

We may become subject to third parties' claims alleging infringement of their patents and proprietary rights, or we may be involved in lawsuits to protect or enforce our patents and other proprietary rights, which could be costly and time consuming, delay or prevent the development and commercialization of our product candidates, or put our patents and other proprietary rights at risk.

Our commercial success depends, in part, upon our ability to develop, manufacture, market, and sell our product candidates without alleged or actual infringement, misappropriation, or other violation of the patents and proprietary rights of third parties. Litigation relating to patents and other intellectual property rights in the biopharmaceutical and pharmaceutical industries is common, including patent infringement lawsuits and interferences, oppositions, and reexamination proceedings before the U.S. Patent and Trademark Office, or USPTO, and foreign patent offices. The various markets in which we plan to operate are subject to frequent and extensive litigation regarding patents and other intellectual property rights. In addition, many companies in intellectual property-dependent industries, including in the biopharmaceutical and pharmaceutical industries, have employed intellectual property litigation as a means to gain an advantage over their competitors. Numerous U.S., European, and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates. Some claimants may have substantially greater resources than we do and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us. As the biopharmaceutical and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the intellectual property rights of third parties.

We may be subject to third-party claims including infringement, interference or derivation proceedings, post-grant review and inter partes review before the USPTO, or similar adversarial proceedings or litigation in the U.S. and other jurisdictions. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, and the holders of any such patents may be able to block our ability to commercialize the applicable product candidate unless we obtained a license under the applicable patents, or until such patents expire or are finally determined to be invalid or unenforceable. Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our compositions, formulations, or methods of treatment, prevention, or use, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires or is finally determined to be invalid or unenforceable. In addition, defending such claims would cause us to incur substantial expenses and could cause us to pay substantial damages, if we are found to be infringing a third party's patent rights. These damages potentially include increased damages and attorneys' fees if we are found to have infringed such rights willfully. As an example of the foregoing risks, we are aware of a third-party patent family which currently includes a patent granted by the European Patent Office, or EPO, containing claims that appear to cover the use of BPS-804 in the treatment of OI. The patent owner could assert such patent against us, which could present the foregoing risks and impose limitations in our ability to develop, manufacture or sell BPS-804 for such use in the EU, unless we obtain a license under such patent, such patent is determined to be invalid or unenforceable by the EPO or a national court in one or more relevant territories, or such patent is revoked or otherwise limited by the EPO. This patent is currently the subject of ongoing opposition proceedings before the EPO, but there can be no assurance as to the outcome of such proceedings.

Further, if a patent infringement suit is brought against us or our third-party service providers, our development, manufacturing or sales activities relating to the product or product candidate that is the subject of the suit may be delayed or terminated. As a result of patent infringement claims, or in order to avoid potential infringement claims, we may choose to seek, or be required to seek, a license from

the third party, which would be likely to include a requirement to pay license fees or royalties or both. These licenses may not be available on acceptable terms or at all. Even if a license can be obtained on acceptable terms, the rights may be nonexclusive, which would give our competitors access to the same intellectual property rights. If we are unable to enter into a license on acceptable terms, we could be prevented from commercializing one or more of our product candidates, or forced to modify such product candidates, or to cease some aspect of our business operations, which could harm our business significantly. We might, if possible, also be forced to redesign our product candidates so that we no longer infringe the third-party intellectual property rights, which may result in significant cost and delay to us, or which redesign could be technically infeasible. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

If we were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the United States and in Europe, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness, or non-enablement. Third parties might allege unenforceability of our patents because someone connected with prosecution of the patent withheld relevant information, or made a misleading statement, during prosecution. The outcome of proceedings involving assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity of patents, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution. There is a risk that in connection with such proceedings, a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention. Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. An adverse outcome in a litigation or proceeding involving one or more of our patents could limit our ability to assert those patents against those parties or other competitors, and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. In addition, if the breadth or strength of protection provided by our patents is threatened, it could dissuade companies from collaborating with us to license, develop, or commercialize our current or future product candidates. Furthermore, our patents and other intellectual property rights also will not protect our technology if competitors design around our protected technology without infringing our patents or other intellectual property rights.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. 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. Such litigation or proceedings could substantially increase our operating losses and reduce our resources available for development 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 substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have an adverse effect on our ability to compete in the marketplace. There could also be public announcements of the results of hearings, motions, or other

interim proceedings or developments. If securities analysts or investors view these announcements in a negative light, the price of our ADSs and ordinary shares could be adversely affected.

We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent which might adversely affect our ability to develop, manufacture and market our product candidates.

We cannot guarantee that any of our, our licensors', or the previous owners' patent searches or analyses, including but not limited to the identification of relevant patents, the scope of patent claims, or the expiration of relevant patent applications or patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and patent application in the United States, Europe and elsewhere that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction. For example, in the United States, patent applications filed before November 29, 2000 and, upon request, certain patent applications filed after that date that will not be filed outside the United States, remain confidential until those patent applications issue as patents. Patent applications in the United States, EU, and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our product candidates could have been filed by others without our knowledge, including any such patent applications that may claim priority from patent applications for patents that we have determined will expire before we commercialize our products. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates or the use of our product candidates. Moreover, as we study our product candidates during development, we may learn new information regarding their structure, composition, properties, or functions that may render third-party patent applications or patents that we had not identified as being, or that we had not believed to be, relevant to our product candidates instead to be relevant to or necessary for the commercialization of our product candidates in a jurisdiction. The scope of a patent claim is determined by an interpretation of the law, the written disclosure in the patent, and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending patent application may be incorrect. We may incorrectly determine that our product candidates are not covered by a third-party patent or may incorrectly predict whether a third party's pending patent application will issue with claims of relevant scope. Our determination of the expiration date or the possibility of an extension of patent term of any patent in the United States, Europe, or elsewhere that we consider relevant also may be incorrect. Any of the foregoing circumstances, failures, or errors may negatively impact our ability to develop and market our product candidates.

If we fail to comply with our obligations under our existing and any future intellectual property licenses with third parties, we could lose license rights that are important to our business, and our business may be substantially harmed as a result.

We are party to agreements with Novartis and AstraZeneca, under which we in-license certain intellectual property and were assigned, in the case of Novartis, or granted an option to acquire, in the case of AstraZeneca, certain patents and patent applications related to our business. We may enter into additional license agreements in the future. Our existing license agreements impose and any future license agreements are likely to impose various diligence, milestone payment, royalty, insurance and other obligations on us. Any uncured, material breach under these license agreements could result in the loss of our rights to practice such in-licensed intellectual property, and could compromise our development and commercialization efforts for any current or future product candidates.

We may not be successful in maintaining necessary rights to our product candidates or obtaining patent or other intellectual property rights important to our business through acquisitions and in-licenses.

We currently own and have in-licensed rights to intellectual property, including patents, patent applications and know-how, relating to our product candidates, and our success will likely depend on

maintaining these rights. Because our programs may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to continue to acquire, in-license, maintain, or use these proprietary rights. In addition, our product candidates may require specific formulations to work effectively and the rights to those formulations or methods of making those formulations may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes, or other third-party intellectual property rights that we identify as necessary for the development and commercialization of our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies also are pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources, and greater clinical development and commercialization capabilities.

In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We may also be unable to license or acquire third-party intellectual property rights on a timely basis, on terms that would allow us to make an appropriate return on our investment, or at all. Even if we are able to obtain a license to intellectual property of interest, we may not be able to secure exclusive rights, in which case others could use the same rights and compete with us. If we are unable to successfully obtain a license to third-party intellectual property rights necessary for the development of our product candidates or a development program on acceptable terms, we may have to abandon development of our product candidates or that development program.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance and annuity fees on any issued patent are due to be paid to the USPTO and foreign patent agencies over the lifetime of a patent. In addition, the USPTO and other foreign patent agencies require compliance with a number of procedural, documentary, fee payment, and other similar provisions during the patent application process. While an inadvertent failure to make payment of such fees or to comply with such provisions can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which such non-compliance will result in the abandonment or lapse of the patent or patent application, and the partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, and non-payment of fees and failure to properly legalize and submit formal documents within prescribed time limits. If we or our licensors fail to maintain the patents and patent applications covering our product candidates or if we or our licensors otherwise allow our patents or patent applications to be abandoned or lapse, our competitors might be able to enter the market, which would hurt our competitive position and could impair our ability to successfully commercialize our product candidates in any indication for which they are approved.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

Although we are not currently experiencing any claims challenging the inventorship of our patents and patent applications or ownership of our intellectual property, we may in the future be subject to claims that former employees or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. While it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. For

example, the assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, or we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Changes in patent laws or patent jurisprudence could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other biopharmaceutical and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical and pharmaceutical industries involve both technological complexity and legal complexity. Therefore, obtaining and enforcing biopharmaceutical and pharmaceutical patents is costly, time-consuming and inherently uncertain. In addition, the America Invents Act, or the AIA, which was passed in September, 2011, resulted in significant changes to the U.S. patent system.

An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to a “first-to-file” system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. A third party that files a patent application in the USPTO after that date but before us could therefore be awarded a patent covering an invention of ours even if we made the invention before it was made by the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application, but circumstances could prevent us from promptly filing patent applications on our inventions.

Among some of the other changes introduced by the AIA are changes to the limitation where a patent may be challenged, thus providing opportunities for third parties to challenge any issued patent in the USPTO. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action.

Accordingly, a third party may attempt to use the USPTO proceedings to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. It is not clear what, if any, impact the AIA will have on the operation of our business. However, the AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our licensors’ patent applications and the enforcement or defense of our or our licensors’ issued patents.

Additionally, the U.S. Supreme Court has ruled on several patent cases in recent years either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. Similarly, the complexity and uncertainty of European patent laws have also increased in recent years. In addition, the European patent system is relatively stringent in the type of

amendments that are allowed during prosecution. Complying with these laws and regulations could limit our ability to obtain new patents in the future that may be important for our business.

If we do not obtain protection under the Hatch-Waxman Amendments and similar non-U.S. legislation for extending the term of patents covering our product candidates, our ability to compete effectively could be impaired.

Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch Waxman Amendments. The Hatch Waxman Amendments permit a patent term extension of up to five years for a patent covering an approved product or method of use as compensation for patent term lost during product development and the FDA regulatory review process. Similar patent term extensions may be available in other jurisdictions. For example, a Supplementary Protection Certificate in Europe may be applied for approval to recover some of the time lost between the patent application filing date and the date of first marketing authorization. However, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents, or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue from applicable products could be reduced, possibly materially.

If our trademarks and trade names are not adequately protected, we may not be able to build name recognition in our markets of interest and our competitive position may be adversely affected.

We currently own registered trademarks. We may not be able to obtain trademark protection in territories that we consider of significant importance to us. In addition, any of our trademarks or trade names, whether registered or unregistered, may be challenged, opposed, infringed, cancelled, circumvented or declared generic, or determined to be infringing on other marks, as applicable. We may not be able to protect our rights to these trademarks and trade names, which we will need to build name recognition by potential collaborators or customers in our markets of interest. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

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

We consider proprietary trade secrets and confidential know-how and unpatented know-how to be important to our business. In addition to seeking patents for some of our technology and product candidates, we also may rely on trade secrets or confidential know-how to protect our technology, especially where patent protection is believed to be of limited value. However, trade secrets and confidential know-how are difficult to maintain as confidential.

To protect this type of information against disclosure or appropriation by competitors, our policy is to require our employees, consultants, contractors and advisors to enter into confidentiality agreements with us. We also seek to preserve the integrity and confidentiality of our data, trade secrets, and know-how by maintaining physical security of our premises and physical and electronic security of our information technology systems. Monitoring unauthorized uses and disclosures is difficult, and we cannot know whether the steps we have taken to protect our proprietary technologies will be effective. In addition, current or former employees, consultants, contractors, and advisers may unintentionally or willfully disclose our confidential information to competitors, and confidentiality agreements may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. We

therefore cannot guarantee that our trade secrets and other proprietary and confidential information will not be disclosed or that competitors will not otherwise gain access to our trade secrets. Enforcing a claim that a third party obtained illegally and is using trade secrets or confidential know-how is expensive, time consuming, and unpredictable. The enforceability of confidentiality agreements may vary from jurisdiction to jurisdiction. Furthermore, if a competitor lawfully obtained or independently developed any of our trade secrets, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret.

Failure to protect or maintain trade secrets and confidential know-how could adversely affect our business and our competitive position. Moreover, our competitors may independently develop substantially equivalent proprietary information and may even apply for patent protection in respect of the same. If successful in obtaining such patent protection, our competitors could limit our use of our own trade secrets or confidential know-how.

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. These claims may be costly to defend and if we do not successfully do so, we may be required to pay monetary damages and lose valuable intellectual property rights or personnel.

Some of our employees, including our senior management, were previously employed at other biopharmaceutical or pharmaceutical companies, including our competitors or potential competitors. Some of these employees executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. Although we try to ensure that our employees do not use the know-how, trade secrets, or other proprietary information of others in their work for us, we may be subject to claims that we or these employees have used or disclosed confidential information or intellectual property, including know-how, trade secrets, or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

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. A loss of key research personnel or their work product could hamper or undermine our ability to develop and commercialize our product candidates, which would severely harm our business. In addition, if such intellectual property rights were to be awarded to a third party, we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all, which could hamper or undermine our ability to develop and commercialize our product candidates, which would severely harm our business. Even if we successfully prosecute or defend against such claims, litigation could result in substantial costs and distract management from the development and commercialization of our product candidates.

Our proprietary information may be lost or we may suffer security breaches.

In the ordinary course of our business, we collect and store sensitive data, including intellectual property, clinical trial data, proprietary business information, personal data and personally identifiable information of our clinical trial subjects and employees, in our data centers and on our networks. The secure processing, maintenance and transmission of this information is critical to our operations. Despite our security measures, our information technology and infrastructure and those of our CROs or other contractors or consultants may be vulnerable to attacks by hackers or breached due to employee error, malfeasance, or other disruptions. The loss of clinical trial data from completed, ongoing, or planned trials could result in delays in our regulatory approval efforts and significantly increase our

costs to recover or reproduce the data. Although, to our knowledge, we have not experienced any such material security breach to date, any such breach could compromise our networks and the information stored there could be accessed, publicly disclosed, lost, or stolen. Any such access, disclosure, or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, and significant regulatory penalties; disrupt our operations; damage our reputation; and cause a loss of confidence in us and our ability to conduct clinical trials, which could adversely affect our reputation and delay our clinical development of our product candidates.

Risks Related to Employee Matters and Managing Growth

Our future growth and ability to compete depends on retaining our key personnel and recruiting additional qualified personnel.

Our success depends upon the continued contributions of our key management, including all of our senior management team, and scientific and technical personnel, many of whom have been instrumental for us and have substantial experience with rare and specialty diseases and the biopharmaceutical and pharmaceutical industries. The loss of key managers and senior physicians or scientists could delay our acquisition and development activities. In addition, the competition for qualified personnel in the biopharmaceutical and pharmaceutical fields is intense, and our future success depends upon our ability to attract, retain and motivate highly skilled scientific, technical, and managerial employees. We face competition for personnel from other companies and organizations. If our recruitment and retention efforts are unsuccessful in the future, it may be difficult for us to achieve our development objectives, raise additional capital, and implement our business strategy.

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 acquisition and 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 or acquire new 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 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.

Risks Related to the Global Offering and Our ADSs and Ordinary Shares

The price of our ADSs and ordinary shares may be volatile and may fluctuate due to factors beyond our control.

The trading market for publicly traded emerging drug development companies has been highly volatile and is likely to remain highly volatile in the future. The market price of our ADSs and ordinary shares may fluctuate significantly due to a variety of factors, including:

- positive or negative results from, or delays in, testing or clinical trials conducted by us or our competitors;
- delays in entering into strategic relationships with respect to development or commercialization of our product candidates or entry into strategic relationships on terms that are not deemed to be favorable to us;
- technological innovations or commercial product introductions by us or competitors;

- changes in government regulations;
- developments concerning proprietary rights, including patents and litigation matters;
- public concern relating to the commercial value or safety of our product candidates;
- financing or other corporate transactions;
- publication of research reports or comments by securities or industry analysts;
- general market conditions in the biopharmaceutical and pharmaceutical industries or in the economy as a whole;
- the loss of any of our key scientific or senior management personnel;
- sales of our ADSs or ordinary shares by us, our senior management and board members, holders of our ADSs or our security holders in the future; or
- other events and factors, many of which are beyond our control.

These and other market and industry factors may cause the market price and demand for our ADSs and ordinary shares to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from readily selling their ADSs or ordinary shares and may otherwise negatively affect the liquidity of our ADSs and ordinary shares. In addition, the stock market in general, and emerging companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. In the past in the United States, when the market price of a security has been volatile, holders of that security have sometimes instituted securities class action litigation against the issuer. If any of the holders of our ADSs or ordinary shares were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the attention of our senior management would be diverted from the operation of our business. Any adverse determination in litigation could also subject us to significant liabilities.

We will incur increased costs as a result of operating as a company with securities listed in the United States, and our senior management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a company with securities listed in the United States, and particularly after we no longer qualify as an emerging growth company, we will incur significant legal, accounting, and other expenses that we did not incur previously. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of Nasdaq, and other applicable securities rules and regulations impose various requirements on non-U.S. reporting public companies, including the establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our senior management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified senior management personnel or members for our board of directors. In addition these rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we will be required to furnish a report by our senior management on our internal control over financial reporting. However, while we remain 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.

To prepare for eventual compliance with Section 404, once we no longer qualify as an emerging growth company, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented, and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

There has been no public market for our ADSs prior to the U.S. offering, and an active market may not develop in which investors can resell our ADSs.

Prior to the U.S. offering, there has been no public market for our ADSs, although our ordinary shares have traded on AIM. We cannot predict the extent to which an active market for our ADSs will develop or be sustained after the U.S. offering, or how the development of such a market might affect the market price for our ADSs. The initial public offering price of our ADSs in the U.S. offering will be determined by negotiations between us and the underwriters taking into account the most recent closing price of our ordinary shares on AIM prior to the pricing date and prevailing market conditions, among other factors, and may not be indicative of the price at which our ADSs will trade following completion of the U.S. offering. Investors may not be able to sell their ADSs at or above the initial public offering price.

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

Following the global offering and after our ADSs begin trading on Nasdaq, our ordinary shares will continue to be admitted to trading on AIM. We cannot predict the effect of this dual listing on the value of our ADSs and ordinary shares. However, the dual listing of our ADSs and ordinary shares may dilute the liquidity of these securities in one or both markets and may adversely affect the development of an active trading market for our ADSs. The price of our ADSs could also be adversely affected by trading in our ordinary shares on AIM.

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

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

Following the global offering, our executive officers, board of directors, and certain of our existing shareholders will continue to own a majority of our ordinary shares (including ordinary shares represented by ADSs) and as a result, will have control or significant influence over us, and your interests may conflict with the interests of these shareholders.

As of March 31, 2018, after giving effect to the closing of the global offering, our executive officers, board of directors, and greater than 3% shareholders and their respective affiliates, in the aggregate, will own approximately 80% of our ordinary shares (including ordinary shares in the form of ADSs).

Depending on the level of attendance at our general meetings of shareholders, these shareholders either alone or voting together as a group may be in a position to control or significantly influence the outcome of decisions taken at any such general meeting. Any shareholder or group of shareholders controlling more than 50% of the share capital present and voting at our general meetings of shareholders may control any shareholder resolution requiring a simple majority, including the appointment of board members, certain decisions relating to our capital structure, the approval of certain significant corporate transactions, and amendments to our Articles of Association. These shareholders may have interests that differ from yours and may vote in a way with which you disagree and which may be adverse to your interests. Among other consequences, this concentration of ownership may have the effect of delaying or preventing a change in control and might therefore negatively affect the market price of our ADSs and ordinary shares.

Future sales, or the possibility of future sales, of a substantial number of our ADSs or ordinary shares could adversely affect the price of our ADSs and ordinary shares.

Future sales of a substantial number of our ADSs or ordinary shares, or the perception that such sales will occur, could cause a decline in the market price of our ADSs and ordinary shares. Based on the number of ordinary shares outstanding as of March 31, 2018, after giving effect to the closing of the global offering, we will have 86,987,891 ordinary shares outstanding (including ordinary shares in the form of ADSs). ADSs and ordinary shares issued and sold in the global offering may be resold in the public market immediately without restriction, unless sold in the United States by an affiliate. A significant portion of these ordinary shares, and potentially of our ADSs, will be subject to the lock-up agreements described in the sections titled “Ordinary Shares and ADSs Eligible for Future Sale” and “Underwriting.” If, after the termination of these lock-up agreements, these shareholders sell substantial amounts of ADSs or ordinary shares in the public market, or the market perceives that such sales may occur, the market price of our ADSs or ordinary shares and our ability to raise capital through an issue of equity securities in the future could be adversely affected.

If you purchase ordinary shares or ADSs in the global offering, you will suffer immediate dilution of your investment.

We expect the initial public offering price of our ADSs in the US offering and the offering price of our ordinary shares in the European private placement to be substantially higher than the net tangible book value per ADS and per ordinary share prior to the global offering. Therefore, if you purchase ADSs or ordinary shares in the global offering, you will pay a price per ADS and per ordinary share that substantially exceeds our net tangible book value per ADS and per ordinary share after the global offering. To the extent any of our outstanding share options or warrants are exercised, or convertible notes are converted, for ordinary shares, you may experience further dilution. Based on the assumed initial public offering price of \$17.62 per ADS and £3.14 per ordinary share, which reflect the last reported sale price of our ordinary shares on AIM on April 4, 2018, you will experience immediate dilution of \$12.94 per ADS and £2.29 per ordinary share, representing the difference between our net tangible book value per ADS and per ordinary share after giving effect to the global offering and the assumed offering prices for our ADSs and ordinary shares in the global offering. See “Dilution.”

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

Under English law, a company’s accumulated realized profits must exceed its accumulated realized losses on a non-consolidated basis before dividends can be paid. Therefore, we must have distributable profits before issuing a dividend. We have 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. In addition, our credit facility prohibits us from paying dividends on our equity securities, and any future debt agreements may likewise preclude us from

paying dividends. As a result, capital appreciation, if any, on our ADSs or ordinary shares will be your sole source of gains for the foreseeable future, and you will suffer a loss on your investment if you are unable to sell your ADSs or ordinary shares at or above the offering price for each. Investors seeking cash dividends should not purchase our ADSs or ordinary shares in the global offering.

We have broad discretion in the use of the net proceeds from the global offering and may not use them effectively.

Our senior management will have broad discretion in the application of the net proceeds from the global offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our ADSs or ordinary shares. The failure by our senior management to apply these funds effectively could result in financial losses, cause the price of our ADSs or ordinary shares to decline, and delay the development of our product candidates. Pending their use, we may invest the net proceeds from the global offering in a manner that does not produce income or that loses value.

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

Our ordinary shares are currently traded on AIM. Investment in equities traded on AIM is sometimes perceived to carry a higher risk than an investment in equities quoted on exchanges with more stringent listing requirements, such as the main market of the London Stock Exchange or Nasdaq. This is because AIM imposes less stringent corporate governance and ongoing reporting requirements than these other exchanges. In addition, AIM requires only half-yearly financial reporting, rather than the quarterly financial reporting required for domestic U.S.-listed companies. 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-quoted 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 prices may be volatile and subject to significant fluctuations. Therefore, the market price of our ADSs, our ordinary shares, or the ordinary shares underlying our ADSs may not reflect the underlying value of our company.

Purchasers of ADSs in the U.S. offering 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 described in this prospectus, holders of our ADSs will not be able to exercise voting rights attaching to the ordinary shares represented by our ADSs on an individual basis. Holders of our ADSs will appoint the depositary or its nominee as their representative to exercise the voting rights attaching to the ordinary shares represented by our ADSs. Purchasers of ADSs in the U.S. offering may not receive voting materials in time to instruct the depositary to vote, and it is possible that they, or persons who hold their ADSs through brokers, dealers, or other third parties, will not have the opportunity to exercise a right to vote. Furthermore, the depositary will not be liable for any failure to carry out any instructions to vote, for the manner in which any vote is cast or for the effect of any such vote. As a result, purchasers of ADSs in the U.S. offering may not be able to exercise voting rights and may lack recourse if their ADSs are not voted as requested. In addition, in their capacity as ADS holders, purchasers of ADSs in the U.S. offering will not be able to call a shareholders' meeting.

Purchasers of ADSs in the U.S. offering may not receive distributions on our ordinary shares represented by our ADSs or any value for them if it is illegal or impractical to make them available to holders of ADSs.

The depositary for our ADSs has agreed to pay to purchasers of ADSs in the U.S. offering cash dividends or other distributions it or the custodian receives on our ordinary shares after deducting its fees and expenses. Purchasers of our ADSs will receive these distributions in proportion to the number

of our ordinary shares their ADSs represent. However, in accordance with the limitations set forth in the deposit agreement, it may be unlawful or impractical to make a distribution available to holders of ADSs. We have no obligation to take any other action to permit the distribution of our ADSs, ordinary shares, rights or anything else to holders of our ADSs. This means that purchasers of ADSs in the U.S. offering 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 them. These restrictions may negatively impact the value of our ADSs.

Purchasers of ADSs in the U.S. offering may be subject to limitations on transfer of their ADSs.

ADSs are transferable on the books of the depositary. However, the depositary may close its transfer books at any time or from time to time when it deems expedient in connection with the performance of its duties. In addition, the depositary may refuse to deliver, transfer, or register transfers of ADSs generally when our books or the books of the depositary are closed, or at any time if we or the depositary deems it advisable to do so because of any requirement of law or of any government or governmental body, or under any provision of the deposit agreement, or for any other reason in accordance with the terms of the deposit agreement.

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

We are incorporated under English law. The rights of holders of ordinary shares and, therefore, certain of the rights of holders of ADSs, are governed by English law, including the provisions of the U.K. 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. See “Description of Share Capital and Articles of Association—Differences in Corporate Law” and “Description of Share Capital and Articles of Association—Articles of Association—Other U.K. Law Considerations—City Code on Takeovers and Mergers.” in this prospectus for a description of the principal differences between the provisions of the U.K. Companies Act 2006 applicable to us and, for example, the Delaware General Corporation Law relating to shareholders’ rights and protections.

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

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

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

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

We qualify as a foreign private issuer and, as a result, we will not be subject to U.S. proxy rules and will be subject to reporting obligations under the Securities Exchange Act of 1934, as amended, or the Exchange Act, that, to some extent, are more lenient and less frequent than those of a U.S. domestic public company.

Upon the closing of the U.S. offering, we will report under the Exchange Act, as a non-U.S. company with foreign private issuer status. Because we qualify as a foreign private issuer under the Exchange Act, we are exempt from certain provisions of the Exchange Act that are applicable to U.S. domestic public companies, including (i) the sections of the Exchange Act regulating the solicitation of proxies, consents, or authorizations in respect of a security registered under the Exchange Act; (ii) the sections of the Exchange Act requiring insiders to file public reports of their stock ownership and trading activities and liability for insiders who profit from trades made in a short period of time; and (iii) the rules under the Exchange Act requiring the filing with the SEC of quarterly reports on Form 10-Q containing unaudited financial and other specified information or current reports on Form 8-K, upon the occurrence of specified significant events. In addition, foreign private issuers are not required to file their annual report on Form 20-F until 120 days after the end of each fiscal year, while U.S. domestic issuers that are accelerated filers are required to file their annual report on Form 10-K within 75 days after the end of each fiscal year. Foreign private issuers also are exempt from Regulation Fair Disclosure, aimed at preventing issuers from making selective disclosures of material information. As a result of the above, you may not have the same protections afforded to shareholders of companies that are not foreign private issuers.

As a foreign private issuer and as permitted by the listing requirements of Nasdaq, we may follow U.K. corporate governance rules instead of the corporate governance requirements of Nasdaq.

As a foreign private issuer, we may follow our home country corporate governance rules instead of the corporate governance requirements of Nasdaq. For example, we are exempt from Nasdaq regulations that require a listed U.S. company 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;
- promptly disclose any waivers of the code for directors or executive officers that should address certain specified items;
- have an independent nominating committee;
- solicit proxies and provide proxy statements for all shareholder meetings; and
- seek shareholder approval for the implementation of certain equity compensation plans and issuances of ordinary shares.

For an overview of our corporate governance principles, including those which comply with certain of the requirements above, see “Description of Share Capital and Articles of Association—Articles of Association.”

In accordance with our Nasdaq listing, our Audit Committee is required to comply with the provisions of Section 301 of the Sarbanes-Oxley Act of 2002 and Rule 10A-3 of the Exchange Act, both of which also are applicable to Nasdaq-listed U.S. companies. Because we are a foreign private issuer, however, our Audit Committee is not subject to additional Nasdaq requirements applicable to

listed U.S. companies, including an affirmative determination that all members of the Audit Committee are “independent” using more stringent criteria than those applicable to us as a foreign private issuer.

To the extent we determine to follow U.K. corporate governance practices instead of Nasdaq governance requirements, you may not have the same protections afforded to shareholders of companies that are subject to these Nasdaq requirements.

We may lose our foreign private issuer status, which would then require us to comply with the Exchange Act’s domestic reporting regime and cause us to incur significant legal, accounting and other expenses.

In order to maintain our current status as a foreign private issuer, either (a) a majority of our ordinary shares, including ordinary shares in the form of ADSs, must be either directly or indirectly owned of record by non-residents of the United States or (b)(i) a majority of our executive officers or directors are not U.S. citizens or residents, (ii) more than 50 percent of our assets must be located outside the United States and (iii) our business must be administered principally outside the United States. If we lose our status as a foreign private issuer, we would be required to comply with the Exchange Act reporting and other requirements applicable to U.S. domestic issuers, which are more detailed and extensive than the requirements for foreign private issuers. We may also be required to make changes in our corporate governance practices in accordance with various SEC and Nasdaq rules. The regulatory and compliance costs to us under U.S. securities laws if we are required to comply with the reporting requirements applicable to a U.S. domestic issuer may be significantly higher than the cost we would incur as a foreign private issuer. As a result, we expect that the loss of foreign private issuer status would increase our legal and financial compliance costs and would make some activities highly time consuming and costly. We also expect that if we were required to comply with the rules and regulations applicable to U.S. domestic issuers, it would make it more difficult and expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced coverage or incur substantially higher costs to obtain coverage. These rules and regulations could also make it more difficult for us to attract and retain qualified members of our board of directors.

We are an “emerging growth company,” and we cannot be certain if the reduced reporting requirements applicable to “emerging growth companies” will make our ADSs or ordinary shares less attractive to investors.

We are an “emerging growth company” as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404, exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. As an emerging growth company, we are required to report only two years of financial results and selected financial data in this prospectus compared to three and five years, respectively, for comparable data reported by other public companies. We may take advantage of these exemptions until we are no longer an emerging growth company. We could be an emerging growth company for up to five years, although circumstances could cause us to lose that status earlier, including if the aggregate market value of our ADSs and ordinary shares held by non-affiliates exceeds \$700 million as of any June 30 (the end of our second fiscal quarter) before that time, in which case we would no longer be an emerging growth company as of the following December 31 (our fiscal year-end). We cannot predict if investors will find our ADSs or ordinary shares less attractive because we may rely on these exemptions. If some investors find our ADSs or ordinary shares less attractive as a result, there may be a less active trading market for our ADSs or ordinary shares and the price of our ADSs or ordinary shares may be more volatile.

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 our ADSs or ordinary shares.

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, or any subsequent testing by our independent registered public accounting firm, 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. Inadequate 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 our ADSs or ordinary shares.

Management will be required to assess the effectiveness of our internal controls annually. However, for as long as we are an “emerging growth company” under the JOBS Act, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404. An independent assessment of the effectiveness of our internal controls could detect problems that our management’s assessment might not. Undetected material weaknesses in our internal controls could lead to financial statement restatements requiring us to incur the expense of remediation and could also result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

If securities or industry analysts do not publish research, or publish inaccurate or unfavorable research, about our business, the price of our ADSs and ordinary shares and our trading volume could decline.

The trading market for our ADSs and ordinary shares will depend in part on the research and reports that securities or industry analysts publish about us or our business. If no or too few securities or industry analysts commence or continue coverage on us, the trading price for our ADSs and ordinary shares would likely be negatively affected. If one or more of the analysts who cover us downgrade our ADSs or ordinary shares or publish inaccurate or unfavorable research about our business, the price of our ADSs and ordinary shares would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, demand for our ADSs or ordinary shares could decrease, which might cause the price of our ADSs and ordinary shares and trading volume to decline.

We believe we will likely be classified as a passive foreign investment company for U.S. federal income tax purposes for the current year, which could result in adverse U.S. federal income tax consequences to U.S. investors in our ADSs or ordinary shares.

Because we do not expect to earn revenue from our business operations during the current taxable year, and because our sole source of income currently is interest on bank accounts held by us, we believe we will likely be classified as a “passive foreign investment company,” or PFIC, for the current taxable year. A non-U.S. company will be considered a PFIC for any taxable year if (i) at least 75% of its gross income is passive income (including interest income), or (ii) at least 50% of the value of its assets (based on an average of the quarterly values of the assets during a taxable year) is attributable to assets that produce or are held for the production of passive income. If we are classified as a PFIC in any year with respect to which a U.S. Holder (as defined below under “Material Tax Considerations—U.S. Federal Income Taxation”) owns our ADSs or ordinary shares, we will continue to be treated as a PFIC with respect to such U.S. Holder in all succeeding years during which the U.S. Holder owns ADSs or ordinary shares, regardless of whether we continue to meet the PFIC test

described above, unless the U.S. Holder makes a specified election once we cease to be a PFIC. If we are classified as a PFIC for any taxable year during which a U.S. Holder holds our ADSs or ordinary shares, certain adverse U.S. federal income tax consequences could apply to such U.S. Holder, including (i) the treatment of all or a portion of any gain on disposition as ordinary income, (ii) the application of a deferred interest charge on such gain and the receipt of certain dividends and (iii) the obligation to comply with certain reporting requirements. See “Material Tax Considerations—Passive Foreign Investment Company Rules.”

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains statements that constitute forward-looking statements. Many of the forward-looking statements contained in this prospectus can be identified by the use of forward-looking words such as “anticipate,” “believe,” “could,” “estimate,” “expect,” “intend,” “plan,” “potential” and “should,” among others.

Forward-looking statements appear in a number of places in this prospectus and include, but are not limited to, statements regarding our intent, belief, or current expectations. Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. Such statements are subject to substantial risks and uncertainties, and actual results may differ materially from those expressed or implied in the forward-looking statements due to various important factors, including, but not limited to, those identified under “Risk Factors.” In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a guarantee by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all.

Forward-looking statements include, but are not limited to, statements about:

- the development of our product candidates, including statements regarding the expected initiation, timing, progress, and availability of data from our clinical trials;
- the potential attributes and benefit of our product candidates and their competitive position;
- our ability to successfully commercialize, or enter into strategic relationships with third parties to commercialize, our product candidates, if approved;
- our expectations regarding the use of proceeds from the global offering;
- our estimates regarding expenses, future revenues, capital requirements, and our need for additional financing;
- our ability to acquire or in-license new product candidates;
- potential strategic relationships; and
- the duration of our patent portfolio.

Forward-looking statements speak only as of the date they are made, and we do not undertake any obligation to update them in light of new information or future developments or to release publicly any revisions to these statements in order to reflect later events or circumstances or to reflect the occurrence of unanticipated events.

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

MARKET AND INDUSTRY DATA

Certain industry data and market data included in this prospectus were obtained from independent third-party surveys, market research, publicly available information, reports of governmental agencies, and industry publications and surveys. All of the market data used in this prospectus involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. We believe that the information from these industry publications and surveys included in this prospectus is reliable. The industry in which we operate is subject to a high degree of uncertainty and risk due to a variety of factors, including those described in “Risk Factors.” These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

TRADEMARKS, SERVICE MARKS AND TRADENAMES

Solely for convenience, the trademarks, service marks, logos and trade names referred to in this prospectus are without the ® and ™ symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensors to these trademarks, service marks, and trade names. This prospectus contains additional trademarks, service marks, and trade names of others, which are the property of their respective owners. All trademarks, service marks, and trade names appearing in this prospectus are, to our knowledge, the property of their respective owners. We do not intend our use or display of other companies' trademarks, service marks, copyrights, or trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

EXCHANGE RATE INFORMATION

The following table presents information on the exchange rates between the pound sterling and the U.S. dollar for the periods indicated. Such U.S. dollar amounts are not necessarily indicative of the amounts of U.S. dollars that could actually have been purchased upon exchange of pounds sterling at the dates indicated.

<u>Period-end(1)</u>	<u>Average for period(2)</u>	<u>Low</u>	<u>High</u>
(U.S. dollars per pound sterling)			

Year Ended December 31:

2013	1.6574	1.5641	1.4837	1.6574
2014	1.5578	1.6484	1.5517	1.7165
2015	1.4746	1.5284	1.4648	1.5882
2016	1.2337	1.3555	1.2155	1.4800
2017	1.3529	1.2890	1.2118	1.3578

- (1) In the event that the period end fell on a day for which data are not available, the exchange rate on the prior most recent business day is given.
- (2) The average of the noon buying rate of the Federal Reserve Bank of New York for pounds sterling on the last day of each full month during the relevant year or each business day during the relevant month indicated.

<u>Low</u>	<u>High</u>
(U.S. dollars per pound sterling)	

Month Ended:

September 30, 2017	1.2972	1.3578
October 31, 2017	1.3063	1.3304
November 2017	1.3067	1.3506
December 2017	1.3316	1.3529
January 2018	1.3513	1.4264
February 2018	1.3794	1.4247
March 2018	1.3755	1.4236

On March 30, 2018, the exchange rate between the pound sterling and the U.S. dollar was \$1.4027 per £1.00.

PRICE RANGE OF OUR ORDINARY SHARES

Our ordinary shares have been trading on AIM under the symbol “MPH” since June 9, 2016.

The following table presents, for the periods indicated, the reported high and low sale prices, including intra-day sales, of our ordinary shares on AIM in pounds sterling and U.S. dollars. For the convenience of the reader, we have translated pound sterling amounts in the table below into U.S. dollars at the noon buying rate of the Federal Reserve Bank of New York on March 30, 2018, which was £1.00 to \$1.4027.

	Price Per Ordinary Share £		Price Per Ordinary Share \$	
	High	Low	High	Low
Year Ended December 31:				
2016 (beginning June 9, 2016)	3.40	2.40	4.77	3.37
2017	3.59	2.60	5.04	3.65
Quarterly:				
Second Quarter 2016 (beginning June 9, 2016)	3.03	2.40	4.25	3.37
Third Quarter 2016	3.40	2.71	4.77	3.80
Fourth Quarter 2016	3.00	2.41	4.21	3.38
First Quarter 2017	3.10	2.60	4.35	3.65
Second Quarter 2017	3.60	2.90	5.05	4.07
Third Quarter 2017	3.14	2.85	4.40	4.00
Fourth Quarter 2017	3.39	3.00	4.76	4.21
Most Recent Six Months:				
September 2017	3.12	3.00	4.38	4.21
October 2017	3.40	3.00	4.77	4.21
November 2017	3.35	3.15	4.70	4.42
December 2017	3.34	3.15	4.69	4.42
January 2018	3.26	3.20	4.57	4.49
February 2018	3.23	3.04	4.53	4.26
March 2018	3.18	3.01	4.46	4.22

On April 4, 2018, the last reported sale price of our ordinary shares on AIM was £3.14 per ordinary share (\$4.40 per ordinary share based on the exchange rate set forth above).

USE OF PROCEEDS

We estimate that the net proceeds to us from the global offering will be approximately \$62.0 million (or approximately \$69.0 million if the underwriters exercise in full their option to purchase additional ADSs), assuming an initial public offering price of \$17.62 per ADS in the U.S. offering and an offering price of £3.14 per ordinary share in the European private placement, which reflect the last reported sale price of our ordinary shares on AIM on April 4, 2018, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Each £0.1 (\$0.14) increase or decrease in the assumed offering price of £3.14 (\$4.40) per ordinary share, which reflects the last reported sale price of our ordinary shares on AIM on April 4, 2018, would increase or decrease our net proceeds from the global offering by £1.5 million (\$2.1 million), assuming that the number of ordinary shares (including ordinary shares in the form of ADSs) offered by us, as set forth on the cover of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. An increase or decrease of 1,000,000 in the number of ordinary shares (including ordinary shares in the form of ADSs) offered by us in the global offering, as set forth on the cover page of this prospectus, would increase or decrease our net proceeds by approximately £2.9 million (\$4.1 million), assuming no change in the assumed initial public offering price per ADS or in the assumed offering price per ordinary share and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from the global offering, together with our existing cash resources, as follows:

- approximately \$50.0 million to advance the clinical development of BPS-804 for the treatment of OI in adults and children, which we expect will be sufficient to complete our ongoing Phase 2b clinical trial in adults that we initiated in May 2017 and to initiate our planned Phase 2b/3 clinical trial of BPS-804 in children in 2018;
- approximately \$10.0 million to advance the clinical development of AZD-9668 for the treatment of severe AATD, which we expect will be sufficient to complete our planned Phase 2 proof-of-concept trial;
- approximately \$15.0 million to advance the clinical development of BGS-649 for the treatment of HH in obese men, which we expect will be sufficient to complete our ongoing Phase 2b six-month extension study and to commence further late stage clinical development; and
- the remainder to fund general research and development activities, working capital and other general corporate purposes, including the costs relating to entering into any third-party strategic relationship for development and commercialization of BCT-197.

The expected use of the net proceeds from the global offering represents our intentions based upon our current plans and business conditions. We may also use a portion of the net proceeds to in-license, acquire, or invest in additional products or assets, businesses, or technologies, although currently we have no specific agreements, commitments, or understandings in this regard. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the closing of the global offering or the amounts that we will actually spend on the uses set forth above. Predicting the costs necessary to develop product candidates can be difficult. The amounts and timing of our actual expenditures and the extent of clinical development may vary significantly depending on numerous factors, including the progress of our development efforts, the status of and results from ongoing clinical trials or clinical trials we may commence in the future, as well as any collaborations that we may enter into with third parties and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from the global offering.

We anticipate that our existing cash resources, together with the anticipated net proceeds from the global offering, will enable us to fund our operating expenses and capital expenditure requirements into the first quarter of 2020. We have based this estimate on assumptions that may prove to be incorrect, and we could use our available capital resources sooner than we currently expect.

Pending their use, we plan to invest the net proceeds from the global offering in short- and intermediate-term interest-bearing obligations and certificates of deposit.

DIVIDEND POLICY

We have never paid or declared any cash dividends on our ordinary shares, and we do not anticipate paying any cash dividends on our ordinary shares in the foreseeable future. We intend to retain all available funds and any future earnings to fund the development and expansion of our business. Under English law, among other things, we may only pay dividends if we have sufficient distributable reserves (on a non-consolidated basis), which are our accumulated realized profits that have not been previously distributed or capitalized less our accumulated realized losses, so far as such losses have not been previously written off in a reduction or reorganization of capital.

In addition, the terms of our existing loan agreement with Silicon Valley Bank and Kreos Capital V (UK) Limited, or Kreos, preclude us from paying cash dividends without Kreos's consent.

CAPITALIZATION

The table below sets forth our cash and short-term deposits and short-term investments and capitalization as of December 31, 2017 derived from our audited consolidated financial statements to be included elsewhere in this prospectus:

- on an actual basis; and
- on an as adjusted basis to give effect to the sale of 15,892,917 ordinary shares (including 11,352,084 ordinary shares in the form of ADSs) in the global offering at the assumed initial public offering price of \$17.62 per ADS in the U.S. offering and the assumed offering price of £3.14 per ordinary share in the European private placement, which reflect the last reported sale price of our ordinary shares on AIM on April 4, 2018, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this table in conjunction with our consolidated financial statements included elsewhere in this prospectus and the sections of this prospectus titled “Exchange Rate Information,” “Use of Proceeds,” “Selected Consolidated Financial Data,” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations.” For the convenience of the reader and except as otherwise indicated, we have translated pound sterling amounts in the table below as of December 31, 2017 into U.S. dollars at the noon buying rate of the Federal Reserve Bank of New York on December 29, 2017, which was £1.00 to \$1.3529. 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.

	As of December 31, 2017			
	Actual	As Adjusted(1)		
	(in thousands)			
Cash and short-term deposits and short-term investments	£ 52,545	\$ 71,088	£ 96,745	\$ 133,088
Total interest bearing loans and borrowings	£ 20,752	\$ 28,075	£ 20,752	\$ 28,075
Warrant liability	1,346	1,822	1,346	1,822
Equity:				
Issued capital	213	289	261	355
Share premium	118,227	159,949	162,380	221,882
Other capital reserves	16,359	22,132	16,359	22,132
Other reserves	7,000	9,470	7,000	9,470
Accumulated loss	(79,316)	(107,307)	(79,316)	(107,307)
Total equity	62,483	84,534	106,684	146,532
Total capitalization	£ 84,582	\$ 114,431	£ 128,782	\$ 176,429

- (1) Each £0.1 (\$0.14) increase or decrease in the assumed offering price of £3.14 (\$4.40) per ordinary share, which reflects the last reported sale price of our ordinary shares on AIM, would increase or decrease the as adjusted amount of each of cash and short-term deposits and short-term investments, total equity and total capitalization by £1.5 million (\$2.1 million), assuming the number of ordinary shares (including ordinary shares in the form of ADSs) offered by us in the global offering, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. An increase or decrease of 1,000,000 in the number of ordinary shares (including ordinary shares in the form of ADSs) offered by us in the global offering, as set forth on the cover page of

this prospectus, would increase or decrease the as adjusted amount of each of cash and short-term deposits and short-term investments, share premium, total equity and total capitalization by £2.9 million (\$4.1 million), assuming no change in the assumed initial public offering price per ADS or in the assumed offering price per ordinary share and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. U.S. dollar translations in this footnote were made at the exchange rate on March 30, 2018.

The table above excludes:

- 11,916,424 ordinary shares issuable upon the exercise of share options outstanding as of December 31, 2017 at a weighted average exercise price of £1.42 per ordinary share;
- 100,820 ordinary shares that may be issued upon exercise of share options issued under our Deferred Bonus Share Plan, as described in “Management—Equity Compensation Arrangements,” as of December 31, 2017;
- 1,799,382 ordinary shares that may be issued upon conversion of the Novartis Notes as of December 31, 2017;
- 696,490 ordinary shares issuable upon the exercise of warrants to purchase ordinary shares outstanding as of December 31, 2017 at a weighted average exercise price of £3.16 per ordinary share; and
- 1,430,000 ordinary shares issuable upon exercise of share options to be granted to our directors under our Share Option Plan for Non-Executive Directors and to our executive officers under our Share Option Scheme, upon the effectiveness of the registration statement of which this prospectus forms a part, at an exercise price per share equal to the offering price per ordinary share in the European private placement, as more fully described in “Management—Incentive Award Arrangements.”

DILUTION

If you invest in our ADSs or ordinary shares, your interest will be diluted to the extent of the difference between the offering price per ADS or ordinary share paid by purchasers in the global offering and our as adjusted net tangible book value per ADS or ordinary share after completion of the global offering. For the convenience of the reader and except as otherwise indicated, we have translated pound sterling amounts in this section as of December 31, 2017 into U.S. dollars at the noon buying rate of the Federal Reserve Bank of New York on December 29, 2017, which was £1.00 to \$1.3529.

At December 31, 2017, we had a historical net tangible book value of £29.5 million (\$39.9 million), corresponding to a net tangible book value of £0.41 per ordinary share (equal to \$2.24 per ADS). Net tangible book value per ordinary share represents the amount of our total assets less our total liabilities, excluding goodwill and other intangible assets, divided by the total number of our ordinary shares outstanding as of December 31, 2017.

After giving effect to the sale by us of 15,892,917 ordinary shares (including 11,352,084 ordinary shares in the form of ADSs) in the global offering at an assumed initial public offering price of \$17.62 per ADS in the U.S. offering and an assumed offering price of £3.14 per ordinary share in the European private placement, which reflect the last reported sale price of our ordinary shares on AIM on April 4, 2018 and, for the price per ADS, the exchange rate on March 30, 2018, and after deducting the estimated underwriting discounts and commissions and estimated expenses payable by us, our as adjusted net tangible book value as of December 31, 2017 would have been £73.7 million (\$101.9 million), representing an as adjusted net tangible book value of £0.85 per ordinary share and \$4.68 per ADS. This represents an immediate increase in net tangible book value of £0.44 per ordinary share (equal to \$2.44 per ADS) to existing shareholders and an immediate dilution of £2.29 per ordinary share and \$12.94 per ADS to new investors purchasing ordinary shares or ADSs in the global offering. Dilution per ordinary share or ADS to new investors is determined by subtracting the as adjusted net tangible book value per ADS or ordinary share after the global offering from the assumed initial public offering price per ADS or the assumed offering price per ordinary share, as applicable, paid by new investors.

The following table illustrates this dilution to new investors purchasing ADSs or ordinary shares in the global offering.

	As of December 31, 2017	
	Ordinary Shares	ADSs
Assumed offering price	£ 3.14	\$17.62
Net tangible book value per ordinary share or ADS	£ 0.41	\$2.24
Increase in net tangible book value per ordinary share or ADS attributable to the global offering	0.44	2.44
As adjusted net tangible book value per ordinary share or ADS after the global offering	0.85	4.68
Dilution per ADS or ordinary share to new investors in the global offering	<u>£ 2.29</u>	<u>\$12.94</u>

If the underwriters exercise in full their option to purchase an additional 425,703 ADSs, our as adjusted net tangible book value after the global offering would be £0.89 per ordinary share and \$4.91 per ADS, representing an immediate increase in as adjusted net tangible book value of £0.48 per ordinary share and \$2.67 per ADS to existing shareholders and immediate dilution of £2.25 per

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ordinary share and \$12.71 per ADS to new investors participating in the global offering, based on the assumed initial public offering price of \$17.62 per ADS in the U.S. offering and the assumed offering price of £3.14 per ordinary share in the European private placement, which reflect the last reported sale price of our ordinary shares on AIM on April 4, 2018 and, for the price per ADS, the exchange rate on March 30, 2018.

Each £0.1 (\$0.14) increase or decrease in the assumed offering price of £3.14 (\$4.40) per ordinary share, which reflects the last reported sale price of our ordinary shares on AIM on April 4, 2018, would increase or decrease the as adjusted net tangible book value after the global offering by £0.02 per ordinary share and \$0.10 per ADS and the dilution to new investors in the global offering by £0.02 per ordinary share and \$0.10 per ADS, assuming that the number of ordinary shares (including ordinary shares in the form of ADSs) offered by us in the global offering, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. An increase of 1,000,000 in the number of ordinary shares (including ordinary shares in the form of ADSs) offered by us in the global offering, as set forth on the cover page of this prospectus, would increase the as adjusted net tangible book value after the global offering by £0.03 per ordinary share and \$0.17 per ADS and decrease the dilution to new investors participating in the global offering by £0.03 per ordinary share and \$0.17 per ADS, assuming no change in the assumed initial public offering price per ADS or in the assumed offering price per ordinary share and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. A decrease of 1,000,000 in the number of ordinary shares (including ordinary shares in the form of ADSs) offered by us in the global offering, as set forth on the cover page of this prospectus, would decrease the as adjusted net tangible book value after the global offering by £0.03 per ordinary share and \$0.17 per ADS, and increase the dilution to new investors participating in the global offering by £0.03 per ordinary share and \$0.17 per ADS, assuming no change in the assumed initial public offering price per ADS or in the assumed offering price per ordinary share and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. U.S. dollar translations in this paragraph have been made at the exchange rate on March 30, 2018.

The following table summarizes, as of December 31, 2017, on the as adjusted basis described above, the number of ordinary shares purchased from us (including ordinary shares in the form of ADSs), the total consideration paid to us and the average price per ordinary share and per ADS paid by existing shareholders and by new investors purchasing ordinary shares or ADSs in the global offering. The table below and the two paragraphs that follow the table are based on an assumed initial public offering price of \$17.62 per ADS in the U.S. offering and an assumed offering price of £3.14 per ordinary share in the European private placement, which reflect the last reported sale price of our ordinary shares on AIM on April 4, 2018, before deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us and reflect the exchange rate on March 30, 2018:

	Ordinary Shares Purchased ⁽¹⁾		Total Consideration		Average Price per Ordinary Share	Average Price per ADS
	Number	Percent	Amount	Percent		
Existing shareholders	71,094,974	81.7%	\$144,329,161	67%	\$ 2.78	\$ 11.13
New investors	15,892,917	18.3	70,000,000	33	4.40	17.62
Total	86,987,891	100.0%	\$214,329,161	100.0%		

(1) Including ordinary shares in the form of ADSs.

Each £0.1 (\$0.14) increase or decrease in the assumed offering price of £3.14 (\$4.40) per ordinary share, which reflects the last reported sale price of our ordinary shares on AIM on April 4, 2018, would

increase or decrease the total consideration paid by new investors by £1.6 million (\$2.23 million) and would increase or decrease the percentage of total consideration paid by new investors by 1.0%, assuming that the number of ordinary shares (including ordinary shares in the form of ADSs) offered by us in the global offering, as set forth on the cover page of this prospectus, remains the same. An increase or decrease of 1,000,000 in the number of ordinary shares (including ordinary shares in the form of ADSs) offered by us, as set forth on the cover page of this prospectus, would increase or decrease the total consideration paid by new investors by £3.1 million (\$4.4 million) and would increase or decrease the percentage of total consideration paid by new investors by 1.4%, assuming no change in the assumed initial public offering price per ADS or in the assumed offering price per ordinary share.

If the underwriters exercise in full their option to purchase an additional 425,703 ADSs, the following will occur:

- the percentage of our ordinary shares held by existing shareholders will decrease to 80.2% of the total number of our ordinary shares outstanding after the global offering; and
- the percentage of our ordinary shares held by new investors will increase to approximately 19.8% of the total number of our ordinary shares outstanding after the global offering.

The tables above are based on 71,094,974 ordinary shares outstanding as of December 31, 2017. The tables above exclude:

- 11,916,424 ordinary shares issuable upon the exercise of share options outstanding as of December 31, 2017 at a weighted average exercise price of £1.42 per ordinary share;
- 100,820 ordinary shares that may be issued upon exercise of share options issued under our Deferred Bonus Share Plan, as described in “Management—Equity Compensation Arrangements,” as of December 31, 2017;
- 1,799,382 ordinary shares that may be issued upon conversion of the Novartis Notes, as of December 31, 2017;
- 696,490 ordinary shares issuable upon the exercise of warrants to purchase ordinary shares outstanding as of December 31, 2017 at a weighted average exercise price of £3.16 per ordinary share; and
- 1,430,000 ordinary shares issuable upon exercise of share options to be granted to our directors under our Share Option Plan for Non-Executive Directors and to our executive officers under our Share Option Scheme, upon the effectiveness of the registration statement of which this prospectus forms a part, at an exercise price per share equal to the offering price per ordinary share in the European private placement, as more fully described in “Management—Incentive Award Arrangements.”

To the extent that share options or warrants are exercised, the Novartis Notes convert to ordinary shares, or we issue additional ADSs or ordinary shares in the future, there will be further dilution to investors participating in the global offering. In addition, we may choose to raise additional capital because of market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. If we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our shareholders.

SELECTED CONSOLIDATED FINANCIAL DATA

You should read the following selected consolidated financial data together with the audited consolidated financial statements and the sections titled “Exchange Rate Information” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations.” We have derived the consolidated statement of comprehensive loss data for the years ended December 31, 2016 and 2017 and the consolidated balance sheet data as of December 31, 2017 from our consolidated financial statements included elsewhere in this prospectus. Our historical results are not necessarily indicative of the results that should be expected in any future period.

We maintain our books and records in pounds sterling, and we prepare our financial statements in accordance with IFRS as issued by the IASB. We report our financial results in pounds sterling. For the convenience of the reader, we have translated pound sterling amounts as of and for the years ended December 31, 2016 and 2017 into U.S. dollars at the noon buying rate of the Federal Reserve Bank of New York on December 29, 2017, which was £1.00 to \$1.3529. 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.

Year Ended December 31,			
2016		2017	
(£)	(\$)	(£)	(\$)

(in thousands, except per ordinary share data)

Consolidated Statement of Comprehensive Loss Data:

Research and development expenses	(24,563)	(33,231)	(34,607)	(46,819)
General and administrative expenses	(11,617)	(15,716)	(10,697)	(14,472)
Operating loss	(36,179)	(48,947)	(45,304)	(61,292)
Finance income	375	507	827	1,119
Finance charge	(180)	(243)	(1,090)	(1,475)
Net foreign exchange gain/(loss)	2,263	3,061	(1,384)	(1,873)
Net loss before tax	(33,722)	(45,622)	(46,951)	(63,520)
Income tax benefit	5,331	7,213	8,152	11,029
Loss attributable to equity holders of the Company	(28,390)	(38,409)	(38,799)	(52,491)
Total comprehensive loss attributable to equity holders of the Company	(28,390)	(38,409)	(38,799)	(52,491)
Basic and diluted loss per share	(0.63)	(0.85)	(0.56)	(0.76)

As of December 31,

2016		2017	
(£)	(\$)	(£)	(\$)

(in thousands)

Consolidated Balance Sheets Data:

Cash and short-term deposits and short-term investments	53,578	72,486	52,545	71,088
Total assets	86,765	117,384	96,335	130,332
Issued capital	193	261	213	289
Share premium	99,975	135,256	118,227	159,949
Accumulated loss	(40,579)	(54,900)	(79,316)	(107,307)
Total equity	79,257	107,226	62,483	84,534
Total liabilities	7,508(1)	10,158(1)	35,417(2)	47,916(2)

(1) Includes £3.1 million (\$3.9 million) aggregate principal amount of, and accrued interest on, the Novartis Notes. See “Related Party Transactions—Other Transactions with Novartis—Novartis Notes.”

(2) Includes £2.0 million (\$2.7 million) aggregate principal amount of, and accrued interest on, the Novartis Notes. See “Related Party Transactions—Other Transactions with Novartis—Novartis Notes.”

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with the information in "Selected Consolidated Financial Data" and our Consolidated Financial Statements, including the notes thereto. The following discussion is based on our financial information prepared in accordance with IFRS as issued by the IASB, which may differ in material respects from generally accepted accounting principles in other jurisdictions, including generally accepted accounting principles in the United States. The following discussion includes forward-looking statements that involve risks, uncertainties, and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of many factors, including but not limited to those described under "Risk Factors" and elsewhere in this prospectus.

Our financial statements are presented in pounds sterling. For the convenience of the reader, we have translated information in the tables below presented in pounds sterling into U.S. dollars at the noon buying rate of the Federal Reserve Bank of New York on December 31, 2017 which was £1.00 to \$1.3529. 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 are a multi-asset biopharmaceutical company focused on the acquisition, development, and commercialization of innovative therapeutics that aim to improve outcomes for patients with rare and specialty diseases. Our portfolio consists of four clinical-stage product candidates, each of which we acquired from large pharmaceutical companies. We are developing BPS-804 for the treatment of OI, AZD-9668 for the treatment of severe AATD, BCT-197 for the treatment of AECOPD and BGS-649 for the treatment of HH in obese men. Each of our product candidates has generated positive clinical data for our target indication or for a related indication. We believe our portfolio is well diversified because each of our product candidates employs a different mechanism of action and targets a separate indication. We intend to develop and directly commercialize our rare disease product candidates. For our specialty disease product candidates, we intend to develop them through late-stage clinical milestones and then seek strategic relationships for further clinical development and/or commercialization.

Our strategy is to selectively acquire product candidates that have already received significant investment from pharmaceutical companies and that have substantial pre-clinical, clinical, and manufacturing data packages. Since our inception in March 2015, we have successfully executed on this strategy by acquiring our current product candidates from Novartis and AstraZeneca. We have commenced or completed large, randomized, placebo-controlled Phase 2 clinical trials for three of our product candidates. In December 2017, we reported top-line data from our completed Phase 2 dose-ranging clinical trial for BCT-197, and in March 2018 we reported top-line data from our phase 2b study for BGS-649. We intend to commence additional late-stage clinical trials in 2018.

We do not have any approved products and, as a result, have not generated any revenue from product sales. Our ability to generate revenue sufficient to achieve profitability will depend on our successful development and eventual commercialization of our product candidates, if approved. Since our inception, we have incurred significant operating losses. For the years ended December 31, 2016 and 2017, we incurred net losses of £28.4 million and £38.8 million respectively. As of December 31, 2016 and 2017, we had an accumulated loss of £40.6 million and £79.3 million, respectively.

We expect to continue to incur significant expenses and operating losses for the foreseeable future as we advance the clinical development of our product candidates and seek regulatory approval. In

addition, if we obtain regulatory approval for any of our product candidates and do not enter into a third-party commercialization relationship, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales, and distribution. We also expect to incur expenses in connection with the in-license or acquisition of additional product candidates and the potential clinical development of any such product candidates. Furthermore, upon the closing of the global offering, we expect to incur additional costs associated with operating as a U.S. public company listed on the Nasdaq in addition to operating as a U.K. public company listed on AIM, including significant legal, accounting, investor relations, and other expenses that we did not previously incur.

As a result of these anticipated expenditures, we will need additional financing to support our continuing operations. 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, which may include collaborations with third parties. 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. We will need to generate significant revenue to achieve profitability, and we may never do so.

We were incorporated in March 2015 and are headquartered in London, United Kingdom. Since June 9, 2016, our shares have traded on AIM under the symbol “MPH.” Since our inception, we have raised a total of £102.9 million in gross proceeds from private and public placements of our ordinary shares to institutional investors and £3.5 million from the issuance of the Novartis Notes. In August 2017, we also entered into a credit facility in the amount of £20.0 million which was fully drawn by December 31, 2017. As of December 31, 2017, we had cash and short-term deposits and short-term investments of £52.5 million.

We are organized into a single segment following management’s view of the business as a single portfolio of product candidates. Research and development expenses are monitored at a product candidate level; however, decisions over resource allocation are made at an overall portfolio level. Our financing is managed and monitored on a consolidated basis.

Asset Purchase Agreements with Novartis

In July 2015, three of our wholly owned subsidiaries, Mereo BioPharma 3 Limited, Mereo BioPharma 2 Limited, and Mereo BioPharma 1 Limited, or the Subsidiaries, entered into asset purchase agreements, or the Purchase Agreements, to acquire from Novartis rights to BPS-804, BCT-197, and BGS-649, or the Compounds, respectively, and certain related assets, or, together with the Compounds, the Novartis Assets.

In connection with the acquisition of the Novartis Assets, we issued 3,849,000 of our ordinary shares to Novartis pursuant to a subscription agreement. See “Related Party Transactions—Subscription Agreement.” In addition, we paid Novartis \$1.5 million for a payment made by Novartis to a third party in full satisfaction of all monetary obligations of Novartis to such third party with respect to BCT-197. Under the Purchase Agreements, we have agreed to make tiered royalty payments to Novartis based on annual worldwide net sales of products that include the Compounds, or the Acquired Novartis Products, at percentages ranging from the high single digits to low double digits. In the event that the parties agree or it is otherwise determined in accordance with the Purchase Agreements that we require third-party intellectual property rights to exploit the Acquired Novartis Products, we are entitled to offset a specified percentage of amounts paid to such third parties in consideration for such intellectual property rights against the royalties due to Novartis. The royalty payments are payable for a period of ten years after the first commercial sale of an Acquired Novartis Product.

We further agreed that in the event of a change in control that involves the transfer, license, assignment, or lease of all or substantially all of a Subsidiary's assets, including a Compound and related assets, we will pay Novartis a percentage of the proceeds of such transaction, with the majority of the proceeds being retained by us. No payment, however, is required with respect to any transaction of Mereo BioPharma Group plc involving its equity interests, a merger or consolidation of it, or a sale of any of its assets.

We also entered into a sublicense agreement with Novartis, or the Sublicense Agreement, pursuant to which Novartis granted us an exclusive, worldwide, royalty-bearing sublicense for certain therapeutic antibody products directed against sclerostin, or the Antibody Products, including BPS-804. Under the Sublicense Agreement, we have agreed to pay Novartis royalties in the low single digits on worldwide net sales of Antibody Products. We have also agreed to pay Novartis up to \$3.25 million in development and regulatory milestones, and to use commercially reasonable efforts to develop and commercialize an Antibody Product.

License Agreement with AstraZeneca

In October 2017, our wholly owned subsidiary Mereo BioPharma 4 Limited entered into an exclusive license and option agreement, or the License Agreement, to obtain from AstraZeneca an exclusive worldwide, sub-licensable license under AstraZeneca's intellectual property rights relating to certain products containing a NE inhibitor, including products that contain AZD-9668, with an option to acquire such intellectual property rights, following commencement of a pivotal trial and payment of related milestone payments, or the Option, together with the acquisition of certain related assets.

Upon entering into the License Agreement, we made an upfront payment of \$3.0 million to AstraZeneca in cash and issued 490,798 new ordinary shares for an aggregate upfront payment equal to \$5.0 million. In connection with certain development and regulatory milestones, we have agreed to make payments of up to \$115.5 million in the aggregate and issue additional ordinary shares to AstraZeneca for licensed products containing AZD-9668. In addition, we have agreed to make payments to AstraZeneca based on specified commercial milestones of the product. In the event that we sub-license AZD-9668, we have also agreed to pay a specified percentage of sublicensing revenue to AstraZeneca. Otherwise, we have agreed to make royalty payments to AstraZeneca equal to ascending specified percentages of tiered annual worldwide net sales by us or our affiliates of licensed products (subject to certain reductions), ranging from the high single digits to low double digits.

Financial Operations Overview

Revenue

We do not currently have any approved products. Accordingly, we have not generated any revenue and do not expect to do so unless we obtain regulatory approval and commercialize any of our product candidates or until we receive revenues from collaborations with third parties, neither of which may occur.

Research and Development Expenses

Research and development expenses include:

- employee-related expenses, such as salaries, share-based compensation, and other benefits, for our research and development personnel;
- costs for production of drug substance and drug product and development of our manufacturing processes by CMOs;
- fees and other costs paid to CROs, consultants, and other suppliers to conduct our clinical trials and pre-clinical and non-clinical studies; and

- costs of facilities, materials, and equipment related to drug production and our clinical trials and pre-clinical and non-clinical studies.

Our direct research and development expenses are allocated on a product-by-product basis. We allocate employee-related expenses for our research and development personnel and other related expenses to specific product candidate development programs.

Product candidates in a later stage of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later stage clinical trials. We expect that our research and development expense will increase substantially as we continue to advance the clinical development of our product candidates, including through our ongoing and planned Phase 2b clinical trials of BPS-804, our planned Phase 2 proof-of-concept trial for AZD-9668, and our ongoing Phase 2b clinical trial and late-stage clinical development for BGS-649; hire additional clinical, scientific, and commercial personnel; and acquire or in-license future product candidates and technologies. As a result, we expect our research and development expenses will increase for the foreseeable future.

The successful development, approval, and commercialization of our product candidates is highly uncertain. At this time, we cannot reasonably estimate the nature, timing, and estimated costs of the efforts that will be necessary to complete the development of, or the period, if any, in which material net cash inflows may commence from any of our product candidates.

Our future expenditure on developing our product candidates is therefore highly uncertain. This is due to numerous risks and uncertainties associated with developing our drugs, including the uncertainty of:

- the scope, rate of progress, and expense of our research and development activities;
- the progress and results of our clinical trials and our pre-clinical and non-clinical studies;
- the terms and timing of regulatory approvals, if any;
- establishment of arrangements with our third-party manufacturers to obtain manufacturing supply;
- protection of our rights in our intellectual property portfolio;
- launch of commercial sales of any of our product candidates, if approved, whether alone or in collaboration with others;
- third party strategic relationships for late-stage clinical development and/or commercialization of our specialty product candidates and performance of our strategic partners under these arrangements;
- acceptance of any of our product candidates, if approved, by patients, the medical community and payors;
- competition with other therapies; and
- continued acceptable safety profile of any of our product candidates following approval.

Any of these variables with respect to the development of our product candidates or any other future candidate that we may develop could result in a significant change in the costs and timing associated with their development. For example, if the FDA, the EMA, or another regulatory authority were to require us to conduct pre-clinical studies and clinical trials beyond those we currently anticipate will be required for the completion of clinical development or if we experience significant delays in enrollment in any clinical trials, we could be required to expend significant additional financial resources and time on the completion of our clinical development programs. We may never succeed in obtaining regulatory approval for any of our product candidates.

General and Administrative Expenses

Our general and administrative expenses principally consist of salaries and related benefits, including share-based compensation, for personnel in our executive, finance and other administrative

functions. Other general and administrative costs include facility-related costs and professional services fees for auditing, tax and general legal services, as well as expenses associated with our requirements of being a listed public company on AIM.

We expect that our general and administrative costs will increase in the future as our business expands and we increase our headcount to support the expected growth in our operating activities. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, lawyers and accountants, among other expenses. In addition, we expect to continue to grant share-based compensation awards to existing and future key management personnel and other employees. Additionally, we anticipate increased costs associated with being a U.S. public company, including expenses related to services associated with maintaining compliance with Nasdaq rules and SEC requirements, director compensation, insurance, and investor relation costs. If any of our product candidates that we intend to directly commercialize obtains regulatory approval, we expect that we will incur expenses associated with building a sales and marketing team.

Finance Income

Finance income consists of interest earned on our short-term cash deposits.

Finance Charge

Finance charge consists of interest on the Novartis Notes, interest on our credit facility and losses on short term deposits. For further information on the terms of the Novartis Notes and our credit facility see “—Indebtedness.”

Net Foreign Exchange Gain/(Loss)

Our functional currency is pound sterling. We initially record transactions in foreign currencies at the rate ruling on the date the transaction first qualifies for recognition. Net foreign exchange gain/(loss) consists of the difference arising on settlement or translation of our foreign currencies, which are primarily held in U.S. dollars.

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. As of December 31, 2016 and 2017, we had cumulative carryforward tax losses of £16.3 million and £36.4 million, respectively. Subject to any relevant restrictions, we expect these to be available to carry forward and offset against future operating profits. As a company that carries out extensive research and development (“R&D”) activities, we benefit from the U.K. R&D small or medium-sized enterprise 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 of up to 33.35% of eligible R&D expenditure. Qualifying expenditures largely comprise employment costs for research staff, subcontracted CRO and CMO costs, consumables and certain internal overhead costs incurred as part of research projects. Certain subcontracted qualifying research expenditures are eligible for a cash rebate of up to 21.67%. Our effective cash rebate on qualifying R&D expenditure in 2017 was £8.2 million and we expect to receive this in 2018. Our cash rebate for 2016 was £5.3 million and we received this in May 2017. The cash rebate due for 2017 has increased by £2.8 million reflecting the higher level of qualifying R&D spend in 2017. We may not be able to continue to claim payable research and development tax credits in the future because we may no longer qualify as a small or medium-sized company.

In the event we generate revenues in the future, we may benefit from the U.K. “patent box” regime that allows profits attributable to revenues from patents or patented products to be taxed at an effective rate of 10%. This relief applies to profits earned from April 1, 2013. When taken in combination with the

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enhanced relief available on our R&D expenditures, we expect a long-term lower rate of corporation tax to apply to us. If, however, there are unexpected adverse changes to the U.K. R&D tax credit regime or the “patent box” regime, or for any reason we are unable to qualify for such advantageous tax legislation, or we are unable to use net operating loss and tax credit carryforwards and certain built-in losses to reduce future tax payments, our business, results of operations, and financial condition may be adversely affected.

Results of Operations

The following table sets forth our results of operations for the years ended December 31, 2016 and 2017.

	Year Ended December 31,			
	2016		2017	
	(£)	(\$)	(£)	(\$)
	(in thousands)			
Research and development expenses	(24,563)	(33,231)	(34,607)	(46,819)
General and administrative expenses	(11,617)	(15,716)	(10,697)	(14,472)
Operating loss	(36,179)	(48,947)	(45,304)	(61,292)
Finance income	375	507	827	1,119
Finance charge	(180)	(243)	(1,090)	(1,475)
Net foreign exchange gain/(loss)	2,263	3,061	(1,384)	(1,873)
Net loss before tax	(33,722)	(45,622)	(46,951)	(63,520)
Income tax benefit	5,331	7,213	8,152	11,029
Loss attributable to equity holders of the Company	(28,390)	(38,409)	(38,799)	(52,491)

Comparison of the Years Ended December 31, 2016 and 2017

Research and Development Expenses

The following table sets forth our research and development expenses by product development program for the years ended December 31, 2016 and 2017.

	Year Ended December 31,			
	2016		2017	
	(£)	(\$)	(£)	(\$)
	(in thousands)			
BPS-804	4,804	6,499	13,380	18,100
BCT-197	9,734	13,169	10,014	13,548
BGS-649	9,432	12,761	10,801	14,613
AZD-9668	—	—	2	3
Unallocated costs	593	803	410	555
Total research and development expenses	24,563	33,231	34,607	46,819

Our total R&D, expenses increased by £10.0 million, or 41%, from £24.6 million in 2016 to £34.6 million in 2017. This was a result of increased spending on clinical development as we continued the Phase 2 programs for BCT-197 and BGS-649 and commenced the adult Phase 2b program for BPS-804. Total R&D expenses included payments we made to CROs and other suppliers for the ongoing clinical development of each of BPS-804, BCT-197, and BGS-649, which increased from £17.9 million in 2016 to £22.8 million in 2017, reflecting the inclusion of expenses relating to the adult Phase 2b study for BPS-804. Additionally, our R&D employee related costs increased from £3.1 million in 2016

to £4.1 million in 2017, reflecting increased headcount, higher other employee-related expenses, including travel, and higher bonus amounts earned in 2017. Our payments to CMOs for the provision of drug substance and drug product and associated manufacturing development to support our clinical trials and the transfer of manufacturing of drug substance and drug product from Novartis to third-party manufacturers increased from £2.9 million in 2016 to £7.3 million in 2017, reflecting ongoing manufacturing activity primarily due to the manufacture of additional clinical trial materials in respect of BPS-804.

Direct research and development expenses related to BPS-804 increased by £8.6 million, from £4.8 million in 2016 to £13.4 million in 2017, due to the commencement of the adult Phase 2b study for BPS-804 during 2017 and the completion of the manufacture of associated clinical trial materials.

Direct research and development expenses related to BCT-197 increased by £0.3 million, from £9.7 million in 2016 to £10.0 million in 2017, due to the completion of the Phase 2 clinical trial for BCT-197 in the fourth quarter of 2017, which trial commenced in the first half of 2016.

Direct research and development expenses related to BGS-649 increased by £1.4 million, from £9.4 million in 2016 to £10.8 million in 2017, due to the continuation of the Phase 2b study for BGS-649 and the commencement of the Phase 2b extension study.

General and Administrative Expenses

General and administrative expenses decreased by £0.9 million, or 7.8%, from £11.6 million in 2016 to £10.7 million in 2017. This decrease was due to a decrease in share-based payment expenses of £2.8 million, reflecting the lower level of share option awards in 2017, partially offset by a rise in other general and administrative costs of £1.9 million, reflecting an increase in payroll-related costs due to a higher headcount and higher bonus amounts earned in 2017, together with additional legal and professional fees in connection with the equity financing in April 2017, the entering into a credit facility in August 2017, and the acquisition of AZD-9668 in October 2017.

Finance Income

Interest earned on our short-term cash deposits increased from £0.4 million in 2016 to £0.8 million in 2017, reflecting higher cash balances held in deposit in 2017.

Finance Charge

Finance charge increased from £0.2 million in 2016 to £1.1 million in 2017, reflecting interest costs on additional borrowings under our credit facility during 2017 and lower costs related to the Novartis Notes after the exercise of a portion of these notes in April 2017. Finance charge in 2017 also included £0.3 million of losses on short term deposits.

Net Foreign Exchange Gain/(Loss)

In 2016, the net foreign exchange gain was £2.3 million, primarily as a result of the unrealized gain on translation of cash deposits held primarily in U.S. dollars at year end, reflecting a strengthening of the U.S. dollar against pounds sterling during the year. In 2017, net foreign exchange loss was £1.4 million, reflecting a weakening of the U.S. dollar against pounds sterling during the year which negatively impacted the translation of our foreign deposits and investments at December 31, 2017.

Income Tax Benefit

We recorded a tax credit of £5.3 million in 2016 and £8.2 million in 2017. The tax credit represents the cash rebate from the U.K. tax authorities we qualified for in respect of eligible research and development activities during the years. Due to the increase in qualifying R&D expenditure in 2017, the 2017 tax credit increased by £2.9 million from the 2016 tax credit. The 2016 tax credit was received in May 2017. We expect to receive the 2017 tax credit of £8.2 million in 2018.

Liquidity and Capital Resources

Overview

Since our inception, we have incurred significant operating losses. We expect to incur significant expenses and operating losses for the foreseeable future as we advance the clinical development of our product candidates. We expect that our research and development and general and administrative costs will increase in connection with conducting clinical trials for our product candidates and any new product candidates we acquire and due to the costs in seeking marketing approval for our product candidates in Europe and the United States as well as other jurisdictions. As a result, we will need additional capital to fund our operations, which we may obtain from additional debt or equity financings, collaborations, licensing arrangements, or other sources.

We do not currently have any approved products and have never generated any revenue from product sales or otherwise. To date, we have financed our operations primarily through the issuances of our equity securities and convertible debt and our credit facility, which we entered into in August 2017. Since we were incorporated, we have raised a total of £102.9 million in gross proceeds from private and public placements of our ordinary shares to institutional investors and £3.5 million from the issuance of the Novartis Notes. In August 2017, we also entered into a credit facility in the amount of £20.0 million which we have fully drawn down during 2017. As of December 31, 2016 and 2017, we had cash and short term deposits and short term investments of £53.6 million and £52.5 million, respectively.

Cash Flows

The table below summarizes our cash flows for the period presented.

	Year Ended December 31,			
	2016		2017	
	(£)	(\$)	(£)	(\$)
	(in thousands)			
Net cash used in operating activities	(29,662)	(40,130)	(32,148)	(43,493)
Net cash from (used in) investing activities	373	504	(3,745)	(5,065)
Net cash from financing activities	68,356	92,480	33,744	45,651
Net increase (decrease) in cash and cash equivalents	39,067	52,854	(2,149)	(2,907)

Operating Activities

The increase in net cash used in operating activities was £2.4 million, from £29.7 million in 2016 to £32.1 million in 2017. This was largely due to the increased loss before taxation due to higher levels of R&D activity in 2017, offset in part by the increase in cash tax credit received from £0.9 million in 2016 to £5.3 million in 2017. In addition there were changes in the add-backs for non-cash expenses as follows: (i) share based payment add-backs were reduced from £6.5 million to £3.7 million, reflecting lower share based payments charge in 2017, (ii) foreign exchange add-backs increased by £3.6 million in 2017, reflecting the movement from a foreign exchange gain of £2.3 million in 2016 to a loss of £1.4 million in 2017, (iii) interest earned increased by £0.5 million in 2017 as a result of higher cash held in deposits throughout 2017 and increased interest rates, (iv) £0.3 million on interest expense on the credit facility entered into in August 2017, (v) £0.3 million of loss on short-term deposits in 2017 and (vi) working capital increased by £5.6 million in 2017, reflecting higher creditor and accrual balances at December 31, 2017 compared to 2016.

Investing Activities

Our net cash from investing activities reduced from £0.4 million in 2016 to net cash used in financing activities of £3.7 million in 2017, largely due to the £2.3 million cash cost of purchasing a

license for AZD-9668 from AstraZeneca in October 2017 and £2.5 million of cash transferred into short-term investments held on deposit, partially offset by £1.1 million of interests received on our short-term deposits.

Financing Activities

Our net cash from financing activities reduced from £68.4 million in 2016 to £33.7 million in 2017. In June 2016, we raised gross proceeds of £56.5 million in the second tranche of a private placement entered into in 2015. In June 2016, in connection with our ordinary shares being admitted to trading on the AIM market, we raised gross proceeds of £11.4 million in private placements of our ordinary shares with institutional investors. In addition, and as part of that transaction, we raised £3.5 million gross proceeds in the form of the Novartis Notes. Our total costs in respect of the foregoing transactions were £3.0 million. In April 2017, we raised gross proceeds of £15.0 million in a placement of ordinary shares with institutional investors, for which the cash cost amounted to £0.8 million. In August 2017, we borrowed the first £10.0 million tranche under our credit facility and in December 2017 we borrowed the second and final tranche under our credit facility for another £10.0 million. In addition, in 2017, we paid an aggregate of £0.3 million of interest on our outstanding borrowings under our credit facility.

Operating and Capital Expenditure Requirements

As of December 31, 2016 and 2017, we had an accumulated loss of £40.6 million and £79.3 million, respectively. We expect to continue to incur significant operating losses in 2018 and for the foreseeable future as we continue our research and development efforts and seek to obtain regulatory approval of our product candidates and any future product candidate we develop.

We expect our expenses to increase substantially in connection with our ongoing development activities related to our product candidates. In addition, upon the closing of the global offering, we expect to incur additional costs associated with operating as a U.S. public company listed on the Nasdaq Global Market in addition to operating as a U.K. public company listed on AIM.

We anticipate that our expenses will increase substantially due to the costs associated with our current and planned clinical trials, our outsourced manufacturing activities and other associated costs including the management of our intellectual property portfolio. These costs will increase further if we:

- seek to develop additional product candidates;
- seek regulatory approvals for any of our product candidates that successfully completes clinical trials;
- potentially establish a sales, marketing, and distribution infrastructure and scale-up manufacturing capabilities to commercialize any products for which we may obtain regulatory approval and chose to commercialize directly;
- expand our intellectual property portfolio;
- add further central clinical, scientific, operational, financial and management information systems, and personnel, including personnel to support our development and to support our operations as a U.S. public company listed on the Nasdaq Global Market; and
- experience any delays or encounter any issues from any of the above, including but not limited to failed studies, complex results, safety issues, or other regulatory challenges.

We expect that our existing cash resources will enable us to fund our currently committed clinical trials and operating expenses and capital expenditure requirements for at least the next 12 months. We expect that these cash resources, together with anticipated net proceeds from the global offering, will enable us to fund our current and planned clinical trials and operating expenses and capital expenditure requirements into the first quarter of 2020. We have based these estimates on assumptions that may prove to be wrong, and we may use our available capital resources sooner than

we currently expect. Because of the numerous risks and uncertainties associated with the development of our product candidates and any future product candidates and because the extent to which we may enter into collaborations with third parties for development of any of our product candidates is unknown, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with completing the research and development of our product candidates. Our future capital requirements will depend on many factors, including:

- the costs, timing, and results of our ongoing Phase 2b clinical trial for BPS-804, our planned pediatric Phase 2b/3 study for BPS-804 in Europe, and our planned Phase 2 clinical trial for AZD-9668 and late-stage clinical development for BGS-649;
- the costs and timing of manufacturing clinical supplies of our product candidates;
- the costs, timing, and outcome of regulatory review of our product candidates, including post-marketing studies that could be required by regulatory authorities;
- the costs, timing, and outcome of potential future commercialization activities, including manufacturing, marketing, sales and distribution, for our product candidates that we commercialize directly;
- the timing and amount of revenue, if any, received from commercial sales of our product candidates;
- the costs and timing of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims, including any claims by third parties that we are infringing upon their intellectual property rights;
- the sales price and availability of adequate third-party coverage and reimbursement for our product candidates;
- the effect of competitors and market developments;
- the extent to which we are able to acquire new product candidates or enter into licensing or collaboration arrangements for our product candidates, although we currently have no commitments or agreements to complete any such transactions; and
- milestone and deferred payments under our license and option agreement with AstraZeneca.

Our revenues, if any, will be derived from sales of any products that we are able to successfully develop, receive regulatory approval for, and commercialize in future years. In the meantime, we will need to obtain substantial additional funds to achieve our business objective.

Adequate additional funds may not be available to us on acceptable terms, or at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a shareholder. Any future debt financing or preferred equity 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 and may require the issuance of warrants, which could potentially dilute your ownership interests.

If we raised additional funds through collaborations, strategic alliances, 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 grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce, or terminate our product development programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Indebtedness

Novartis Notes

On June 3, 2016, as part of the fundraising for our product development programs and for general corporate purposes and in connection with our ordinary shares being admitted to trading on AIM, we issued 3,463,563 unsecured convertible loan notes to Novartis, or the Novartis Notes, for aggregate proceeds of £3,463,563. The Novartis Notes bear interest at 4% per annum payable annually and accruing daily and rank senior to any other unsecured obligations we may have. Novartis may at any time convert all or some of the Novartis Notes, together with accrued interest, into our ordinary shares at a conversion price of £2.21 per ordinary share as long as, following such conversion, Novartis holds no more than 19.5% of the aggregate voting rights of our company. In addition, upon conversion, Novartis is entitled to receive an additional number of our ordinary shares equal to the number of shares into which such Novartis Notes and accrued interest are converted multiplied by 0.93, or the Bonus Shares. At December 31, 2016, Novartis was entitled to receive up to 1,453,520 Bonus Shares.

On April 6, 2017, Novartis delivered to us a notice of conversion with respect to £1,398,552 aggregate principal amount of Novartis Notes. Pursuant to such notice, on April 26, 2017, £1,398,552 aggregate principal amount of Novartis Notes was converted into 632,829 fully paid ordinary shares. Additionally, in connection with such conversion, we issued 588,532 Bonus Shares to Novartis. At December 31, 2017, Novartis was entitled to receive up to 864,998 Bonus Shares.

To the extent any of the Novartis Notes remain outstanding on March 2, 2021, we are obligated to pay Novartis the principal amount of such outstanding Novartis Notes together with any accrued interest.

Credit Facility

On August 7, 2017, we entered into a loan agreement with Silicon Valley Bank and Kreos Capital V (UK) Limited, which provides for total borrowings of £20.0 million. We borrowed £10.0 million on each of August 21, 2017 and December 29, 2017 for general working capital purposes. We are obligated to make interest-only payments on the loan amount until September 30, 2018, and thereafter we are obligated to pay interest and principal in 30 equal monthly installments until March 31, 2021, the maturity date. The loan bears interest at an annual fixed rate equal to 9.0%. In addition a final payment of 7.5% of the principal loan amount is due upon the earlier of the maturity date, prepayment in whole of the loan amount, mandatory repayment, acceleration of the loan, and the loan becoming immediately due and payable due to an event of default. The loan is secured by substantially all of our assets, including intellectual property rights owned or controlled by us.

In connection with the loan agreement, we issued to the lenders warrants to subscribe for 363,156 of our ordinary shares at an exercise price of £3.029 per ordinary share and warrants to subscribe for 333,334 of our ordinary shares at an exercise price of £3.30 per ordinary share.

Contractual Obligations and Commitments

The table below summarizes our contractual obligations at December 31, 2017.

	Payments Due by Period				
	Up to 1 year	1-3 Years	3-5 Years (in thousands)	Over 5 Years	Total
Novartis Notes(1)	£ 83	£ 165	£ 2,079	–	£ 2,327
Bank loan(2)	3,574	17,794	2,983	–	24,351
Operating lease(3)	744	535	–	–	1,279
Total	<u>£ 4,401</u>	<u>£18,494</u>	<u>£5,062</u>	<u>–</u>	<u>£27,957</u>

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- (1) Includes interest. See “—Indebtedness—Novartis Notes.”
 - (2) Includes interest. See “—Indebtedness—Credit Facility.”
 - (3) Reflects payments due for our office lease under a lease agreement that expires in August 2025. We may terminate this agreement in August 2020 and, as such, no amounts due under the agreement after August 2020 are reflected.

As further described above under “—Asset Purchase Agreements with Novartis” and “—License Agreement with AstraZeneca,” under various agreements with Novartis and AstraZeneca, we have agreed to make milestone payments and pay royalties. We have not included any deferred payment obligations, such as milestones or royalties, in the table above, as the amount, timing, and likelihood of such payments are not known and will remain uncertain for the foreseeable future.

In addition, we enter into contracts in the ordinary course of business with CROs, CMOs, and other vendors 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.

Off-Balance Sheet Arrangements

We did not have during the period presented, and we do not currently have, any off-balance sheet arrangements.

Quantitative and Qualitative Disclosures about Market Risk

We are exposed to a variety of financial risks. Our overall risk management program seeks to minimize potential adverse effects of these financial risks on our financial performance.

Interest Rate Risk

We manage interest rate risk by monitoring short and medium-term interest rates and placing cash on deposit for periods that optimize the amount of interest earned while maintaining access to sufficient funds to meet day-to-day cash requirements. We have a committed borrowing facility in an amount of £20.0 million which was fully drawn as of the date of this prospectus. Loans under the credit facility bear interest at a fixed rate of 9.0% per annum. The interest payable on the Novartis Notes is fixed at 4.0% per annum. Consequently, there is no material exposure to interest rate risk in respect of interest payable.

Credit Risk

We consider all of our material counterparties to be creditworthy. We consider the credit risk for each of our major counterparties to be low. We are, however, dependent on a number of third parties for the delivery of our programs and, in addition, where appropriate we pay upfront deposits and fees in advance of the delivery of services where required. We continue to assess credit risk as part of our management of these third-party relationships.

Liquidity Risk

We manage our liquidity risk by maintaining adequate cash reserves at banking facilities and invested in short term money market accounts, and by continuously monitoring our cash forecasts, our actual cash flows and by matching the maturity profiles of financial assets and liabilities.

Foreign Currency Risk

Foreign currency risk reflects the risk that the value of a financial commitment or recognized asset or liability will fluctuate due to changes in foreign currency rates. The majority of our operating costs

are denominated in pounds sterling, euros, and U.S. dollars. Our financial position, as expressed in pounds sterling, is exposed to movements in foreign exchange rates against the U.S. dollar and the euro. Our main trading currencies are pounds sterling and U.S. dollars. We are exposed to foreign currency risk as a result of operating transactions and the translation of foreign currency bank accounts and short-term deposits. We monitor our exposure to foreign exchange risk. We have not entered into foreign exchange contracts to hedge against foreign exchange fluctuations but maintain cash and investments in U.S. dollars to cover anticipated forward commitments. For the year ended December 31, 2017, we recorded a net foreign exchange loss of £1.4 million, compared to a £2.3 million gain for the year ended December 31, 2016, primarily as a result of the accretion in value of our U.S. dollar cash deposits measured at the balance sheet date compared to the date of conversion. These deposits amounted to \$20.0 million and \$10.5 million as of December 31, 2016 and 2017, respectively.

Critical Accounting Judgments and Estimates

Our financial statements have been prepared in accordance with IFRS as issued by the IASB. In the application of our accounting policies, we are required to make judgments, estimates, and assumptions about the value of assets and liabilities for which there is no definitive third-party reference. The estimates and associated assumptions are based on historical experience and other factors that we considered to be relevant. Actual results may differ from these estimates. We review our estimates and assumptions 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.

The following are our critical judgments and estimates that we have made in the process of applying our accounting policies and that have the most significant effect on the amounts recognized in our consolidated financial statements included elsewhere in this prospectus.

Measurement of Share-Based Compensation

We have granted share options and awards under the following four equity award plans: (i) the Mereo BioPharma Group Limited Share Option Scheme, or the 2015 Plan; (ii) the Mereo BioPharma Group plc Share Option Scheme, or the Share Option Plan; (iii) the Mereo BioPharma Group plc Long Term Incentive Plan, or LTIP; and (iv) the Mereo BioPharma Group plc Deferred Bonus Share Plan, or DBSP.

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 options using either the Black-Scholes model, or for options with performance conditions, a simulation model. We charge the fair value to the statement of comprehensive income over the expected vesting period.

2015 Plan

Under the 2015 Plan, we have granted share options to our employees, including our senior executives, and our non-executive directors. For all employees, share options vest over four years with 25% vesting 12 months after the vesting start date and the balance vesting equally over the next 36 months. For non-executive directors, share options vest over three years in three equal annual installments. There have been no performance conditions attached to the share options granted under the 2015 Plan. Certain rules apply for accelerated vesting and exercise of share options in the event of an offer for the company.

We measure the share options under the 2015 Plan at fair value at their grant date in accordance with IFRS 2, "Share-based Payment," using the Black-Scholes model. The exercise price of the share options under the 2015 Plan is in the range of £1.29 to £2.21 per ordinary share and the share options

were granted between September 2015 and May 2016 with an exercise period of 10 years from the date of grant.

Other inputs to determine the fair value included:

Volatility(1)	56%
Risk-free rate	1.48 to 2.07%
Expected dividends	£nil

(1) Measured by reference to a basket of similar companies trading on AIM.

The fair value of such share-based compensation is recognized as an expense over the respective vesting period. Share-based compensation expense under the 2015 Plan was £6.2 million in 2016.

Since there is no historical data in relation to the expected life of the share options, the contractual life of the options was used in calculating the expense for the year. Volatility was estimated by reference to the share price volatility of a group of comparable companies over a retrospective year equal to the expected life of the share options.

Share Option Plan

Under the Share Option Plan, we granted 1,593,188 share options to executive officers and other employees and 15,000 options lapsed. The weighted-average remaining contractual life for the share options outstanding as of December 31, 2017 was 9.4 years. The weighted-average fair value of options granted during the year was £1.85 per share. Share options outstanding at the end of the year had an exercise price of between £3.03 and £3.23 per share.

The weighted-average inputs to the models used for the fair value of share options granted during the year ended December 31, 2017 were as follows:

	Year ended December 31, 2016	Year ended December 31, 2017
Expected volatility (%)	–	49-51
Risk-free interest rate (%)	–	1.06-1.33
Expected life of share options (years)	–	10
Market price of ordinary shares (£)	–	3.03-3.23
Model used	–	Black Scholes

Since there is no historical data in relation to the expected life of the share options, the contractual life of the options was used in calculating the expense for the year. Volatility was estimated by reference to the share price volatility of a group of comparable companies over a retrospective year equal to the expected life of the share options.

Long Term Incentive Plan

Under the LTIP, share options were granted to executive officers on June 9, 2016 and April 4, 2017. 75% of these share options have specific performance conditions and vest up to 33.3% on June 9, 2019 (Tranche 1), 33.3% on June 9, 2020 (Tranche 2) and 33.3% on June 9, 2021 (Tranche 3) depending on achieving share price increases relative to the share price at January 1 2019, January 1, 2020 and January 1, 2021 relative to the share price at admission to AIM. The share options were granted at a weighted-average fair value of £1.34 per ordinary share and have an exercise price of £nil.

Other inputs used to determine the fair value of the strategic element of the LTIP share options were:

	Tranche 1	Tranche 2	Tranche 3
Volatility	48.9%	48.9%	48.9%
Risk-free rate	0.48%	0.61%	0.74%
Expected dividends	£nil	£nil	£nil

We measure the fair value of the share price element of the LTIP share options at their grant date in accordance with IFRS 2, "Share-based Payment," using a Monte Carlo simulation model. Share options have an exercise period of one year from vesting date.

25% of the LTIP share options are subject to strategic targets and share options vest three years from the date of grant. LTIP share options were granted at a weighted-average fair value of £1.34 per ordinary share and have an exercise price of £nil. We measure the fair value of the strategic element of the LTIP share options using the Black-Scholes model.

Other inputs used to determine the fair value of LTIP share options were:

Volatility	48.9%
Risk-free rate	0.74%
Expected dividends	£nil

The fair value of the total share-based compensation is recognized as an expense over the respective vesting period. Share-based compensation expense under the LTIP was £0.3 million in 2017 and £0.1 million in 2016.

Deferred Bonus Share Plan

Under the DBSP, share options were granted to executive officers on April 4, 2017 in respect of the year ended December 31, 2016. Share options have no performance conditions, an exercise price of £nil, a normal vesting date of 3 years from grant and are exercisable within one year of vesting.

Since the DBSP awards are equity-settled, they are valued using the grant date model based on the fair value at the date of issue. Given there are no market conditions nor any non-vesting conditions, the value of the awards will be the monetary value of the shares issued at the date of issue.

The fair value of such share-based compensation is recognized as an expense over the respective vesting period. Share-based compensation expense under the DBSP was £0.3 million in 2017 and £0.2 million in 2016.

We account for related social security contributions on all share options as cash-settled share-based payment transactions. We recognize a liability over the vesting period in respect of share options to be exercised. The total charge in respect of social security was £1.1 million in 2017 and £1.0 million in 2016.

We expect to grant additional share options that will result in additional share-based compensation expense.

Measuring the Fair Value of Our Intangible Assets

At each reporting date, we review the carrying value of our intangible assets to determine whether there is any indication that those assets have been impaired. If such an indication exists, the

recoverable amount of the asset, being the higher of the asset's fair value less costs to sell and value in use, is compared to the asset's carrying value. Any excess of the asset's carrying value over its recoverable amount is expensed to the income statement.

We consider the future development costs, the probability of successfully progressing each program to product approval and likely commercial returns after product approval, among other factors, when reviewing for indicators of impairment. The results of this testing did not indicate any impairment of the acquired products' rights in the years ended December 31, 2016 and December 31, 2017.

The acquired development programs are assets which are not used in launched products. These assets have not yet begun to be amortized but have been tested for impairment by assessing their value in use. Value-in-use calculations for each program are utilized to calculate the recoverable amount. The calculations use pre-tax cash flow projections covering the period through product development to commercial sales up to the later of loss of patent protection or market exclusivity, which extend beyond five years from the balance sheet date; no cash flows are included after this date. Approved products are assumed to be out-licensed such that we receive upfront fees, milestone payments, and royalties on sales; therefore, we do not incur any costs of commercialization after out-licensing.

Key assumptions we have used for the value-in-use calculations are described as follows:

- development costs to obtain regulatory approval—costs are estimated net of any contributions expected from collaborative arrangements with future partners. Our directors have developed cost estimates based on our previous experience and in conjunction with the expertise of our clinical development partners;
- launch dates of products—these reflect our expected date of launch for products based on the timeline of development programs required to obtain regulatory approval. The assumptions are based on our directors' prior experience together with the outcome of discussions with regulators;
- probability of successful development—we estimate probabilities of success for each phase of development based on industry averages and knowledge of specific programs;
- out-licensing upfront fees, milestones, and royalty rates on sales—we estimate these amounts based on prior experience and access to values from similar transactions in the industry, which are collated and accessible from specialist third-party sources;
- sales projections—these are based on our internal projections using external market data and market research commissioned by us;
- profit margins and other operational expenses—these are based on our internal projections of current product manufacturing costings, with input from manufacturing partners where applicable, and estimates of operating costs based on our prior industry experience;
- cash flow projections—the periods over which cash flows are forecast (based on the current patent protection periods relevant to the asset), are as follows:
 - BCT-197—18 years;
 - BGS-649—17 years;
 - BPS-804—14 years; and
 - AZD-9668—16 years
- discount rates—the discount rate is estimated on a pre-tax basis reflecting our estimated cost of capital and is applied consistently across each of the operating segments. The cost of capital in 2017 was reviewed in 2017 and was 15.3%. In 2016, the cost of capital was 11.2%.

At this stage of product development, we believe the key sensitivity for all three development programs is the probability of successful completion of clinical trials in order to obtain regulatory

approval for sale. Therefore, full impairment of a development program is expected should such related trials be unsuccessful and development halted.

Determining whether an intangible asset is impaired requires an estimation of whether there are any indications that its carrying value is not recoverable.

Fair Value of Warrants

In connection with the borrowings under the credit facility in 2017, we issued to the lenders warrants to subscribe for an aggregate of 363,156 of our ordinary shares at an exercise price of £3.029 per ordinary share and warrants to subscribe for an aggregate of 333,334 of our ordinary shares at an exercise price of £3.30 per ordinary share.

The fair value of the warrants is measured using the Black-Scholes model taking into account any appropriate amendments to inputs in respect of volatility and remaining expected life of the warrants.

The weighted-average inputs to the models used for the fair value of warrants granted during the period ended December 31, 2017 were as follows:

	Year ended December 31 2017
Expected volatility (%)	50-51
Risk-free interest rate (%)	1.10-1.25
Expected life of share options (years)	9.6-10
Market price of ordinary shares (£)	3.00-3.25
Model used	Black Scholes

The fair value of the warrants at December 31, 2017 was £1.3 million. The carrying value of the loan at December 31, 2017 was £18.8 million.

Fair Value of Provision for Deferred Cash Consideration

Provision for deferred cash consideration represents the potential future cash payments in respect of the AZD-9668 acquisition. As this is in respect of a product which is not yet approved, this provision for deferred cash consideration includes all contingent payments up to the point of exercise of the right to acquire the intellectual property and excludes potential downstream milestones, royalties or other payments because they are unquantifiable. The provision is recognized as a liability at each balance sheet date with the amounts calculated as the risk adjusted net present value of certain future payments we may make. The payments are dependent on reaching specific milestones based on the commencement and outcome of clinical trials.

The total amount of provision for deferred cash consideration at December 31, 2017 was £2.1 million.

Key inputs used to determine the value of the provision for deferred consideration include:

Discount rate:	15.3%
Likely payment date:	Based on the expected timing of the planned Phase 2 study for AZD-9668
Risk adjustment:	Standard risk adjustments for orphan asset development programs

Fair Value of Deferred Equity Consideration

Deferred equity consideration is accounted for as equity-settled share-based payment transactions in accordance with IFRS 2. Fair value is determined by the share price at the date of purchase.

Deferred Tax and Current Tax Credits

Tax on the profit or loss for the year comprises current and deferred tax. Tax is recognized in the statement of operations, except to the extent that it relates to items recognized directly in equity, in which case it is recognized in equity. Current tax is the expected tax payable on the taxable income or loss for the year, using tax rates enacted or substantively enacted at the balance sheet date, and any adjustment to tax payable in respect of previous years. Tax credits are accrued for the year based on calculations that conform to the U.K. research and development tax credit regime applicable to small and medium-sized companies.

We may not be able to continue to claim research and development tax credits in the future under the current research and development tax credit scheme, when we become a U.S. public company because we may no longer qualify as a small or medium-sized company. However, we may be able to file under a large-company scheme. Deferred tax is recognized on temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for taxation purposes. The amount of deferred tax is based on the expected manner of realization or settlement of the carrying amount of assets and liabilities, using tax rates enacted or substantively enacted at the balance sheet date. A deferred tax asset is recognized only to the extent that it is probable that future taxable profits will be available against which the asset can be utilized. No deferred tax assets are recognized on our losses carried forward because there is currently no indication that we will make sufficient profits to utilize these tax losses.

Recent Accounting Pronouncements

We refer to Note 27 to our consolidated financial statements for the year ended December 31, 2017 included elsewhere in this prospectus for a discussion of new standards and interpretations not yet adopted by us.

JOBS Act

In April 2012, the U.S. Jumpstart Our Business Startups Act of 2012, or the JOBS Act, was enacted. Section 107(b) of the JOBS Act provides that an “emerging growth company,” or EGC, can take advantage of an extended transition period for complying with new or revised accounting standards. Thus, an EGC can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. Given that we currently report and expect to continue to report under IFRS as issued by the IASB, we have irrevocably elected not to avail ourselves of this extended transition period, and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

BUSINESS

Overview





We are a multi-asset biopharmaceutical company focused on the acquisition, development, and commercialization of innovative therapeutics that aim to improve outcomes for patients with rare and specialty diseases. Our portfolio consists of four clinical-stage product candidates, each of which we acquired from large pharmaceutical companies. We are developing BPS-804 for the treatment of osteogenesis imperfecta, or OI, AZD-9668 for the treatment of severe alpha-1 antitrypsin deficiency, or AATD, BCT-197 for the treatment of acute exacerbations of chronic obstructive pulmonary disease, or AECOPD, and BGS-649 for the treatment of hypogonadotropic hypogonadism, or HH, in obese men. Each of our product candidates has generated positive clinical data for our target indication or for a related indication. We believe our portfolio is well diversified because each of our product candidates employs a different mechanism of action and targets a separate indication. We intend to develop and directly commercialize our rare disease product candidates. For our specialty disease product candidates, we intend to develop them through late-stage clinical milestones and then seek strategic relationships for further clinical development and/or commercialization.

Our strategy is to selectively acquire product candidates that have already received significant investment from pharmaceutical companies and that have substantial pre-clinical, clinical, and manufacturing data packages. Since our inception in March 2015, we have successfully executed on this strategy by acquiring our current product candidates from Novartis Pharma AG, or Novartis, and AstraZeneca AB, or AstraZeneca. We have commenced or completed large, randomized, placebo-controlled Phase 2 clinical trials for three of these product candidates. In December 2017, we reported top-line data from our completed Phase 2 dose-ranging clinical trial for BCT-197, and in March 2018, we reported top-line data from our Phase 2b dose-ranging clinical trial for BGS-649. We intend to commence additional late-stage clinical trials in 2018.

Our team has extensive experience in the pharmaceutical and biotechnology sector in the identification, acquisition, development, manufacturing, and commercialization of product candidates in multiple therapeutic areas. Our senior management team has long-standing relationships with senior executives of large pharmaceutical companies, which we believe enhances our ability to identify and acquire additional product candidates.

Our Pipeline

The following table summarizes our pipeline. We have global commercial rights to all of our product candidates.

Product Candidate Indication	Phase 1	Phase 2a	Phase 2b	Phase 3	Last Milestone	Next Anticipated Milestone
BPS-804 (setrusumab) Osteogenesis Imperfecta					Phase 2b initiated	Commence pediatric Phase 2b/3 study in Europe and Canada in the second half of 2018
AZD-9668 (alvelestat) Severe Alpha-1 Antitrypsin Deficiency					Positive Phase 2 data in bronchiectasis	Initiate Phase 2 trial in AATD in the second half of 2018
BCT-197 (acumapimod) Acute Exacerbations of COPD					Positive Phase 2 data	Enter into strategic relationship for further clinical development
BGS-649 (leflutrolole) Hypogonadotropic Hypogonadism in Obese Men					Positive Phase 2b data	Phase 2b extension study data in 4Q 2018

Our portfolio consists of the following product candidates:

- **BPS-804:** BPS-804, or setrusumab, is a novel antibody we are developing as a treatment for OI, a rare genetic disease that results in bones that can break easily and is commonly known as brittle bone disease. OI is a debilitating orphan disease for which there are no treatments approved by the U.S. Food and Drug Administration, or FDA, or European Medicines Agency, or EMA. It is estimated that OI affects a minimum of 20,000 people in the United States and approximately 32,000 people in Germany, Spain, France, Italy, and the United Kingdom. BPS-804 is designed to inhibit sclerostin, a protein that inhibits the activity of bone-forming cells. We believe BPS-804's mechanism of action is well suited for the treatment of OI and has the potential to become a novel treatment option for patients that could reduce fractures and improve patient quality of life.

In 2016, we obtained orphan drug designation in OI for BPS-804 in the United States and the European Union, or EU, and in February 2017, BPS-804 was accepted into the adaptive pathways program in the EU. In addition, in November 2017, BPS-804 was admitted to the PRIME scheme of the EMA. Prior to our acquisition of BPS-804, Novartis conducted four clinical trials in 106 patients and healthy volunteers. A Phase 2 clinical trial of BPS-804 showed statistically significant improvements in bone formation biomarkers and bone mineral density. In May 2017, we initiated a randomized, double-blind, placebo-controlled Phase 2b clinical trial for BPS-804 in adults in the United States, Europe and Canada. We expect the results from this trial, if favorable, along with validation of our use of high resolution peripheral quantitative computerized tomography, or HRPqCT, as a biomarker for fracture, may be sufficient to support the submission of a Conditional Marketing Authorisation, or CMA, to the EMA for BPS-804 for the treatment of adults with OI in the EU. We also intend to commence a Phase 2b/3 clinical trial of BPS-804 in children with OI in the second half of 2018 in Europe and Canada, with fracture rate as the primary endpoint. We expect the results from this trial, if favorable, may be sufficient to validate our use of HRPqCT and support the submission of a CMA to the EMA for BPS-804 for the treatment of children with severe OI in the EU.

In the United States, the FDA has denied our request for a Type C meeting to discuss the initiation of a pediatric Phase 2b study for BPS-804 for the treatment of patients with severe OI. The FDA has cited that a serious cardiovascular safety concern exists in adults treated with sclerostin inhibitors that has yet to be resolved. We do not believe the FDA's concern is related to BPS-804. Given the undetermined risk/benefit assessment in adults, the FDA believes it is premature to conduct a study of sclerostin inhibitors in children. If this safety issue is resolved, we plan on submitting our proposed Phase 2b/3 study for BPS-804 in children with severe OI to the FDA to expand the proposed trial into the United States. We believe the FDA's position does not impact our ability to conduct our clinical development activities of BPS-804 in Europe and Canada for children with severe OI and our clinical development activities of BPS-804 in Europe, the United States and Canada for adults with OI.

- **AZD-9668:** AZD-9668, or alvelestat, is a novel, oral small molecule we are developing for the treatment of severe AATD, a potentially life-threatening rare, genetic condition caused by a lack of alpha-1 antitrypsin, or AAT, a protein that protects the lungs from enzymatic degradation. This degradation leads to severe debilitating diseases, including early-onset pulmonary emphysema, a disease that irreversibly destroys the tissues that support lung function. There are an estimated 50,000 patients in North America and 60,000 patients in Europe with severe AATD. AZD-9668 is designed to inhibit neutrophil elastase, or NE, a neutrophil protease, which is a key enzyme involved in the destruction of lung tissue. We believe the inhibition of NE has the potential to protect AATD patients from further lung damage.

Prior to our license of AZD-9668, AstraZeneca conducted 12 clinical trials involving 1,776 subjects, including trials in bronchiectasis and cystic fibrosis, or CF. Although these trials were

conducted in diseases other than AATD, we believe the data demonstrated potential clinical benefit and biomarker evidence of treatment effect for AATD patients. We intend to initiate a Phase 2 proof-of-concept clinical trial in patients with severe AATD in the second half of 2018.

- **BCT-197:** BCT-197, or acumapimod, is a p38 MAP kinase inhibitor we are developing as an oral first-line acute therapy for patients with AECOPD. Chronic obstructive pulmonary disease, or COPD, is a non-fully-reversible, progressive lung disease in which inflammation plays a central role. There are an estimated 16 million people in the United States and 13 million people in Europe diagnosed with COPD. Of all hospital admissions in the United States related to COPD, approximately 63% are for AECOPD patients. We believe BCT-197 offers a potential new treatment for controlling inflammation by targeting pathways that drive the pathological mechanism behind AECOPD.

Since there are currently no approved therapies in the United States or the EU to treat AECOPD, we believe that there is significant medical need for a drug which is disease-modifying. We believe BCT-197 could potentially prevent AECOPD instead of just treating the symptoms and has the potential to improve quality of life, slow the progression of the disease, and significantly reduce direct healthcare costs.

Prior to our acquisition of BCT-197, Novartis conducted five clinical trials in 459 patients and healthy volunteers, including a Phase 2a trial in AECOPD patients that showed a clinically meaningful improvement in lung function at all doses and a statistically significant improvement in lung function at the highest dose. In December 2017, we reported top-line data from our completed placebo-controlled Phase 2 dose-ranging clinical trial for BCT-197. The trial was conducted in 282 patients with AECOPD to explore two different dosing regimens on top of standard of care, which included steroids, antibiotics, and bronchodilators. Both dosing regimens showed a statistically significant change in FEV1 from baseline to Day 7, meeting the trial's primary endpoint on an intent-to-treat patient population basis. Treatment with BCT-197 also showed a statistically significant reduction in the number of COPD exacerbations that required hospitalization. In addition, BCT-197 was reported to be safe and well tolerated. Based on these results, we plan to enter into one or more strategic relationships with third parties for further clinical development and, if approved, commercialization, of BCT-197.

- **BGS-649:** BGS-649, or leflutrolole, is a once-weekly oral therapy we are developing for the treatment of HH in obese men. HH is a clinical syndrome that results from inadequate levels of testosterone. Based on World Health Organization, or WHO, estimates and scientific data, we estimate there are approximately seven million cases of HH in obese men in the United States and approximately five million cases of HH in obese men in Europe. In these men, a decline in testosterone is exacerbated by high levels of the aromatase enzyme, which is present in fat tissue and leads to a reduction in testosterone. BGS-649 is designed to inhibit the aromatase enzyme and is being developed to restore normal levels of testosterone without causing excessively high testosterone levels or reducing the levels of luteinizing hormone, or LH, or follicular stimulating hormone, or FSH. Both LH and FSH play key roles in sperm formation and LH plays a key role in endogenous testosterone formation. In contrast to current therapies for HH, which involve the exogenous administration of testosterone and lead to further down regulation of LH and FSH, we believe that BGS-649, by preserving sperm formation through LH and FSH production, may present a benefit to patients.

Prior to our acquisition of BGS-649, Novartis conducted seven clinical trials in 131 patients and healthy volunteers, including a Phase 2 proof-of-concept trial for HH in obese men in which BGS-649 normalized testosterone levels in all patients and demonstrated an increase in LH and FSH levels. In March 2018, we reported top-line data from our completed Phase 2b dose-ranging clinical trial of BGS-649 for the treatment of HH in obese men. The trial enrolled 271 patients who were administered placebo or one of three doses of BGS-649. The

trial met its primary endpoint of normalizing testosterone levels in at least 75% of subjects after 24 weeks of treatment and all of the secondary endpoints, including normalizing testosterone in at least 90% of patients after 24 weeks of treatment at the two highest doses and improvement in LH and FSH levels at all three doses. BGS-649 was reported to be well-tolerated in the trial. A subset of patients have entered into a six-month extension study, and we expect data from the extension study in the fourth quarter of 2018. We intend to advance BGS-649 into late-stage clinical development.

Our Strategy

We intend to become a leading biopharmaceutical company focused on the acquisition, development and commercialization of innovative therapeutics that aim to improve outcomes for patients with rare and specialty diseases. The key elements of our strategy to achieve this goal include:

- **Rapidly develop and directly commercialize our rare disease product candidates.** We have commenced a Phase 2b clinical trial of BPS-804 for the treatment of OI in adults in the United States, Europe and Canada. If the results from this trial are favorable and our use of HRPqCT as a biomarker for fracture is validated, we intend to submit a CMA to the EMA for the treatment of adults with OI in the EU. We also intend to commence a Phase 2b/3 clinical trial of BPS-804 for the treatment of OI in children in the second half of 2018 in Europe and Canada. We expect that the results from this trial, if favorable, will be sufficient to validate our use of HRPqCT and support the submission of a CMA to the EMA for BPS-804 for the treatment of children with severe OI in the EU. We intend to initiate a Phase 2 clinical trial of AZD-9668 for the treatment of severe AATD in the second half of 2018 and, if the results are favorable and pending regulatory feedback, continue to develop AZD-9668 toward approval and commercialization. We plan to establish our own sales and marketing organization in the United States and Europe for BPS-804 and AZD-9668 and any future rare disease product candidates.
- **Efficiently advance our specialty disease product candidates and explore strategic relationships with third parties for further clinical development and/or commercialization.** Based on the top-line results from our Phase 2 clinical trial of BCT-197, we plan to enter into one or more strategic relationships with third parties for BCT-197 to undertake the next phase of clinical development and, if approved, commercialization. In March 2018, we reported top-line Phase 2b data for BGS-649 for the treatment of HH. We intend to continue late-stage clinical development of BGS-649 and plan to enter into strategic relationships with third parties for commercialization, if approved. We may also enter into strategic relationships with third parties to complete the clinical development of BGS-649.
- **Leverage our expertise in business development to expand our pipeline of product candidates.** Our senior management team has extensive relationships with large pharmaceutical and biotechnology companies, as evidenced by the acquisition of our four clinical-stage product candidates. We intend to leverage these relationships to grow our pipeline with a focus on rare diseases. We intend to continue to identify, acquire, develop, and ultimately commercialize novel product candidates that have received significant investment from large pharmaceutical companies. We will continue to focus on acquiring product candidates with either proof-of-concept clinical data in our target indication or with clinical data in a related disease and a strong scientific rationale that supports development in our target indication. Using a disciplined approach, we intend to continue building a diverse portfolio of product candidates that we believe have compelling market potential, robust pre-clinical, clinical, and manufacturing data packages, and a clear regulatory pathway.
- **Continue to be a partner of choice for large pharmaceutical and biotechnology companies.** We believe that we are a preferred partner for large pharmaceutical and biotechnology companies as they seek to unlock the potential in their development pipelines

and deliver therapeutics to patients in areas of high unmet medical need. We have strong relationships with these companies, as evidenced by our agreements with Novartis and AstraZeneca, and a track record of structuring transactions that enable us to leverage our core development capabilities while creating value for all stakeholders. We intend to continue to enter into strategic relationships that align our interests with those of large pharmaceutical and biotechnology companies and that we believe to be mutually beneficial.

BPS-804 (setrusumab) for the Treatment of Osteogenesis Imperfecta

Overview

We are developing BPS-804 (setrusumab) for the treatment of OI. BPS-804 is a novel, intravenously administered antibody that is designed to inhibit sclerostin, a protein that inhibits the activity of bone-forming cells, known as osteoblasts. We believe that by blocking sclerostin, BPS-804 has the potential to induce or increase osteoblast function and maturation of these cells, increasing bone formation and reducing bone resorption, thereby reducing fractures in OI patients.

Background of Osteogenesis Imperfecta

OI is a genetic disorder characterized by fragile bones and reduced bone mass, resulting in bones that break easily, loose joints and weakened teeth. In severe cases, patients may experience hundreds of fractures in a lifetime. In addition, people with OI often suffer from muscle weakness, early hearing loss, fatigue, curved bones, scoliosis (curved spine), brittle teeth, respiratory problems and short stature. The disease can be extremely debilitating and even fatal in newborn infants with a severe form of the disease. OI is a rare condition that affects a minimum of 20,000 people, an incidence rate of 6.2 out of 100,000, in the United States, according to estimates by the Osteogenesis Imperfecta Foundation, and approximately 32,000 people, an incidence rate of 10 out of 100,000, in Germany, Spain, France, Italy, and the United Kingdom, according to estimates by Orphanet.

There are eight recognized forms of OI, designated type I through type VIII. Type I is the least severe form, while type II is the most severe and frequently causes death at or shortly after birth. The most prevalent form of OI is type I, which is estimated to occur in approximately 50% to 60% of OI patients. The less severe forms of OI, such as type I and type IV, are characterized by broken bones, often as a result of minor trauma. Patients typically have a blue or gray tint to the sclera, the part of the eye that is usually white, and are at risk of hearing loss in adulthood. Individuals affected by less severe types of OI are usually of normal height and have normal life spans.

In addition to the features of less severe forms of OI, type III patients are characterized by frequent bone fractures starting even before birth, respiratory problems, short stature, a disorder of tooth development, and reduced life expectancy as a result of respiratory failure and cardiac failure. Type III OI is characterized by extreme growth deficiency and typically scoliosis, and patients may require wheelchairs for mobility. The most severe forms of OI, particularly type II, may be characterized by an extremely small, fragile rib cage, and underdeveloped lungs. Infants with these abnormalities have life-threatening problems related to breathing and often die shortly after birth.

Current Treatment Landscape for Osteogenesis Imperfecta

There are no approved therapies for the treatment of OI in the United States or the EU. The only treatments available to OI patients are the acute management of fractures as they occur and bisphosphonate drugs, which are not approved for this indication but are commonly used off-label in children.

Current treatment of OI is directed towards management of fractures with casting or surgical fixation. Following either of these, physical therapy will often be required. Preventative surgeries, such

as intramedullary, or in-bone, nailing fixation are also undertaken. Supportive care for the disease involves surgery to correct deformities, internal splinting of bones with metal rods, bracing to support weak limbs and decrease pain, physical therapy, and muscle strengthening and aerobic conditioning to improve bone mass and strength.

Many OI patients are treated off-label with drugs indicated for osteoporosis. Bisphosphonate drugs slow down the rate at which osteoclasts, which are cells which resorb or take away bone, reduce the bones' mass. These include Aredia (pamidronate), Fosamax (alendronate) and Reclast (zoledronic acid). However, bisphosphonate drugs are not approved by the FDA or the EMA for use in OI. We are not aware of any long-term clinical studies demonstrating an improvement in fractures in adults and the effect of long-term therapy with these drugs remains unclear. Therefore, we believe the effect of bisphosphonate drugs on fractures, growth, bone deformity, mobility, and pain remains unclear in both adults and children. Despite not being approved, bisphosphonates are effectively the standard of care in children, especially those with more severe disease.

Our Approach

Our product candidate for treating OI is BPS-804, a fully human monoclonal antibody that is designed to inhibit sclerostin. Sclerostin is produced in osteocytes, which are mature bone cells that are thought to be the mechanoreceptor cells that regulate the activity of bone-building osteoblasts and bone-resorbing osteoclasts. Sclerostin inhibits the activity of osteoblasts. We believe that by blocking sclerostin, BPS-804 has the potential to induce or increase osteoblast activity and maturation of these cells, increasing bone formation and reducing bone resorption, thereby reducing fractures in OI patients.

Clinical Development of BPS-804

The following table summarizes the historical, current and planned clinical trials of BPS-804:

Historical Trials			Current Trials			Planned Trials			
Phase	Population	Subjects Treated with BPS-804	Phase	Population	Planned Enrollment	Phase	Population	Planned Enrollment	Target Start
Phase 1	Healthy Volunteers (postmenopausal women)	30	Phase 2b	OI (adult)	120	Phase 2b/3	OI (pediatrics)	~150	2018
Phase 2	Hypophosphatasia	8							
Phase 2	Women with Low Bone Mineral Density	36							
Phase 2	OI	9							

Phase 1 and Phase 2 Clinical Trials in Other Indications

Novartis performed a Phase 1 single ascending dose trial in 30 healthy female volunteers. A range of doses of BPS-804 were administered and were shown to be well tolerated. A Phase 2 ascending dose trial was also performed in eight adult patients with hypophosphatasia, a rare disorder characterized by abnormal development of bones and teeth. Three different BPS-804 doses were administered and a positive effect on bone formation biomarkers was observed.

Additionally, Novartis performed a Phase 2 clinical trial in a total of 44 postmenopausal women with low bone mineral density, in which 36 subjects were treated with BPS-804. The trial had four arms, with patients dosed weekly for three weeks (4 doses), monthly for three months (4 doses) and quarterly for one quarter (2 doses), and a placebo group. In this trial, BPS-804 increased bone mineral density up to 7.8%, 7.3% and 4.3% in the weekly, monthly and quarterly groups, respectively.

Phase 2 Clinical Trial in Osteogenesis Imperfecta

Novartis conducted a Phase 2 randomized, open-label, intra-patient dose-escalating proof-of-concept trial in the United States, Canada and Europe in adults with OI. The objectives were:

- to evaluate safety and tolerability of BPS-804;
- to evaluate the effect of BPS-804 on lumbar spine bone mineral density measured by dual-energy X-ray absorptiometry, or DEXA, scan; and
- to determine the pharmacodynamic effect of BPS-804 when administered as multiple dose escalating intravenous infusions on:
 - serum bone formation markers, including procollagen 1 N-terminal propeptide, or P1NP, procollagen 1 C terminal propeptide, or P1CP, osteocalcin, or OC, and bone-specific alkaline phosphatase, or BSAP; and
 - serum bone resorption markers, including C-telopeptides of type I collagen cross-links, or CTX-1, and N-telopeptides of type I collagen cross-links.

The trial included 14 patients with types I, III and IV OI, nine of which were treated and five of which were observed as a reference group in parallel during the trial to provide comparative data. The reference patients did not receive drug or placebo. The patients were treated with three doses of BPS-804 two weeks apart, over four weeks, and were followed for a total of 21 weeks after the last dose. DEXA studies were performed at day 141 and bone biomarkers were measured on days eight, 15, 29, 36, 43, 57, 85, 113 and 141, for both groups.

Treatment with BPS-804 showed a statistically significant increase in lumbar spine bone mineral density from baseline, which was sustained at day 141 of the trial, 16 weeks after the last dose of BPS-804, with a mean increase in lumbar spine bone mineral density in treated patients of 4%, as shown in the table below:

Parameter	BPS-804			Reference		
	Number of patients	Ratio of geometric mean to baseline	p-value	Number of patients	Ratio of geometric mean to baseline	p-value
Bone Mineral Density	9	1.04	0.038*	4**	1.01	0.138

* Statistically significant, meaning a less than 5% chance (or p-value less than 0.05) that the observed results occurred by chance alone.

** One patient in the reference group did not complete the study and is not included in the results.

Bone turnover comprises two processes: the removal of bone and the laying down of new bone. Markers in blood can be used to assess the formation and resorption of bone. P1NP and CTX-1 are the markers of bone formation and resorption, respectively, that are recommended for clinical use and are considered the two reference markers by the International Osteoporosis Foundation and International Federation of Clinical Chemistry.

Treatment with BPS-804 also showed a statistically significant improvement in all measured bone formation biomarkers at day 43 of the trial, as shown in the table below, as well as a trend of reduction in the CTX-1 biomarker of bone resorption:

Bone formation biomarker	BPS-804			Reference			Ratio of geometric means 90% confidence interval
	Number of patients	Ratio of geometric mean to baseline	p-value	Number of patients	Ratio of geometric mean to baseline	p-value	
P1NP	9	1.84	<0.001*	5	1.06	0.651	1.75
P1CP	9	1.53	0.003*	5	1.05	0.6	1.45
BSAP	9	1.59	<0.001*	5	0.87	0.582	1.83
OC	9	1.44	0.012*	5	0.81	0.436	1.78

* Statistically significant.

These results showed a statistically significant upregulation in the activity of P1NP, P1CP, BSAP, and increased OC levels, while the corresponding biomarkers remained unchanged or declined moderately in the reference group.

We believe that the observed increase in lumbar spine bone mineral density in patients treated with BPS-804, along with the bone biomarker data, support the bone anabolic effects of BPS-804 in adult patients with moderate OI and support the potential for BPS-804 to stimulate bone formation and reduce bone resorption after three doses.

Summary of Safety Results

In the trials conducted by Novartis, BPS-804 was generally well tolerated. In the Phase 2 OI clinical trial, there was one non-drug related significant adverse event in the reference group. The most common adverse events were headaches, influenza, arthralgia and fatigue both in patients who received BPS-804 and in the reference group.

Current and Planned Phase 2b Clinical Trials in Osteogenesis Imperfecta

In May 2017, we commenced a Phase 2b clinical trial of BPS-804 in the United States, Europe and Canada. The Phase 2b clinical trial is a multi-center, randomized double-blind, placebo-controlled trial of BPS-804 in which we intend to enroll approximately 140 adult OI patients. Similar to the Phase 2 clinical trial conducted by Novartis, we plan to enroll patients with types I, III and IV OI.

The primary endpoint of this trial is the change in trabecular volumetric bone mineral density measured by HRpQCT and change in bone strength using finite element analysis, or FEA. HRpQCT enables the measurement of relevant parameters of bone density, microstructure, and strength. FEA uses data from HRpQCT measurements to provide a predictive measure of the whole bone strength and biomechanical risk of fracture. Additional endpoints include further measures of bone parameters measured by HRpQCT, bone turnover markers and quality of life scores. Based on our interactions with the EMA, we believe that the results from this trial, if favorable, and validation of our use of HRpQCT as a biomarker for fracture, from our planned Phase 2b/3 trial in children with OI, will be sufficient to support the submission of a CMA for BPS-804 for the treatment of adults with OI in the EU.

In addition, in the second half of 2018, we intend to commence a Phase 2b/3 clinical trial of BPS-804 for the treatment of OI in children aged 5 to 18 in Europe and Canada. We intend to enroll approximately 150 patients in this trial, with fracture rate as the primary endpoint. Based on our interactions with the EMA, we expect the results from this trial, if favorable, will be sufficient to validate our use of HRpQCT and support the submission of a CMA for BPS-804 for the treatment of children with severe OI in the EU.

In the United States, the FDA has denied our request for a Type C meeting to discuss the initiation of a pediatric Phase 2b study for BPS-804 for the treatment of patients with severe OI. The FDA has cited that a serious cardiovascular safety concern exists in adults treated with sclerostin inhibitors that has yet to be resolved. We do not believe the FDA's concern is related to BPS-804. Given the undetermined risk/benefit assessment in adults, the FDA believes it is premature to conduct a study of sclerostin inhibitors in children. If this safety issue is resolved, we plan on submitting our proposed European Phase 2b/3 study for BPS-804 in children with severe OI to the FDA to expand the proposed trial into the United States. We believe the FDA's position does not impact our ability to conduct our clinical development activities of BPS-804 in Europe and Canada for children with severe OI and our clinical development activities of BPS-804 in Europe, the United States and Canada for adults with OI.

AZD-9668 (alvelestat) for the Treatment of Severe Alpha-1-Antitrypsin Deficiency

Overview

We are developing AZD-9668 (alvelestat) for the treatment of severe AATD, a potentially life-threatening rare, genetic condition that results in severe debilitating diseases, including early-onset pulmonary emphysema. AZD-9668 is a novel, oral small molecule designed to inhibit NE. Scientific data indicate that the increased risk of lung tissue injury in AATD patients may be due to inadequately controlled NE caused by insufficient AAT. We believe that by inhibiting NE, AZD-9668 has the potential to reduce the destruction of lung tissue and stabilize clinical deterioration in severe AATD patients.

Background of Alpha-1-Antitrypsin Deficiency

AATD is a genetic disease. There are estimated to be 50,000 people in North America and 60,000 in Europe with severe AATD, which we define as AATD in patients with either a PiZZ genotype or NullNull genotype. The major function of AAT in the lungs is to protect the connective tissue from NE released from triggered neutrophils. In the majority of people, the lungs are defended from NE attack by AAT, which is a highly effective inhibitor of NE. Severe AATD patients, however, produce minimal or no AAT and are, therefore, unable to defend against NE attack. As a result, severe AATD patients commonly experience degeneration of lung function, such as early-onset pulmonary emphysema, which significantly affects quality of life and life expectancy.

AATD is the result of a mutation of the SERPINA1 gene. Most people with AATD inherit two copies of the defective PiZ allele, or gene variant, of the SERPINA1 gene, resulting in a PiZZ genotype. Patients with a PiZZ genotype have approximately 15% of normal AAT levels. Individuals who inherit two copies of the Null allele, resulting in a NullNull genotype, do not produce any AAT. These two groups are at very high risk of developing lung disease. AATD patients with the PiZZ genotype experience a decline in the amount of air that can be forcibly exhaled in one second, or FEV1, a standard measure of exhalation. The annual mortality rate in this genotype estimated to be 4%. Given that individuals with the NullNull genotype do not produce any AAT, we believe that they are likely to experience an even greater annual decline in FEV1.

Current Treatment Landscape for Alpha-1-Antitrypsin Deficiency

AATD patients are monitored by pulmonary functions tests, including spirometry. Treatment involves bronchodilators and inhaled corticosteroid medications and pulmonary rehabilitation, with increased intensity of therapy guided by disease severity. Surgical options include lung volume reduction surgery and lung transplantation. Both are highly invasive, and transplantation is only an option for a portion of patients with end-stage disease despite optimal therapy.

Augmentation therapy is available for AATD, using a partially purified plasma preparation highly enriched for AAT that is administered weekly by intravenous infusion. This therapy was approved by the FDA based on its biochemical efficacy, or its ability to raise blood levels of AAT, but not based on

clinical outcome data. Several observational studies have suggested that AAT augmentation therapy may slow the rate of decline in lung function in a subgroup of AATD patients with moderate-to-severe airflow obstruction. In a randomized, controlled trial of augmentation therapy, patients had some reduction in the progression of emphysema, as assessed by measuring lung density using computed tomography. The study did not show significant slowing in the decline in FEV1.

We believe that current therapies for AATD are inadequate. Surgical options are limited to a few patients, are highly invasive, have variable results, and do not address the underlying pathology of AATD. AAT augmentation therapy, while FDA approved, was not approved on the basis of clinical outcome data. In addition, AAT augmentation therapy requires potentially inconvenient weekly intravenous infusions.

Our Approach

Our product candidate for treating severe AATD is AZD-9668, a potent, specific oral small molecule that is designed to inhibit NE. We believe that by inhibiting NE, AZD-9668 has the potential to reduce the enzymatic destruction of lung tissue. Furthermore, we believe that convenient oral dosing of AZD-9668 could provide a significant advantage compared to the current treatments for AATD of surgery or weekly intravenous AAT augmentation therapy.

Clinical Development of AZD-9668

The following table summarizes the historical and planned clinical trials of AZD-9668:

Historical Trials				Planned Trials			
Phase	# of Studies	Population	Subjects Treated with AZD-9668	Phase	Population	Planned Enrollment	Target Start
Phase 1	7	Healthy Volunteers / COPD	143	Phase 2	AATD	~150	2018
Phase 2	3	COPD	958				
Phase 2	1	CF	26				
Phase 2	1	Bronchiectasis	22				

Phase 2 Clinical Trials

Although prior clinical trials of AZD-9668 were in indications other than AATD, we believe that the clinical benefit observed in these trials and the biomarker evidence of treatment effect make AZD-9668 a promising potential product candidate for treating severe AATD. In particular, we believe the results from the Phase 2 clinical trials in bronchiectasis and CF are most relevant in assessing AZD-9668's potential to treat severe AATD.

Phase 2 Clinical Trial in Bronchiectasis

AstraZeneca conducted a double-blind, placebo-controlled Phase 2 clinical trial in bronchiectasis in a total of 38 patients, 22 of whom were treated with AZD-9668, using a 60 mg dose of AZD-9668 administered twice daily for four weeks. Bronchiectasis is a disease characterized by localized, irreversible dilatation of parts of the bronchial tree, caused by destruction of the structural components of the bronchial wall that result from a vicious cycle of transmural infection and inflammation. Neutrophils play a key role in inflammation in bronchiectasis with airway neutrophilia resulting in high concentrations of neutrophil proteases, such as NE, which may be inadequately neutralized by anti-proteases.

The results of this four-week trial showed a statistically significant improvement at day 28 versus placebo in mean FEV1 of 100 ml ($p=0.006$) and a clinically meaningful improvement of 130 ml ($p=0.079$) in mean slow vital capacity, which measures the volume of air on a slow full expiration of air in the patient's lungs. The effect on the St. George's Respiratory Questionnaire, a questionnaire that

measures quality of life in patients with diseases of airways obstruction, favored AZD-9668 overall and in each measured domain, with a more than four-unit difference in the overall score, demonstrating clinical relevance. In addition, although the data did not show statistical significance in desmosine levels in urine, the treatment group showed a reduction in desmosine levels while the placebo group showed an increase in desmosine levels.

We believe that bronchiectasis and AATD share common pathological features such as damage to structural parts of the bronchial tree caused by neutrophil proteases that support the potential for AZD-9668 to treat severe AATD, a disease driven primarily by insufficient inhibition of NE.

Phase 2 Clinical Trial in Cystic Fibrosis

AstraZeneca conducted a double-blind, placebo-controlled Phase 2 clinical trial in CF in a total of 56 patients, 26 of whom were treated with AZD-9668, using a 60 mg dose of AZD-9668 administered twice daily for four weeks. CF is a disease that results in thickened secretions and endobronchial infections. These chronic infections are associated with an exaggerated inflammatory response in the airways and neutrophil infiltration of the lungs. The presence of neutrophils in the airways, and the resulting high concentrations of neutrophil proteases, such as NE, suggest that neutrophils are contributors in the pathogenesis of the proteolytic lung destruction associated with CF.

The trial was designed to examine the safety and efficacy of AZD-9668 and its effect on the biomarkers of lung damage. The trial did not demonstrate a statistically significant benefit in lung function, which we believe was due to the anti-proteolytic mechanism of action of AZD-9668 only addressing one component of the pathology of CF. However, there was a statistically significant reduction in free desmosine in urine corrected for creatinine ($p=0.002$), and a reduction in plasma desmosine of 16%. Desmosine and isodesmosine are unique cross linking amino acids in elastin. Elastin is a protein that makes up the structure of the alveoli in the lungs and provides the pressure that allows for easy breathing, but is vulnerable to breakdown by NE. The reduction in desmosine in this trial indicates a reduction in the breakdown of elastin, which we believe suggests the utility of desmosine as a clinical biomarker with direct relevance to the proposed mechanism of action in severe AATD.

We believe that the data from this trial provide proof of concept for mechanistic effect and the use of desmosine as a biomarker of lung degradation in diseases of high or unopposed NE, such as severe AATD.

Summary of Safety Results

In the clinical trials conducted by AstraZeneca, no treatment-related serious adverse events were identified. A dose of up to 120 mg twice daily was well tolerated in Phase 1 clinical trials and a dose of 60 mg twice daily was well tolerated in the CF, bronchiectasis and COPD Phase 2 trials. Across the 1,149 patients and healthy volunteers treated with AZD-9668, 16 patients had an elevation of liver enzymes with alanine transaminase or aspartate transaminase enzyme concentrations elevated to greater than three times the upper limit of normal, but no patient met the criteria of Hy's law of drug-induced liver injury and no dose dependency was observed. Independent safety review committees evaluated this data and recommended that the trials continue.

Planned Phase 2 Clinical Trial in Severe AATD

We intend to commence a Phase 2 proof-of-concept clinical trial of AZD-9668 for severe AATD in the second half of 2018. We anticipate this trial will be a 12-week, double-blind, placebo-controlled clinical trial examining two doses of AZD-9668 compared to placebo with primary endpoints of elastin breakdown and binding to NE or NE inhibition as determined using biomarkers. We anticipate desmosine will be the elastin breakdown product that is the biomarker endpoint. We believe that by

inhibiting NE, AZD-9668 will reduce the breakdown of elastin and therefore the amount of desmosine. Planned secondary endpoints are plasma Aa-Val(360), a biomarker of NE activity, NE activity in sputum, and lung function tests, including FEV1.

We plan to enroll only patients with PiZZ or NullNull genotypes with confirmed emphysema and declining FEV1, who have not received AAT augmentation therapy or have undergone a wash-out period following AAT augmentation therapy. We estimate that we will need to recruit approximately 150 patients for this trial.

If the results from this trial are favorable, we intend to seek regulatory advice on the design of, and commence, a pivotal trial.

BCT-197 (acumapimod) for the Treatment of AECOPD

Overview

We are developing BCT-197 (acumapimod) as a first-line acute therapy in patients with AECOPD. BCT-197 is a novel, orally active p38 MAP kinase inhibitor designed to inhibit the pathological mechanism behind inflammation, which is a key feature of AECOPD. Currently available treatments only manage the symptoms of AECOPD and are comprised primarily of oxygen therapy, corticosteroids, antibiotics, and bronchodilators. We believe BCT-197 offers a potential new treatment by targeting the underlying disease and delivering tangible benefits for patients and payors by potentially preventing AECOPD, or reducing the frequency of exacerbations and reducing readmissions.

Background of COPD and AECOPD

COPD includes chronic bronchitis, emphysema, refractory (non-reversible) asthma, and some forms of bronchiectasis. COPD is a non-fully-reversible, progressive lung disease that was the third largest cause of death in the world in 2010 according to the Global Burden of Disease Study, and the WHO forecasts that it will remain the third largest cause of death in the world in 2030. The National Heart Lung Blood Institute estimates that 16 million people in the United States have been diagnosed with the disease and the same number likely suffer from the disease without being aware of it. The European COPD Coalition estimates that 13 million people in Europe have been diagnosed with COPD. In 2015, according to the WHO, there were over three million deaths from the disease worldwide.

An AECOPD is defined as an acute event characterized by a worsening of the patient's symptoms beyond normal day-to-day variations that requires a change in medication. Typical symptoms include an increase in breathlessness and/or increase in sputum production, which lead to an increase in the frequency or dose of bronchodilators or an increase in corticosteroid use, or the need to seek further medical attention. The risk of AECOPD increases with COPD progression and increases following exacerbations. Increased inflammation is a core feature of an AECOPD. This is demonstrated by inflamed airways and the influx of white blood cells that respond to and can propagate inflammation.

On average, COPD patients suffer one to three AECOPDs per year with an average hospital stay, if admitted, of three to 10 days. Each episode of AECOPD poses significant risk to the patient, including an increased risk of death. Approximately 8% of patients admitted to the hospital for COPD die while in the hospital. The frequency and severity of exacerbations increase with age, disease severity and history of prior AECOPD. The five-year survival rate for those suffering three or more AECOPDs per year is 30%, but those who do not suffer AECOPDs have an 80% survival rate. Moderate to severe cases of AECOPD can also result in greatly diminished quality of life, disability, and serious co-morbidities, including heart disease. After an AECOPD many patients do not return to their pre-AECOPD baseline respiratory function. Furthermore, a patient who has several AECOPDs a

year is typically exposed to large quantities of systemic corticosteroids, which can lead to osteoporosis and diabetes.

AECOPDs account for the greatest proportion of COPD costs. Of all COPD-related hospital admissions in the United States, approximately 63% are for AECOPD patients, representing more than 1.5 million emergency room visits in the United States alone. Based on current estimates of U.S. COPD rates, the direct costs of COPD are estimated at \$4,000 per patient per year. Costs increase in correlation with each progressive stage of the disease. In the United States in 2010, mild COPD patients had median direct costs of \$1,681 per patient per year, moderate patients had direct costs of \$5,037 per patient per year and severe patients had direct costs of \$10,812 per patient per year. Hospital stays make up the greatest proportion of the total COPD burden on the healthcare system, accounting for approximately 45% to 50% of the total direct cost generated by COPD patients. The mean length of hospital stays varies but is typically about 4.7 days. In the United States, the average cost of admission is \$7,500 but more than 20% of patients are re-admitted within 30 days with significantly higher cost.

Current Treatment Landscape of AECOPD

We are not aware of any approved therapies for the treatment of AECOPD in the United States or the EU. The management of AECOPD is directed at relieving symptoms and restoring functional capacity of the airways. In its milder forms, an AECOPD can be controlled with inhaled steroids, bronchodilators, and antibiotics. The bronchodilators reduce the patients' breathlessness by opening up the airways, and corticosteroids reduce inflammation. In more severe cases, AECOPD requires hospitalization, where patients are typically treated with oral or intravenous steroids and antibiotics.

The current recommended management for AECOPD includes beta2 agonists, the addition of anticholinergics or an increase in their dosage, the systemic administration of corticosteroids and antibiotics, and the intravenous administration of methylxanthines, such as aminophylline. Additionally, supporting oxygen therapy is used in order to provide the patient with sufficient blood oxygen levels. While AECOPDs are often triggered by bacterial or viral pathogens or pollutants, antibiotics are often used as the precise etiology is often unknown.

We believe there is a significant medical need for a drug which is disease-modifying and could potentially prevent AECOPD instead of just treating the symptoms. In addition, we believe that a drug that could prevent or reduce AECOPD and also has anti-inflammatory effects would significantly improve the quality of life of AECOPD patients due to improved lung function, fewer infections and possibly reduced risk of rehospitalization and mortality.

Our Approach

Our product candidate for treating AECOPD is BCT-197, an orally administered small molecule that inhibits p38 MAP kinase. p38 MAP kinase is an enzyme that plays a key role in the cellular response to external stress signals. p38 MAP kinase is activated in COPD and AECOPD and is inversely correlated with measures of lung function, in particular, FEV1 and forced vital capacity, which is the amount of air that can be forcibly exhaled from the lungs after maximal inspiration. The higher the p38 MAP kinase activation, the lower we would expect lung function to be. Inhibition of this enzyme has been shown to have anti-inflammatory effects, primarily through the inhibition of the expression of inflammatory mediators or molecules called cytokines. The inflammatory cytokines are key to initiating and escalating the inflammatory response by attracting inflammatory cells and inducing further release of the cytokines by these cells. Key cytokines released in the inflammatory response are tumor necrosis factor alpha, or TNF α , and interleukin-8, which are released in the blood stream, and interleukin-6, which is released from bronchial epithelial cells, all of which are blocked by inhibiting p38 MAP kinase.

We believe that BCT-197 has the following key advantages over current therapies:

- potential to be a rapid-onset treatment targeting inflammatory drivers of AECOPD;
- designed to target anti-inflammatory response systemically and locally with easier oral administration than inhaled treatments;
- simple oral regimen of three doses over five days that can be conveniently administered in either the hospital or an outpatient setting;
- designed to target pathophysiology of acute exacerbations without generalized immune suppression; and
- potential for efficacy in steroid-resistant population.

Clinical Development of BCT-197

The following table summarizes the historical clinical trials of BCT-197. We plan to enter into one or more strategic relationships with third parties for BCT-197 to undertake the next phase of clinical development and, if approved, for commercialization.

Historical Trials			
Phase	# of Studies	Population	Subjects Treated with BCT-197
Phase 1	4*	Healthy Volunteers	152
Phase 2	1	AECOPD	108
Phase 2	1	Acute Kidney Injury	50
Phase 2	1	AECOPD	188

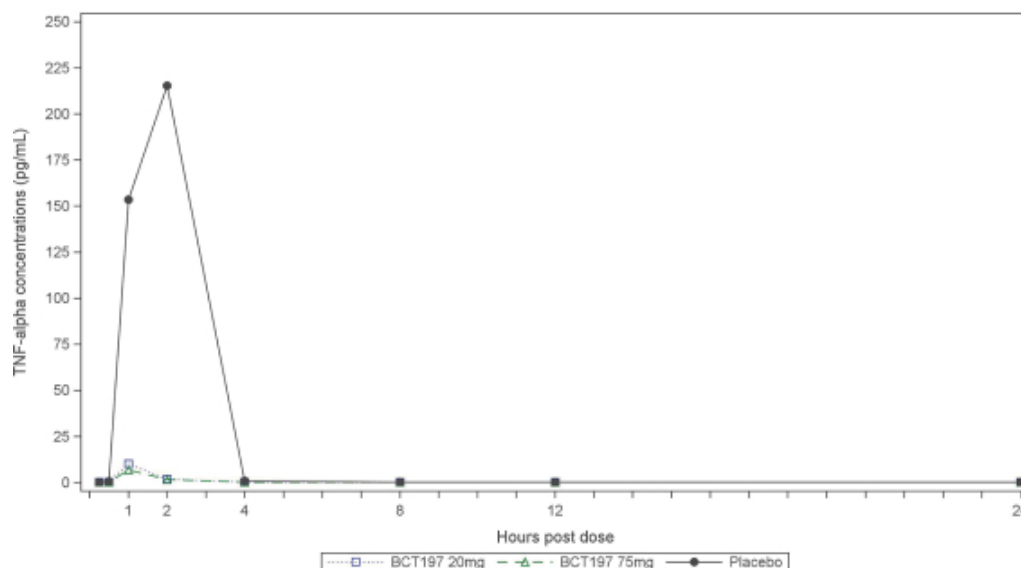
* Includes our 16-patient drug-drug interaction study.

Phase 1 Clinical Trials

Prior to our acquisition of BCT-197, Novartis performed three Phase 1 clinical trials. One of these trials was a three-part Phase 1 clinical trial in a total of 141 healthy volunteers designed to evaluate the safety and anti-inflammatory properties of BCT-197 following lipopolysaccharide, or LPS, challenge, a method of inducing an inflammatory response. Parts 1 and 2 of this trial assessed the ability of BCT-197 to inhibit TNF α , a pro-inflammatory cytokine, *ex vivo* following LPS challenge and Part 3 assessed the same *in vivo*. In Part 1, which was a single ascending dose trial, TNF α was inhibited by a mean of 50% by doses of at least 30 mg, and in Part 2, which was a multi-ascending dose trial, TNF α was inhibited by a mean of 70%.

In Part 3, a three-arm trial, 24 subjects were randomized to receive placebo, 20 mg of BCT-197, or 75 mg of BCT-197. Subjects were exposed to LPS three hours following dosing of BCT-197 or placebo and the concentration of TNF α was measured. In this trial, BCT-197 produced a statistically significant reduction in the levels of TNF α in the treated subjects versus placebo. The following graph shows that the TNF α response was seen in both doses of BCT-197.

TNF α Concentration over Time following LPS Challenge
n=24



In addition, a radiolabeled pharmacology trial was performed in four healthy volunteers. We believe the results of this trial suggest that BCT-197 has pharmacology appropriate for an oral drug.

Phase 2 Clinical Trial in AECOPD

Novartis conducted a double-blind, Phase 2 clinical trial in Europe comparing BCT-197 to the steroid prednisolone and a placebo control. The trial was designed to assess the effect of single and repeated dose of BCT-197 in AECOPD patients. The primary endpoint was to demonstrate an improvement in FEV1 relative to placebo. Secondary and exploratory endpoints included the assessment of safety and tolerability, measurement of the time to recovery, and the determination of the pharmacokinetic properties of BCT-197.

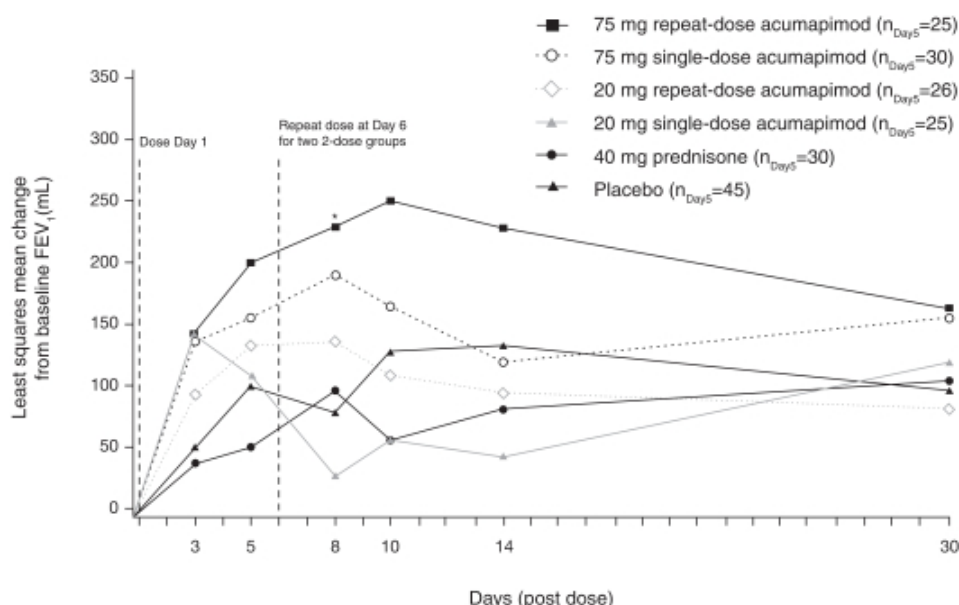
The trial was split into four parts and included a total of 183 patients:

- part 1: 91 patients were randomized to receive either: 75 mg of BCT-197 on day one plus placebo daily for 10 days, prednisolone on day one plus placebo daily for 10 days, or placebo on day one and for 10 days daily;
- part 2: 30 patients were randomized to receive 20 mg of BCT-197 or placebo on day one of the trial. The ratio of patients receiving BCT-197 to patients receiving placebo was five to one;
- part 3: 32 patients were randomized to receive 20 mg of BCT-197 or placebo on days one and six of the trial. The ratio of patients receiving BCT-197 to patients receiving placebo was five to one; and

- part 4: 30 patients were randomized to receive 75 mg of BCT-197 or placebo on days one and six of the trial. The ratio of patients receiving BCT-197 to patients receiving placebo was five to one.

The data on FEV1 were recorded on days three, five, eight, 10, 14 and 30 and showed a clinically meaningful increase in FEV1 (of greater than 100 milliliters) on measuring dates in patients receiving two doses of BCT-197, during a 14-day period, consistent with the duration of most AECOPDs. The following graph summarizes the mean change from baseline in FEV1 values for each dose arm. The change was greatest in the group that received two doses of 75 mg of BCT-197, reaching statistical significance in this group at day 8 ($p=0.022$). On analysis of the area under the curve to Day 14, two doses of 75 mg of BCT-197 demonstrated a statistically significant improvement in FEV1 versus placebo and prednisolone ($p=0.0198$ and 0.0102 respectively).

Mean Change from Baseline in FEV1



Summary of Safety Results

In trials conducted by Novartis, BCT-197 was well tolerated in the target patient population. In the Phase 2a clinical trial, 54% of patients out of 183 experienced one or more adverse events. There were six deaths, none of which were deemed to be attributable to BCT197. Over the six-month follow-up period, 13 patients experienced 15 significant adverse events, excluding deaths: 10 cases of COPD worsening or re-exacerbation, three of pneumonia, one of sinusitis and one of bladder cancer. Six of the COPD adverse events were in the placebo and prednisolone arms, two in the 20 mg repeat dose and two in the 75 mg repeat dose. None of these adverse events were considered by the investigators to be related to BCT-197. There were also two cases of rash in the 75 mg repeat dose arm. Two cases of mild and transient transaminase elevations were reported as adverse events, one in the 20 mg dose group and the other in the 75 mg repeat dose group. Other events were mild to moderate.

Phase 2 Dose-Ranging Clinical Trial in AECOPD

In December 2017, we reported top-line data from our completed dose-ranging Phase 2 clinical trial in the United States and Europe to identify the most effective dosing regimen for AECOPD patients. The primary endpoint of the trial was to demonstrate a change in FEV1 from baseline to Day 7. A total of 282 patients enrolled in the trial.

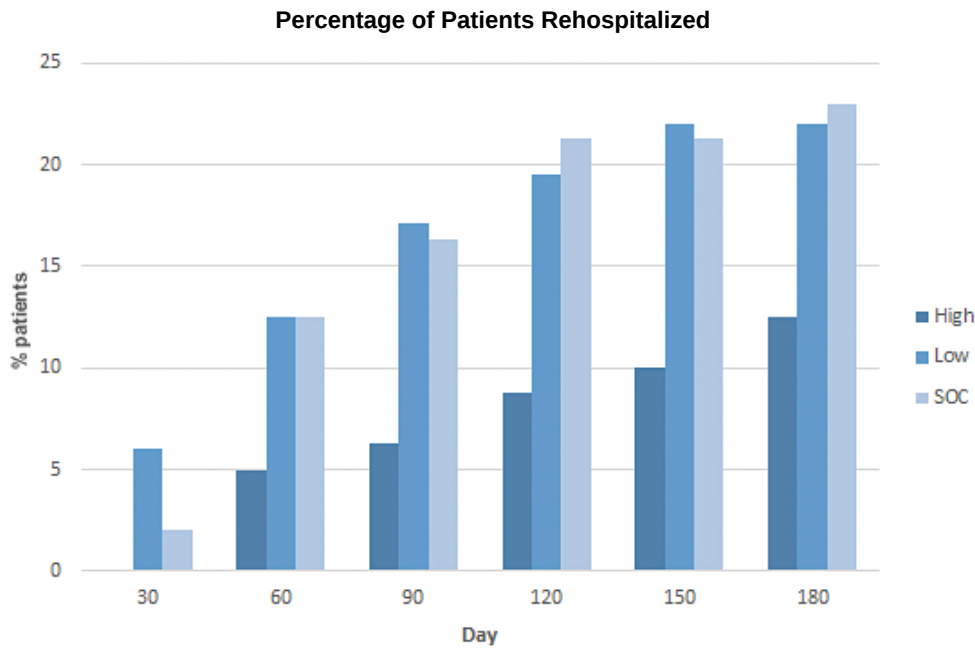
This dose-ranging trial assessed two dosing regimens of BCT-197 and placebo in combination with standard of care, which included steroids, antibiotics, and bronchodilators. Patients were followed for 26 weeks to explore recurrence rates of AECOPD and number of re-hospitalizations. Secondary and exploratory endpoints included clinical failure rate, number of moderate/severe AECOPDs during the trial, the area under the curve of FEV1 over time and time to normalization of FEV1.

The reduction in clinical failure rate was also observed. Clinical treatment failure is defined as a composite endpoint in which any patient fulfils one of more of the following criteria:

- hospitalization or re-hospitalization due to worsening respiratory symptoms;
- worsening of respiratory symptoms requiring the addition of another antibiotic or substitution of a new antibiotic;
- worsening of respiratory symptoms requiring an increase in dose of oral corticosteroids or initiation of new corticosteroids;
- worsening of respiratory symptoms requiring an additional treatment regimen of systemic corticosteroids and/or antibiotics, after completion of the first regimen;
- COPD-related death; or
- any new moderate or severe exacerbation after a period of seven days of resolution from the index AECOPD.

Both dosing regimens of BCT-197 showed a statistically significant change in FEV1 from baseline to Day 7 ($p=0.012$ and $p \leq 0.001$), meeting the trial's primary endpoint on an intent-to-treat patient population basis. The standard of care plus placebo group did not show a significant change from baseline ($p=0.102$). The high- and low-dosage BCT-197 groups showed a mean improvement in FEV1 of 84 ml and 115 ml, respectively, compared to 57 ml for the standard of care plus placebo group. While the BCT-197 groups showed greater improvement when compared to the standard of care plus placebo group, the difference in improvement was not statistically significant.

As shown in the chart below, the high-dose BCT-197 group showed a statistically significant reduction in clinical treatment failure of more than 50% ($p \leq 0.027$ to 0.05) compared to the standard of care plus placebo group, measured by the number of rehospitalizations for the treatment of COPD at Days 90 through 150, with a trend observed as early as Day 30. A trend showing reduced composite clinical treatment failures of 56% to 28% from Day 30 through Day 150 was also observed in the high-dose BCT-197 group. We are currently conducting analysis of the data for the secondary and exploratory endpoints.



In a prespecified subgroup analysis of patients with low blood eosinophils of less than 2%, which comprised 68% of the patients in this trial, BCT-197 showed a trend toward improvement of FEV1 from baseline at Day 7, compared to standard of care plus placebo, which showed almost no improvement. Approximately 50% of COPD patients have low blood eosinophils and are considered to be resistant to treatment with steroids.

In this trial, BCT-197 was observed to be well tolerated. Adverse events included two cases of acneiform rash, which were resolved. No induced liver injuries were observed.

BGS-649 (leflutrozoled) for the Treatment of Hypogonadotropic Hypogonadism

Overview

We are developing BGS-649 (leflutrozoled) for the treatment of HH in obese men. In obese men, a decline in testosterone is exacerbated by high levels of the aromatase enzyme in the fat tissue. The aromatase enzyme converts testosterone to estradiol, thereby reducing testosterone levels. BGS-649 is a novel once-weekly oral aromatase inhibitor designed to normalize testosterone levels and improve HH without causing the excessively high testosterone levels and impaired fertility that may result from exogenous hormone replacement therapy, or TRT, the primary treatment for HH.

Background of Hypogonadotropic Hypogonadism

HH is a clinical syndrome that results from the failure of the testes to produce adequate levels of testosterone. Low testosterone or male hypogonadism is classified in two different types: primary hypogonadism and HH. Primary hypogonadism generally results from the failure of the testes to produce sufficient levels of testosterone, due to testicular trauma, disease (such as mumps), or genetic defects. HH also results from the failure of the testes to produce sufficient levels of testosterone, in this case due to the disruption of the hypothalamic-pituitary-testicular, or HPT, axis, an endocrine pathway, and is typically associated with obesity, aging, stress, or as a side effect of medications. The symptoms of testosterone deficiency are non-specific, which can make the diagnosis difficult. Symptoms that are most commonly associated with testosterone deficiency include reduced or loss of libido, the absence of morning erections and erectile dysfunction. Other common symptoms include fatigue, impaired physical endurance, loss of vitality, lack of motivation and mood disturbance. In physician assessments of the symptoms of HH, patients rate decreased energy levels and impaired sexual function as having the greatest negative impact on quality of life.

The largest group affected by HH is comprised of men over the age of 40 who suffer from chronic diseases, such as obesity or type 2 diabetes. Based on World Health Organization, or WHO, estimates and scientific data, we believe there are approximately seven million cases of HH in obese men, generally defined as men with a body mass index, or BMI, of 30 kilograms per meter squared or more, in the United States and approximately five million cases of HH in obese men in Europe. Over 85% of men with HH are untreated despite access to care. Obesity rates continue to increase in the United States and in other developed and developing countries around the world. In 2016, the WHO estimated that 35.5% and 21.9% of males in the United States and the EU, respectively, were obese. A recent study in obese men, published in the Netherlands Journal of Medicine, showed that HH increased linearly with an increase in BMI.

Current Treatment Landscape of Hypogonadotropic Hypogonadism

The primary treatment for HH is TRT, in which testosterone is administered to normalize testosterone levels. There are several available routes of administering TRT, including intramuscular injections, scrotal patches, transdermal patches, transdermal gel, and implants. The direct replacement of testosterone exposes the patient to significant side effects. The FDA has concluded that there is a possible increased cardiovascular risk associated with TRT. One of the most common and serious side effects associated with TRT is impaired sperm formation. Additional complications caused by excessive testosterone include prostate enlargement, sleep apnea and worsening heart failure, gynecomastia, or breast development in males, and mood swings. Besides these side effects, each of these delivery methods also has considerable drawbacks. For example, intramuscular injections can be painful, gels and patches run the risk of testosterone transmission to other people, and patches can cause skin irritation.

The leading testosterone replacement products on the market are Abbvie's AndroGel and Eli Lilly's Axiron, both of which carry a black box warning. Both products are administered transdermally by applying a gel formulation. Allergan's Androderm is the leading transdermal patch on the market. The most frequently prescribed intramuscular injections are Bayer's Nebido and Endo's Aveed. The leading implant on the market is Endo's Testopel.

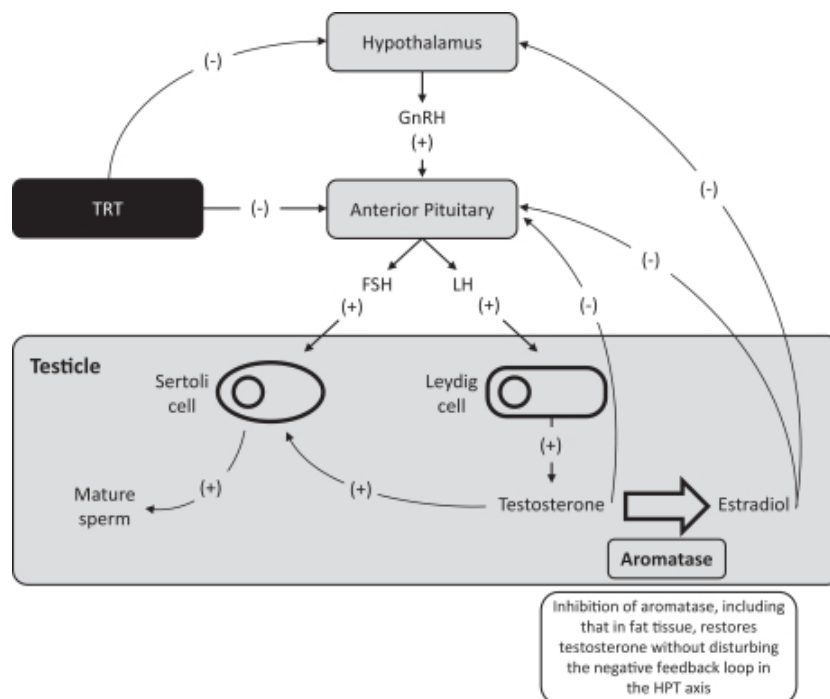
Our Approach

Our product candidate for treating HH in obese men is BGS-649, which is intended for once-weekly oral administration and is designed to inhibit the aromatase enzyme, instead of directly replacing testosterone. The aromatase enzyme converts testosterone to estradiol, thereby reducing testosterone levels. Aromatase is expressed at high levels in fat tissue, and therefore obese men are potentially more prone to HH. BGS-649 is intended to restore normal levels of testosterone without causing the excessively high testosterone levels that may result from TRT. In addition, we believe that the long half-life of BGS-649 of 22 days may allow for convenient weekly dosing.

Testosterone is a hormone that is regulated by three organs in the body, the hypothalamus, anterior pituitary glands and testes, which comprise the HPT axis. The initial stimulus for hormone formation begins in the hypothalamus with the formation of hormones, such as gonadotropin-releasing hormone, or GnRH, that stimulate the pituitary gland to release LH and FSH. LH, in turn, stimulates the testicular production of testosterone, while FSH stimulates sperm formation. As testosterone levels rise, they feedback directly to the hypothalamus and indirectly through estradiol to the hypothalamus and anterior pituitary gland, which reduces the stimulation to produce more hormones, thereby creating a negative feedback loop that maintains normal testosterone levels. In obese men with HH, excessive aromatase enzyme in fat tissue convert testosterone into estradiol, which inhibits the HPT axis by the negative feedback loop.

The administration of exogenous testosterone, such as with TRT, which is not controlled by the HPT feedback loop, rapidly leads to suppression of LH and FSH. Furthermore, as exogenous testosterone is not controlled by the HPT feedback loop, supraphysiological, or excessively high, levels of testosterone can be reached, which have been associated with cardiovascular disease. In contrast to exogenous TRT, BGS-649 is designed to inhibit aromatase and restore testosterone without disturbing the physiological feedback in the HPT axis, thereby maintaining or increasing LH and FSH with minimal risk of reaching supraphysiological levels of testosterone.

The diagram below illustrates the HPT feedback loop process, including the negative effects of TRT:



Clinical Development of BGS-649

The following is a table of the historical, current and planned clinical trials of BGS-649:

Historical Trials				Current Trials			Planned Trials	
Phase	# of Studies	Population	Subjects Treated with BGS-649	Phase	Population	Total Enrollment	Phase	Population
Phase 1	5	Healthy Women / Endometriosis	95	Phase 2b (extension study)	HH obese men	143	Phase 3	HH obese men
Phase 2	1	Endometriosis	12					
Phase 2	1	HH obese men	24					
Phase 2b	1	HH obese men	271					

Phase 2 Proof-of-Concept Clinical Trial in Hypogonadotropic Hypogonadism

Novartis conducted a two-part Phase 2 proof-of-concept trial for HH in obese men in North America.

Part 1 was an open-label trial to evaluate the pharmacokinetics and pharmacodynamics of BGS-649 in obese men. Fourteen patients were enrolled in this 12-week trial with a three-month follow-up phase. Patients received a first dose of BGS-649, and testosterone was measured on days five through seven to allow the physicians to choose subsequent doses with the goal of achieving and maintaining normal testosterone levels. Following the first dose, a range of doses were administered. The average BMI of participants was 34 kilograms per meter squared.

Consistent with the goal of the trial, BGS-649 treatment increased testosterone into the normal range of 300 to 1,000 nanograms per deciliter, or ng/dl, in all patients exposed in Part 1. Mean baseline testosterone was 239 ng/dl, and rose to a mean of 514 ng/dl at week 12 of the trial. Both FSH and LH levels also increased in the BGS-649 group.

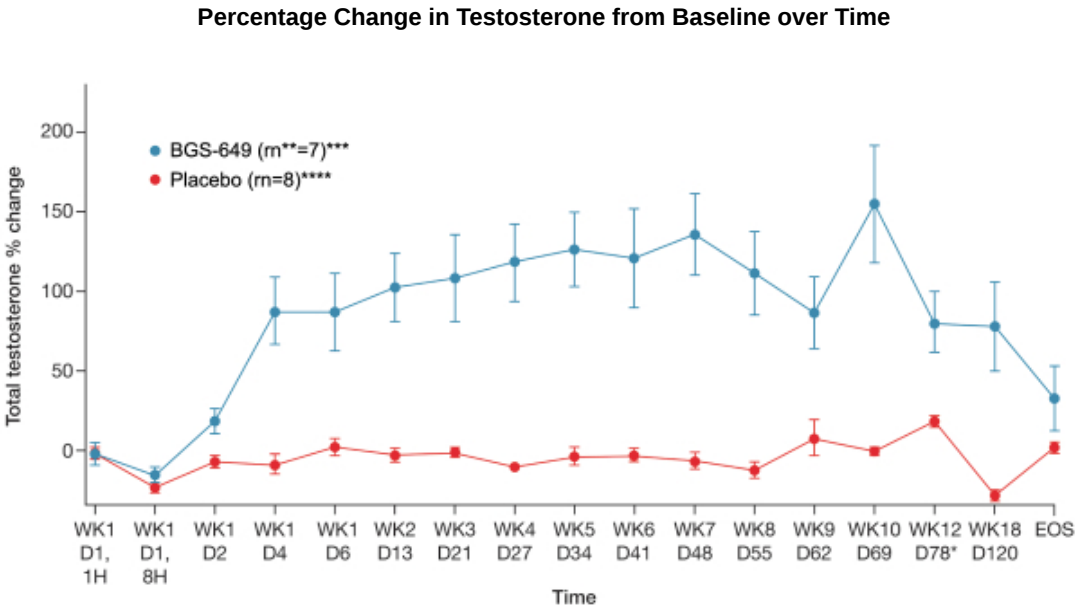
Part 2 was a two-arm, randomized, placebo-controlled, double-blind 12-week trial, with a three-month follow-up trial. The primary objectives were to evaluate the ability of BGS-649 to normalize testosterone and examine if normalized testosterone benefits insulin sensitivity. The secondary endpoints were safety, tolerability, pharmacodynamic effects on glucose, insulin and lipid metabolism.

Fifteen patients were enrolled in Part 2 of the trial, eight in the placebo group and seven in the treatment arm. Originally, 30 patients were to be enrolled. Enrollment was terminated early due to a dosing error at a trial site, which resulted in three placebo patients receiving an active dose of BGS-649. The error was identified after testosterone levels in these three patients normalized, and was confirmed by the presence of BGS-649 in these patients' plasma. The patients who were inadvertently given an initial dose of BGS-649 continued to the end of the trial on placebo. Their results were included in the safety database, but were not included in the efficacy analysis. Therefore, there were five placebo patients. Due to the early termination of the trial, among the placebo patients, one completed the full 12-week protocol, two completed week 10, one completed week seven and one completed week six.

Of the seven patients treated with BGS-649, five completed all 11 doses, one completed week eight and one completed week six prior to termination of the trial. Their subsequent testosterone levels were recorded and included in efficacy analyses, though one patient missed the end-of-trial blood test as he withdrew consent. Despite the early termination, BGS-649 normalized testosterone levels in all patients treated.

The treated patients received a loading dose of BGS-649 on day one, followed by a lower weekly dose of BGS-649. The testosterone levels of all patients treated with BGS-649 normalized after one dose and remained in the normal range throughout the treatment period, with the exception of one patient on day 21, whose level dropped to 279 ng/dl but recovered to a level of 480 ng/dl on day 27. Testosterone levels in the placebo patients occasionally reached the normal range, but this effect was not consistent or sustained. In the BGS-649 arm, the mean testosterone level increased from 273 ng/dl at baseline to 423 ng/dl at week 12. Both FSH and LH levels also increased in the BGS-649 group.

The following graph illustrates the percentage increase in testosterone level relative to baseline in patients receiving a weekly dose of BGS-649 or placebo. The testosterone increase was statistically significant in the BGS-649 group from day 4 ($p=0.012$), with a trend towards return to baseline by the end of the trial, with no evidence of increased total testosterone levels beyond the upper limit of the normal range in any patient exposed to BGS-649.



* Last dose of BGS-649 administered at week 12 (day 78).

** Due to the early termination of this trial, some of these patients did not receive all doses of BGS-649 or placebo. Instead of the total number of patients who completed the trial in each group, the number of patients that were randomly assigned to each group at the start of the trial, or n , is provided in this graph.

*** Five patients received BGS-649 through week 12 of the trial, one patient received BGS-649 through week 10, and one patient received BGS-649 through week eight.

**** One patient received placebo through week 12 of the trial, two patients received placebo through week 10, one patient received placebo through week seven and one patient received placebo through week six. Results from three patients randomly assigned to the placebo group who mistakenly received a dose of BGS-649 are excluded from this graph.

In addition, patients receiving a weekly dose of BGS-649 showed a trend towards an increase in LH and FSH levels in the treated group with a return to baseline by end of trial. These results in the treated group, suggest that the negative feedback loop controlling the gonadotropin levels in the HPT axis was not disrupted.

Summary of Safety Results

In the clinical trials conducted by Novartis, BGS-649 was well tolerated in the 131 treated patients, with no treatment related serious adverse events. In the Phase 2 proof-of-concept trial in HH, there were 41 adverse events, 16 in the BGS-649 group and 25 in the placebo group. In the BGS-649 group, six of the adverse events were moderate and 10 were mild.

In Part 1 of the trial there were 59 adverse events, 16 of which were moderate and 43 of which were mild. These adverse events were transient and resolved spontaneously. Four patients reported spontaneous penile erection, three patients reported an episode of a headache and two patients reported abnormal hair growth, which were suspected of being related to BGS-649. Other common adverse events were oropharyngeal pain, nasal congestion, diarrhea, arthralgia, cough, dizziness and frequent bowel movements. There were no drug-related significant adverse events.

In Part 2 of the trial, the most common adverse events were lack of energy, headache, nasal congestion, somnolence, and spontaneous penile erection, which were distributed broadly across the BGS-649 and placebo groups. None of these adverse events occurred in more than three patients. Special safety parameters, including prostate specific antigen, haematocrit, hemoglobin, high-density lipoprotein, and bone turnover markers, showed no significant effect of BGS-649. We are monitoring these parameters in the current trial.

A reproductive toxicology trial was also performed in rats to evaluate the risk of potential transference of BGS-649 in the semen, and no reproductive toxicology risk was identified. The maximum dosage would equate to a maximum of 4,700 times the human exposure, which should provide a significant safety margin.

Phase 2b Clinical Trial in Hypogonadotropic Hypogonadism

In March 2018, we announced top-line data from our Phase 2b clinical trial of BGS-649 for the treatment of HH in obese men. We enrolled 271 patients in the trial in the United States and Europe. The trial was a multi-center, randomized double-blind, dose-ranging, placebo-controlled trial of BGS-649 in obese males with HH with a BMI of over 30. Subjects were divided into four groups, with 71 receiving placebo and 67, 66 and 67, receiving the low, intermediate or high dose, respectively, of BGS-649.

The primary endpoint of the trial was to measure the percentage of patients whose testosterone levels normalized. The trial was designed to detect whether at least 75% of patients had normalized testosterone levels at week 24.

The secondary endpoints were:

- the ability of BGS-649 to normalize testosterone in at least 90% of patients;
- the effects of BGS-649 on LH and FSH; and
- the proportion of subjects that overshoot testosterone levels at 24 weeks.

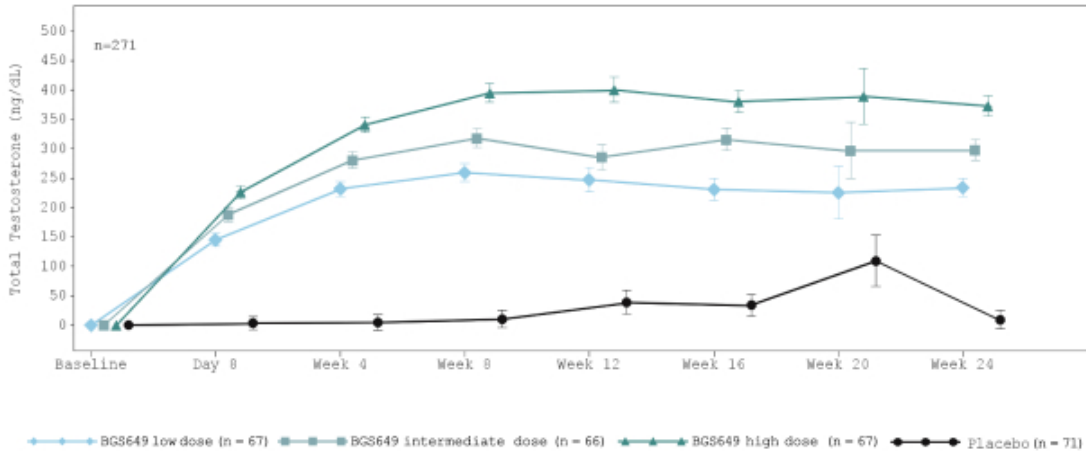
In addition, the trial was designed:

- to investigate the benefit on patient-reported outcomes, or PROs, including the Patient Reported Outcomes Measurement Information System, or PROMIS, Brief Fatigue Inventory, Sex SF and International Index of Erectile Function, which examine the most common complaints HH patients present to a doctor, fatigue and sexual dysfunction;
- to assess the effects of BGS-649 on semen analysis (sperm count and motility), in a subset of patients; and

- to evaluate safety and tolerability, which included analysis of lipid profiles, haematocrit bone turnover markers, and bone mineral density measured by DEXA score.

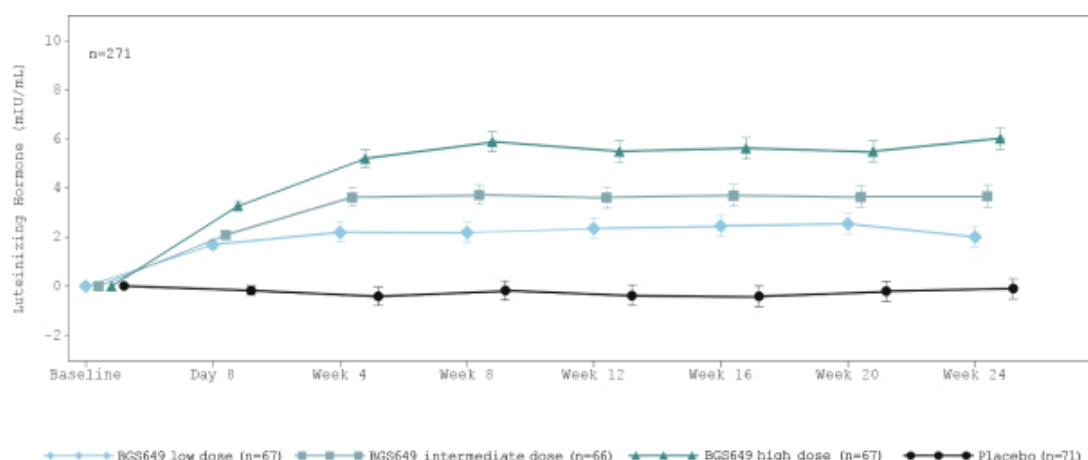
The trial involved a four-week screening phase followed by a 24-week treatment phase and a 12-week follow-up period. All doses of BGS-649 met the primary endpoint, normalizing total testosterone levels in over 75% of subjects after 24 weeks of treatment ($p<0.001$ versus placebo). Normalization of testosterone was observed at the first measurement following the initial dosing of BGS-649 at day 8 in more than 80% of subjects at all three doses. A dose response was also observed in absolute total testosterone levels and over the dosing period, with mean testosterone reaching 458.0 ng/dl (low dose), 512.5 ng/dl (intermediate dose) and 586.5 ng/dl (high dose). The following graph illustrates the increase in mean total testosterone levels from baseline in patients in each of the three dosing arms of BGS-649 and receiving placebo.

Change from Baseline in Mean Total Testosterone

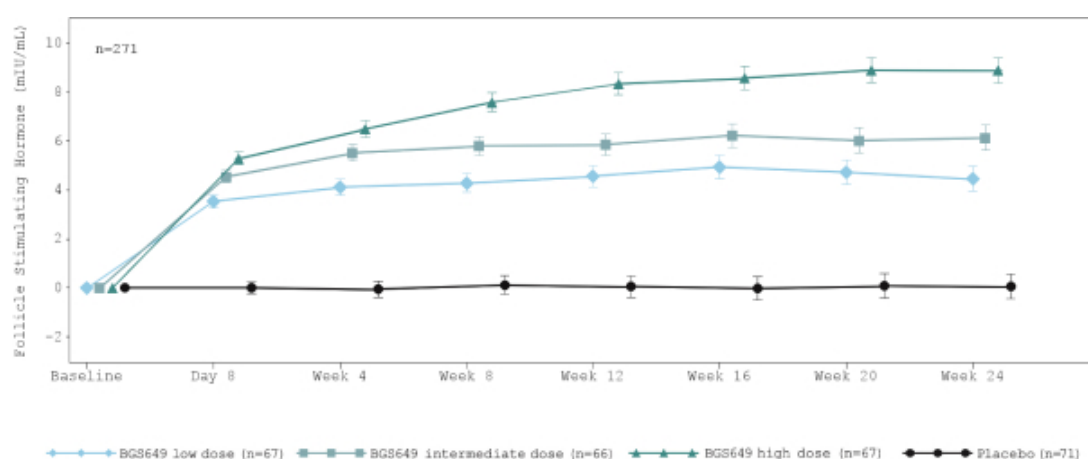


The two highest doses also met the secondary endpoint of normalizing testosterone in 90% of patients at week 24 with the lowest dose normalizing testosterone in 88% of patients at week 24. All three doses of BGS-649 met the remaining secondary endpoints, including the improvement of LH and FSH levels. A statistically significant increase in LH and FSH at all doses at week 24 ($p < 0.001$ for each dose versus placebo) was observed, with an increase following initial dosing at day 8 and an observed dose response. The following graphs illustrate the increase in total LH and total FSH from baseline in patients in each of the three dosing arms of BGS-649 and receiving placebo.

Change from Baseline in Mean Total Luteinising Hormone



Change from Baseline in Mean Total Follicle Stimulating Hormone



The trial also showed an improvement in total motile sperm count across all three doses versus placebo with mean changes at week 20 of 70 million, 14 million and 58 million for the high, intermediate and low doses of BGS-649, respectively, compared with a decrease of 23 million for placebo. Although the trial was not designed to detect statistical significance for this exploratory endpoint, a statistically significant improvement was shown at the highest dose of BGS-649 ($p = 0.03$). No subjects on BGS-649 had testosterone levels greater than 1500 ng/dl at any time during the study.

In addition, a positive trend of treatment effect was observed at eight to 12 weeks for reduction of fatigue as measured by the PROMIS Brief Fatigue Inventory. The trial was not designed to detect statistical significance for this endpoint. Further analysis on the remaining PROs is ongoing and will be combined with the results of the extension study.

BGS-649 was observed to be well tolerated during the trial. An increased incidence of elevated haematocrit levels was observed in each of the treatment arms of the trial, which is consistent with increasing testosterone levels.

A subset of 143 patients have entered into a six-month extension study, to gain long-term data on both efficacy and safety. We expect results from the extension study in the fourth quarter of 2018. The results from this extension study will provide further analysis on the current top-line data reported to further inform our understanding of the PROs and to assist in developing our clinical strategy for BGS-649. We intend to commence additional late-stage clinical studies of BGS-649 in 2019.

Material Agreements

Novartis Agreements

In July 2015, our wholly owned subsidiaries, Mereo BioPharma 3 Limited, Mereo BioPharma 2 Limited, and Mereo BioPharma 1 Limited, or the Subsidiaries, entered into asset purchase agreements, or the Purchase Agreements, to acquire from Novartis rights to, respectively, BPS-804, BCT-197, and BGS-649, or the Compounds, and certain related assets, which, together with the Compounds, we refer to as the Novartis Assets. In connection with the acquisition of the Novartis Assets, we issued 3,849,000 ordinary shares to Novartis pursuant to a subscription agreement. See "Related Party Transactions—Subscription Agreement" for more information. In addition, we paid Novartis \$1.5 million for a payment made by Novartis to a third party in full satisfaction of all monetary obligations of Novartis to such third party with respect to BCT-197. Under the Purchase Agreements, we have agreed to make tiered royalty payments to Novartis based on annual worldwide net sales of products that include the Compounds, or the Acquired Novartis Products, at percentages ranging from the high single digits to low double digits. In the event that the parties agree or it is otherwise determined in accordance with the Purchase Agreements that we require third-party intellectual property rights to exploit the Acquired Novartis Products, we are entitled to offset a specified percentage of amounts paid to such third parties in consideration for such intellectual property rights against the royalties due to Novartis. The royalty payments are payable for a period of ten years after the first commercial sale of an Acquired Novartis Product. We further agreed that in the event of a change in control that involves the transfer, license, assignment, or lease of all or substantially all of a Subsidiary's assets, including a Compound and related assets, we will pay Novartis a percentage of the proceeds of such transaction, with the majority of the proceeds being retained by us. No payment, however, is required with respect to any transaction of Mereo BioPharma Group plc involving its equity interests, a merger or consolidation of it, or a sale of any of its assets.

We granted Novartis an irrevocable, transferable, royalty-free, worldwide and non-exclusive license to use know-how included within the Novartis Assets for Novartis' activities unrelated to any Acquired Novartis Products. We have agreed to use commercially reasonable efforts to develop at least one Acquired Novartis Product. In addition, Novartis agreed to a three-year non-competition restriction in relation to clinical trial activities for the therapeutic treatment of HH in obese men in respect of the BGS-649 Compound and sclerostin in respect of the BGS-804 Compound, subject to exceptions, including where Novartis does not have the ability to control such clinical trial activity and for any of Novartis' existing contracts or relationships.

We also entered into a sublicense agreement with Novartis, or the Sublicense Agreement, pursuant to which Novartis granted us an exclusive, worldwide, royalty-bearing sublicense for certain therapeutic antibody products directed against sclerostin, or the Antibody Products, including BPS-804. Under the Sublicense Agreement, we have agreed to pay Novartis royalties in the low single digits on worldwide net sales of Antibody Products. Royalties will be payable on a country-by-country basis until the later of expiration of the last valid claim of the licensed patents covering the Antibody Products in a country and ten years after the first commercial sale of the Antibody Products in such country, with a maximum royalty term of 12 years after the first commercial sale of the Antibody Products in such country. We have also agreed to pay Novartis up to \$3.25 million in development and regulatory milestones, and to use commercially reasonable efforts to develop and commercialize an Antibody Product. The Sublicense Agreement will expire on the earlier of the termination of the agreement under which Novartis is granting us a sublicense, or the Original License Agreement, and, on a product-by-product and country-by-country basis, the expiration of the royalty term with respect to such Antibody Product in such country. The Original License Agreement has a perpetual term and may be terminated for breach or upon a change in control of the licensing party. We may terminate the Sublicense Agreement upon written notice to Novartis and either party may terminate the Sublicense Agreement for the other party's uncured material breach or bankruptcy.

AstraZeneca Agreement

In October 2017, our wholly owned subsidiary Mereo BioPharma 4 Limited entered into an exclusive license and option agreement, or the License Agreement, to obtain from AstraZeneca an exclusive worldwide, sub-licensable license under AstraZeneca's intellectual property rights relating to certain products containing a NE inhibitor, including products that contain AZD-9668, with an option to acquire such intellectual property rights following commencement of a pivotal trial and payment of related milestone payments, or the Option, together with the acquisition of certain related assets.

Upon entering into the License Agreement, we made a payment of \$3.0 million and issued 490,798 ordinary shares to AstraZeneca, for an aggregate upfront payment equal to \$5.0 million. In connection with certain development and regulatory milestones, we have agreed to make payments of up to \$115.5 million in the aggregate and issue additional ordinary shares to AstraZeneca for licensed products containing AZD-9668. In addition, we have agreed to make payments to AstraZeneca based on specified commercial milestones of the product. In the event that we sub-license AZD-9668, we have also agreed to pay a specified percentage of sublicensing revenue to AstraZeneca. Otherwise, we have agreed to make royalty payments to AstraZeneca equal to ascending specified percentages of tiered annual worldwide net sales by us or our affiliates of licensed products (subject to certain reductions), ranging from the high single digits to low double digits. Royalties will be payable on a licensed product-by-licensed product and country-by-country basis until the later of ten years after the first commercial sale of such licensed product in such country and expiration of the last patent covering such licensed product in such country that would be sufficient to prevent generic entry. Under the License Agreement, we may freely grant sub-licenses to affiliates upon notice to AstraZeneca and we must obtain AstraZeneca's consent, not be unreasonably withheld, to grant sub-licenses to a third party. We have agreed to use commercially reasonable efforts to develop and commercialize at least one licensed product.

The License Agreement will expire on the expiry of the last-to-expire royalty term with respect to all licensed products. Upon the expiration of the royalty term for a licensed product in a particular country, the licenses to us for such product in such country will become fully-paid and irrevocable. Prior to exercise of the Option, if at all, we may terminate the License Agreement upon prior written notice. Either party may terminate the agreement upon prior written notice for the other party's material breach that remains uncured for a specified period of time or insolvency. AstraZeneca has agreed to a three-year non-competition restriction in relation to the direct or indirect commercialization or development of NE

inhibitors for the treatment of AATD. In addition, AstraZeneca agreed not to assert any AstraZeneca intellectual property rights that were included in the scope of the License Agreement against us.

Manufacturing

We do not own or operate manufacturing facilities for the production of our product candidates, nor do we have plans to develop our own manufacturing operations in the foreseeable future. We have entered into manufacturing agreements with a number of drug substance, drug product, and other manufacturers and suppliers for BPS-804, BCT-197, and BGS-649, and we intend to enter into additional manufacturing agreements as necessary. Following our license of AZD-9668, we acquired certain clinical trial materials and we plan to outsource production of further clinical supplies to our own manufacturing suppliers. We also intend to outsource certain product formulation trials. We expect that drug product pre-validation and validation batches will be manufactured to satisfy regulatory requirements where we progress products to late stage trials.

We do not yet have any contractual relationships for the manufacture of commercial supplies of BPS-804, AZD-9668, BCT-197, or BGS-649, and we intend to enter into contractual relationships for commercial supplies prior to commercialization of any product candidates. Any batches of product candidates for commercialization will need to be manufactured in facilities, and by processes, that comply with the requirements of the FDA, the EMA, and the regulatory agencies of other jurisdictions in which we are seeking approval. We employ internal resources to manage our manufacturing contractors and ensure they are compliant with current good manufacturing practices.

Commercialization, Sales and Marketing

We do not have our own marketing, sales, or distribution capabilities. In order to commercialize our product candidates, if approved for commercial sale, we must either develop a sales and marketing infrastructure or collaborate with third parties that have sales and marketing experience. We plan to establish our own sales and marketing organization in the United States and Europe for BPS-804 and AZD-9668, and may seek to directly commercialize our future rare disease product candidates. In markets for which commercialization may be less capital efficient for us, we may selectively pursue arrangements with third parties in order to maximize the commercial potential of BPS-804, AZD-9668, and our future rare disease product candidates. We intend to seek to enter into one or more strategic relationships with third parties for BCT-197 to undertake the next phase of clinical development and, if approved, for commercialization, and to seek to enter into strategic relationships with third parties for further clinical development and/or commercialization of BGS-649.

Competition

We compete directly with other biopharmaceutical and pharmaceutical companies that focus on the treatment of OI, AATD, AECOPD or HH. We may also face competition from academic research institutions, governmental agencies and other various public and private research institutions. We expect to face increasingly intense competition as new technologies become available. Any product candidates, including BPS-804, AZD-9668, BCT-197, and BGS-649 that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

We consider BPS-804's current closest potential competitors in development for the treatment of OI to be Amgen's denosumab (Prolia) an anti-resorptive agent, and Amgen and UCB's anti-sclerostin antibody, romosozumab. Blososumab, an anti-sclerostin antibody, was in Phase 1 development for osteoporosis by Eli Lilly; however, we are not aware of any ongoing clinical trials for this product candidate and we do not believe this product candidate remains under active development. Additionally, Bone Therapeutics is developing osteoblastic cell therapy products. Baylor College of Medicine is also conducting a Phase 1 open label trial of fresolimumab, a TGF-B inhibitor, in adult OI patients.

We consider AZD-9668's current closest potential competitors for the treatment of severe AATD to be alpha1-proteinase inhibitors that are administered intravenously in AAT augmentation therapy. Currently, there are four inhibitors on the market in the United States: Grifols's Prolastin-C, Shire's Aralast, CSL's Zemaira and Kamada's Glassia. Kamada is also investigating an inhaled version of augmentation therapy and Apic Bio and Adverum are in the early stages of developing gene-therapy approaches for AATD. Santhera has licensed an inhaled neutrophil elastase inhibitor and is planning a multiple ascending dose study, with the initial indication targeted being cystic fibrosis.

The current standard of care for AECOPD involves steroids, antibiotics and bronchodilators; however, we are not aware of any drugs specifically approved for the treatment of AECOPD. There are a number of products currently in development, with Verona Pharma, GlaxoSmithKline, and AstraZeneca each conducting Phase 2 clinical trials of drugs for the treatment of COPD. We consider BCT-197's current closest potential competitor in development for the treatment of AECOPD to be Verona Pharma's RPL554, a PDE3 / PDE4 dual inhibitor that is currently being developed as a bronchodilator and anti-inflammatory agent for COPD and asthma patients. GlaxoSmithKline is developing GSK-2269557, a PI3Kd inhibitor, for the treatment of acute and long term use in COPD and asthma, which we believe to be an anti-inflammatory. GSK-2269557 is currently being studied in a Phase 2 clinical trial.

We consider BGS-649's current closest potential competitors for the treatment of HH to be TRT therapies. These include Abbvie's Androgel and Eli Lilly's Axiron, both administered transdermally by applying a gel formulation, which are approved in the United States and Europe, and Merck's Andriol, an oral testosterone therapy, which is approved in Europe but not in the United States. There are also other approved TRT products that are administered via injection and other oral TRTs that are still in the development or registration stages, such as JATENZO from Clarus and TLANDO from Lipocine. The FDA held Advisory Committee meetings in January 2018 for JATENZO and TLANDO. Lipocine has a PDUFA date of May 8, 2018. In addition, Repros is developing a selective estrogen receptor modulator and CHMP/EMA adopted a negative opinion recommending the refusal of its marketing authorization. In December 2017, Allergen announced the acquisition of Repros.

We may face increasing competition for additional new product acquisitions from pharmaceutical companies as new companies emerge with a similar business model and other more established companies focus on acquiring products to develop their pipeline. Many of our competitors have significantly greater financial, manufacturing, marketing, drug development, technical and human resources 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 or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining top qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials.

The key competitive factors affecting the success of BPS-804, AZD-9668, BCT-197 and BGS-649, if approved, are likely to be their efficacy, safety, dosing convenience, price, the effectiveness of companion diagnostics in guiding the use of related therapeutics, the level of generic competition and the availability of reimbursement from government and other third-party payors.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, less expensive, more convenient or easier to administer, or have fewer or less severe effects than any products that we may develop. Our competitors may also obtain FDA, EMA or other regulatory 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. Even if BPS-804, AZD-9668, BCT-197 or BGS-

649 achieve marketing approval, they may be priced at a significant premium over competitive products if any have been approved by then.

Intellectual Property

We have acquired or exclusively licensed a comprehensive intellectual property portfolio from Novartis and AstraZeneca, respectively. We strive to protect and enhance the proprietary technologies, inventions and improvements that we believe are important to our business, including seeking, maintaining and defending patent rights, whether developed internally or acquired or licensed from third parties. Our policy is to seek to protect our proprietary position by, among other methods, pursuing and obtaining patent protection in the United States and in jurisdictions outside of the United States related to our proprietary technology, inventions, improvements, platforms and our product candidates that are important to the development and implementation of our business.

Mereo BioPharma Group plc is the parent company of four wholly-owned subsidiaries: Mereo BioPharma 1 Limited, Mereo BioPharma 2 Limited, Mereo BioPharma 3 Limited and Mereo BioPharma 4 Limited, each of which holds the intellectual property for our product candidates BCT-197, BGS-649, BPS-804 and AZD-9668, respectively. As of March 31, 2018, our patent portfolio comprises approximately 347 issued patents and approximately 43 pending patent applications on a global basis.

BPS-804 (setrusumab)

As of March 31, 2018, our patent portfolio relating to our product candidate BPS-804 consisted of three issued U.S. patents, one pending U.S. patent application, 85 issued foreign patents, four pending foreign patent applications and two pending international patent applications filed under the Patent Cooperation Treaty, or PCT. These patents and patent applications include claims directed to the BPS-804 antibody as well as nucleic acids encoding the antibody and the antibody's use as a medicament; the use of anti-sclerostin antibodies in the treatment of OI; the use of the BPS-804 antibody in the treatment of OI with a specific dosing regimen; and the use of a specific anti-sclerostin antibody in the treatment of OI, with expected expiry dates not earlier than between 2028 and 2037.

The patent portfolio relating to our product candidate BPS-804 includes two patent families:

- The first of these patent families relates to the BPS-804 antibody as well as nucleic acids encoding the antibody and the antibody's use as a medicament. As of March 31, 2018, this patent family included granted patents in Algeria, Argentina, Australia, Canada, China, Colombia, Europe (Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Monaco, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey and United Kingdom), Gulf Cooperation Council countries, Hong Kong, Indonesia, Israel, Japan, Macau, Mexico, New Zealand, Russia, Singapore, South Africa, South Korea and the United States. We expect patents in this family to expire in 2028.
- The second of these patent families relates to the use of anti-sclerostin antibodies in the treatment of OI and the use of the BPS-804 antibody in the treatment of OI at a specific dosing regimen. As of March 31, 2018, this patent family included one U.S. non-provisional application and two pending international patent applications filed under the PCT. We expect patents emanating from this family to expire in 2036/2037.

AZD-9668 (alvelestat)

As of March 31, 2018, our patent portfolio relating to our product candidate AZD-9668 consisted of three issued U.S. patents, no pending U.S. patent applications, 34 issued foreign patents and four pending foreign patent applications. These patents have all been licensed under our agreement with

AstraZeneca. See “—Material Agreements—AstraZeneca Agreement.” These patents and patent applications include claims directed to 2-pyridone derivatives as NE inhibitors and their uses as well as claims to polymorphs of the tosylate salt of a 5-pyrazolyl-2-pyridone derivative, with expected expiry dates not earlier than between 2024 and 2030.

The patent portfolio relating to our product candidate AZD-9668 includes two patent families:

- The first of these patent families relates to 2-pyridone derivatives as NE inhibitors and their use. As of March 31, 2018, this patent family included granted patents in Australia, Canada, China, Europe (France, Germany, Italy, Netherlands, Spain, Sweden, Switzerland, Turkey and United Kingdom), Hong Kong, India, Japan, Mexico, Russia, South Korea and the United States. We expect patents in this family to expire in 2024.
- The second of these patent families relates to polymorphs of the tosylate salt of a 5-pyrazolyl-2-pyridone derivative. As of March 31, 2018, this patent family included granted patents in Australia, Canada, China, Europe (France, Germany, Italy, Netherlands, Spain, Sweden, Switzerland, Turkey and United Kingdom), Hong Kong, Japan, Mexico, Russia and the United States. We expect patents in this family to expire in 2030.

BCT-197 (acumapimod)

As of March 31, 2018, our patent portfolio relating to our product candidate BCT-197 consisted of five issued U.S. patents, no pending U.S. patent applications, 129 issued foreign patents, 13 pending foreign applications, and four pending international patent applications filed under the PCT. These patents and patent applications include claims directed to 5-membered heterocycle-based p38 kinase inhibitors, the use of a pyrazole derivative in the treatment of AECOPD, dosage regimens of BCT-197, the use of BCT-197 in the treatment of specific patient subpopulations, and methods of producing specific polymorphs of BCT-197, with expected expiry dates not earlier than between 2024 and 2038.

The patent portfolio relating to our product candidate BCT-197 includes five patent families:

- The first of these patent families relates to the key composition per se and other 5-membered heterocycle-based p38 kinase inhibitors. As of March 31, 2018, this patent family included granted patents in Algeria, Australia, Canada, China, Colombia, Europe (Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Monaco, Netherlands, Poland, Portugal, Romania, Slovenia, Slovakia, Spain, Sweden, Switzerland, Turkey and United Kingdom), Hong Kong, India, Indonesia, Israel, Japan, Malaysia, Mexico, New Zealand, Norway, Russia, Singapore, South Africa, South Korea and the United States. We expect patents in this family to expire in 2024.
- The second of these patent families relates to the use of pyrazole derivatives in the treatment of AECOPD. As of March 31, 2018, this patent family included granted patents in Algeria, Australia, Canada, China, Europe (Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Germany, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Liechtenstein, Lithuania, Luxembourg, Malta, Mexico, Monaco, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey, Norway and United Kingdom), Hong Kong, Israel, Japan, Mexico, New Zealand, Russia, Singapore, South Africa, South Korea, Taiwan and the United States. We expect patents in this family to expire in 2033.
- The third of these patent families relates to dosage regimens of BCT-197. As of March 31, 2018, this patent family included two PCT patent applications. We expect patents emanating from this family to expire in 2036.

- The fourth of these patent families relates to specific polymorphs of BCT-197. As of March 31, 2018, this patent family included two PCT patent applications. We expect patents emanating from this family to expire in 2037.
- The fifth of these patent families relates to novel regimes for the prevention of AECOPD and the use of BCT-197 in a specific patient subpopulation. As of March 31, 2018, this patent family included four U.K. national patent applications. We expect patents emanating from this family to expire in 2038.

BGS-649 (leflutrozone)

As of March 31, 2018, our patent portfolio relating to our product candidate BGS-649 consisted of three issued U.S. patents, one pending U.S. patent application, 85 issued foreign patents, 13 pending foreign patent applications, and one pending international patent application filed under the PCT. These patents and patent applications include claims directed to BGS-649 formulations the use of BGS-649 in treating hypogonadism according to a specific dosing regimen and combination drug regimens of BGS-649, with expected expiry dates not earlier than between 2032 and 2039. The pending PCT application includes claims directed to the use of BGS-649 in treating endometriosis according to a specific dosing regimen, with an expected expiry date not earlier than 2037.

The patent portfolio relating to our product candidate BGS-649 includes three patent families:

- The first of these patent families relates to BGS-649 formulations and to the use of BGS-649 in treating hypogonadism according to a specific dosing regimen. As of March 31, 2018, this patent family included granted patents in Algeria, Australia, China, Europe (Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Liechtenstein, Lithuania, Luxembourg, Malta, Monaco, Norway, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey, and United Kingdom), GCC, Hong Kong, Indonesia, Israel, Japan, Mexico, New Zealand, Russia, Singapore, South Africa and the United States. We expect patents in this family to expire in 2032.
- The second of these patent families relates to the use of BGS-649 in treating endometriosis according to a specific dosing regimen. As of March 31, 2018, this patent family included a single PCT patent application. We expect patents emanating from this family to expire in 2037.
- The third of these patent families relates to combination drug regimens of BGS-649. As of March 31, 2018 this patent family included two U.K. national patent applications. We expect patents emanating from this family to expire in 2039.

Individual patents extend for varying periods depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, patents issued for regularly filed applications in the United States are granted a term of 20 years from the earliest effective non-provisional filing date. In addition, in certain instances, a patent term can be extended to recapture a portion of the U.S. Patent and Trademark Office, or the USPTO, delay in issuing the patent as well as a portion of the term effectively lost as a result of the FDA regulatory review period. However, as to the FDA component, the restoration period cannot be longer than five years and the total patent term including the restoration period must not exceed 14 years following FDA approval. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically the duration of foreign issued patents is also 20 years from the earliest effective filing date. However, the actual protection afforded by a given patent varies on a product-by-product basis and from country to country, dependent on many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

In addition to patent protection, we also rely upon trademarks, trade secrets and know-how, and continuing technological innovation, to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our collaborators, employees and consultants and invention assignment agreements with our employees. We also have confidentiality agreements or invention assignment agreements with our collaborators and selected consultants. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed through a relationship with a third party. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Our commercial success will also depend in part on not infringing upon the proprietary rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, or our product candidates or processes, obtain licenses or cease certain activities. Our breach of any license agreements or failure to obtain a license to proprietary rights that we may require to develop or commercialize our product candidates may have an adverse impact on us. If third parties have prepared and filed patent applications prior to March 16, 2013 in the United States that also claim technology to which we have rights, we may have to participate in interference proceedings in the USPTO, to determine priority of invention. For more information, please see “Risk Factors—Risks Related to Intellectual Property and Data Protection.”

Government Regulation

Among others, the FDA, the EMA, U.S. Department of Health and Human Services Office of Inspector General, the Centers for Medicare and Medicaid Services, or CMS, and comparable regulatory authorities in state and local jurisdictions and in other countries impose substantial and burdensome requirements upon companies involved in the clinical development, manufacture, marketing and distribution of drugs such as those we are developing. These agencies and other federal, state and local entities regulate, among other things, the research and development, testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion, distribution, post-approval monitoring and reporting, sampling and export and import of our product candidates.

U.S. Government Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations, and biological products, or biologics, under both the FDCA and the Public Health Service Act, or PHSA, and its implementing regulations.

The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before a drug or biologic may be marketed in the United States generally involves the following:

- completion of pre-clinical laboratory tests, animal studies and formulation studies in compliance with the FDA's GLP regulations;

- submission to the FDA of an investigational new drug application, or IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practice, or GCP, requirements to establish the safety and efficacy of the proposed drug product for each indication;
- submission to the FDA of an NDA or BLA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with cGMP 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 potential FDA audits of clinical trials sites and the sponsor's clinical trial records to assure compliance with GCPs and the integrity of the clinical data;
- payment of user fees and FDA review and approval of the NDA or BLA; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

Pre-clinical Studies

Pre-clinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess potential safety and efficacy. The conduct of the pre-clinical tests must comply with federal regulations and requirements, including GLPs. An IND sponsor must submit the results of the pre-clinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Some pre-clinical testing may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical Trials

Clinical trials involve the administration of the investigational new drug or biologic to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives or endpoints of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an institutional review board, or IRB, must review and approve the plan for a clinical trial. This can be a central or local IRB. In the case of a central IRB a single IRB will be the source of record for all sites in a trial; otherwise, a local IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination on their www.clinicaltrials.gov website.

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

- Phase 1: The product candidate is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.
- Phase 2: The product candidate 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 product candidate 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.

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. 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 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.

Special FDA Expedited Review and Approval

The FDA has various programs, including fast track designation, breakthrough therapy designation, accelerated approval, and priority review, which are intended to expedite or simplify the process for the development and FDA review of drugs and biologics that are intended for the treatment of serious or life-threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs and biologics to patients earlier than under standard FDA review procedures.

To be eligible for a fast-track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need by providing a therapy where none exists or a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. Fast-track designation provides opportunities for frequent interactions with the FDA review team to expedite development and review of the product. The FDA may also review sections of the NDA or BLA for a fast-track product on a rolling basis before the complete application is submitted, if the sponsor and FDA agree on a schedule for the submission of the application sections, and the sponsor pays any required user fees upon submission of the first section of the NDA or BLA.

In addition, under the provisions of the Food and Drug Administration Safety and Innovation Act passed in July 2012, a sponsor can request designation of a product candidate as a "breakthrough therapy." A breakthrough therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs or biologics designated as breakthrough therapies are also eligible for accelerated approval. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy.

Products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may be eligible for accelerated approval and may be approved on the basis of adequate and well-controlled clinical trials establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require a sponsor of a product receiving accelerated approval to perform post-marketing studies to verify and describe the predicted effect on IMM or other clinical endpoint, and the product may be subject to accelerated withdrawal procedures.

Once an NDA or BLA is submitted for a product intended to treat a serious condition, the FDA may assign a priority review designation if the FDA determines that the product, if approved, would provide a significant improvement in safety or effectiveness. Under priority review, the FDA must review an application in six months, compared to 10 months for a standard review. Most products that are eligible for fast-track or breakthrough therapy designation are also likely to be considered appropriate to receive a priority review.

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

Orphan Product Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic product candidate if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product). A company must request orphan product designation before submitting an NDA or BLA. If the request is granted, the FDA will publicly disclose the identity of the therapeutic agent and its potential use. We have been granted Orphan Product Designation by the FDA for our product candidate BPS-804 for the treatment of OI. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product is entitled to orphan-product exclusivity. Orphan-product exclusivity means that the FDA may not approve any other applications for the same product for the same indication for seven years, except in certain limited circumstances. If a product candidate designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan-product application, it may not be entitled to exclusivity. Orphan exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same active ingredient for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. Further, the FDA may approve more than one product for the same orphan indication or disease as long as the products contain different active ingredients. Moreover, competitors may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity.

Marketing Approval

Assuming successful completion of the required clinical testing, the results of the pre-clinical 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 or BLA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA or BLA is subject to a substantial application user fee. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, for new molecular entity NDAs and original BLAs, the FDA has 10 months from the filing date in which to complete its initial review of a standard application and respond to the applicant, and six months from the filing date for an application with priority review. The FDA does not always meet its PDUFA goal dates, and the review process is often significantly extended by FDA requests for additional information or clarification. This review typically takes 12 months from the date the NDA or BLA is submitted to the FDA because the FDA has approximately two months to make a "filing" decision.

In addition, under the Pediatric Research Equity Act of 2003, as amended and reauthorized, certain NDAs, BLAs or supplements to an NDA or BLA must contain data that are adequate to assess the safety and effectiveness of the product candidate for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, 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.

The FDA may also require submission of a REMS plan if it determines that a REMS is necessary to ensure that the benefits of the product outweigh its risks. Depending on the specific serious risk(s) to be addressed, the FDA may require that the REMS include a medication guide or patient package insert, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools.

The FDA conducts a preliminary review of all NDAs and BLAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an application 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 reviews an application to determine, among other things, whether the drug is safe and effective (for biologics, the standard is referred to as safe, pure and potent) and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

The FDA may refer an application for a novel drug or biologic candidate to an advisory committee. 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.

Before approving an application, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an application, the FDA may inspect the sponsor and one or more clinical trial sites to assure compliance with GCP requirements and the integrity of the clinical data submitted in an NDA.

After evaluating the application and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally details specific conditions that must be met in order to secure final approval of the application and may require additional clinical or pre-clinical testing in order for FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require additional contraindications, warnings or precautions to be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a product's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a 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-marketing studies or surveillance programs. After approval, some 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 and biologics manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, 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 user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA or BLA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

In addition, manufacturers and other entities involved in the manufacture and distribution of approved products 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 requirements 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 mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition

of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products
- injunctions or the imposition of civil or criminal penalties;
- consent decrees, corporate integrity agreements, debarment, or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information; or
- the FDA or other regulatory authorities may issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Foreign Government Regulation

Our product candidates will be subject to similar laws and regulations imposed by jurisdictions outside of the United States, and, in particular, Europe, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or other transfers of value to healthcare professionals.

In order to market our future products in the European Economic Area (which is comprised of the 28 Member States of the EU plus Norway, Iceland and Liechtenstein), or EEA, and many other foreign jurisdictions, we must obtain separate regulatory approvals. More concretely, in the EEA, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations:

- the Community MA, which is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use of the European Medicines Agency, and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products and medicinal products indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU; and
- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized

for marketing in a Member State of the EEA, this National MA can be recognized in another Member State through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure.

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

Data and marketing exclusivity. In the EEA, new products authorized for marketing, or reference products, qualify for eight years of data exclusivity and an additional two years of market exclusivity upon marketing authorization. The data exclusivity period prevents generic or biosimilar applicants from relying on the pre-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from the initial authorization of the reference product in the EU. The 10-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those 10 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.

Pediatric investigation plan. In the EEA, marketing authorization applications for new medicinal products not authorized have to include the results of studies conducted in the pediatric population, in compliance with a pediatric investigation plan, or PIP, agreed with the EMA's Pediatric Committee, or PDCO. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which marketing authorization is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data are not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the marketing authorization is obtained in all Member States of the EU and study results are included in the product information, even when negative, the product is eligible for a six-months supplementary protection certificate extension.

Orphan drug designation. In the EEA, a medicinal product can be designated as an orphan drug if its sponsor can establish that the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically-debilitating condition affecting not more than five in 10,000 persons in the EU when the application is made, or that the product is intended for the diagnosis, prevention or treatment of a life-threatening, seriously-debilitating or serious and chronic condition in the European Community and that without incentives it is unlikely that the marketing of the drug in the EU would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the drug will be of significant benefit to those affected by that condition.

In the EEA, an application for designation as an orphan product can be made any time prior to the filing of an application for approval to market the product. Marketing authorization for an orphan drug leads to a ten-year period of market exclusivity. During this market exclusivity period, the EMA or the member state competent authorities, cannot accept another application for a marketing authorization,

or grant a marketing authorization, for a similar medicinal product for the same indication. The period of market exclusivity is extended by two years for medicines that have also complied with an agreed PIP.

This period may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan drug designation, for example because the product is sufficiently profitable not to justify market exclusivity. Market exclusivity can be revoked only in very selected cases, such as consent from the marketing authorization holder, inability to supply sufficient quantities of the product, demonstration of “clinical superiority” by a similar medicinal product, or, after a review by the Committee for Orphan Medicinal Products, requested by a member state in the fifth year of the marketing exclusivity period (if the designation criteria are believed to no longer apply). Medicinal products designated as orphan drugs are eligible for incentives made available by the EU and its Member States to support research into, and the development and availability of, orphan drugs. In March 2016, we obtained orphan drug designation for BPS-804 for the treatment of OI in the EU.

Adaptive pathways. The EMA has an adaptive pathways program which allows for early and progressive patient access to a medicine. The adaptive pathways concept is an approach to medicines approval that aims to improve patients’ access to medicines in cases of high unmet medical need. To achieve this goal, several approaches are envisaged: identifying small populations with severe disease where a medicine’s benefit-risk balance could be favorable; making more use of real-world data where appropriate to support clinical trial data; and involving health technology assessment bodies early in development to increase the chance that medicines will be recommended for payment and ultimately covered by national healthcare systems. The adaptive pathways concept applies primarily to treatments in areas of high medical need where it is difficult to collect data via traditional routes and where large clinical trials would unnecessarily expose patients who are unlikely to benefit from the medicine. The approach builds on regulatory processes already in place within the existing EU legal framework. These include: scientific advice; compassionate use; the conditional approval mechanism (for medicines addressing life-threatening conditions); patient registries and other pharmacovigilance tools that allow collection of real-life data and development of a risk-management plan for each medicine.

The adaptive pathways program does not change the standards for the evaluation of benefits and risks or the requirement to demonstrate a positive benefit-risk balance to obtain marketing authorization. In February 2017, BPS-804 was accepted into the adaptive pathways program.

PRIME scheme. In July 2016, the EMA launched its Priority Medicines scheme, or PRIME. PRIME is a voluntary scheme aimed at enhancing the EMA’s support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. Product developers that benefit from PRIME designation can expect to be eligible for accelerated assessment but this is however not guaranteed. The benefits of a PRIME designation includes the appointment of a rapporteur from the Committee for Medicinal Products for Human Use before submission of an MAA, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review earlier in the application process. In November 2017, the EMA granted PRIME designation for BPS-804 for the treatment of OI.

Other U.S. Healthcare Laws

In addition to FDA restrictions on marketing of pharmaceutical and biologic products, other U.S. federal and state healthcare regulatory laws restrict business practices in the pharmaceutical and biotechnology industry, which include, but are not limited to, state and federal anti-kickback, false claims, data privacy and security and physician payment and pricing transparency laws.

The U.S. federal Anti-Kickback Statute prohibits, among other things, any person or entity from knowingly and willfully offering, paying, soliciting, receiving or providing any remuneration, directly or indirectly, overtly or covertly, to induce or in return for purchasing, leasing, ordering, or arranging for or recommending the purchase, lease, or order of any good, facility, item or service reimbursable, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. The term “remuneration” has been broadly interpreted to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements, such as those between pharmaceutical manufacturers on the one hand and prescribers, purchasers, formulary managers and beneficiaries on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases, or recommendations may be subject to scrutiny if they do not meet the requirements of a statutory or regulatory exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the U.S. federal Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all facts and circumstances. Several courts have interpreted the statute’s intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated.

Additionally, the intent standard under the U.S. federal Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, to a stricter standard such that a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the ACA codified case law that a claim including items or services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. The majority of states also have anti-kickback laws, which establish similar prohibitions and in some cases may apply to items or services reimbursed by any third-party payor, including commercial insurers, or to self-pay patients.

The federal false claims and civil monetary penalties laws, including the civil False Claims Act, prohibit any person or entity from, among other things, knowingly presenting, or causing to be presented, a false, fictitious or fraudulent claim for payment to, or approval by, the federal government, knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. A claim includes “any request or demand” for money or property presented to the U.S. government. Actions under the civil False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Violations of the civil False Claims Act can result in very significant monetary penalties and treble damages. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies’ marketing of products for unapproved, or off-label, uses. In addition, the civil monetary penalties statute imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. Many states also have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit, among other actions, knowingly and willfully executing, or

attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, the ACA broadened the reach of certain criminal healthcare fraud statutes created under HIPAA by amending the intent requirement such that a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

In addition, there has been a trend of increased federal and state regulation of payments made to physicians and certain other healthcare providers. The ACA imposed, among other things, new annual reporting requirements through the Physician Payments Sunshine Act for applicable manufacturers for certain payments and "transfers of value" provided to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit timely, accurately and completely the required information for all payments, transfers of value and ownership or investment interests may result in civil monetary penalties. Applicable manufacturers must submit reports by the 90th day of each subsequent calendar year. In addition, certain states require implementation of compliance programs and compliance with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, impose restrictions on marketing practices and/or tracking and reporting of gifts, compensation and other remuneration or items of value provided to physicians and other healthcare professionals and entities.

We may also be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their respective implementing regulations, including the Final HIPAA Omnibus Rule published on January 25, 2013, impose specified requirements relating to the privacy, security and transmission of individually identifiable health information held by covered entities and their business associates. Among other things, HITECH made HIPAA's security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same requirements, thus complicating compliance efforts.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Ensuring that internal operations and business arrangements with third parties comply with applicable healthcare laws and regulations involve substantial costs.

Violations of any of these laws may be punishable by criminal and civil sanctions, including fines and civil monetary penalties, the possibility of exclusion from federal healthcare programs (including Medicare and Medicaid), disgorgement and corporate integrity agreements, which impose, among other things, rigorous operational and monitoring requirements on companies. Similar sanctions and penalties, as well as imprisonment, also can be imposed upon executive officers and employees of such companies. Given the significant size of actual and potential settlements, it is expected that the government authorities will continue to devote substantial resources to investigating healthcare providers' and manufacturers' compliance with applicable laws.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any pharmaceutical or biological product for which we obtain regulatory approval. In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Sales of any products for which we receive regulatory approval for commercial sale will therefore depend, in part, on the availability of coverage and adequate reimbursement from third-party payors. Third-party payors include government authorities, managed care plans, private health insurers and other organizations.

In the United States, the process for determining whether a third-party payor will provide coverage for a pharmaceutical or biologic product typically is separate from the process for setting the price of such product or for establishing the reimbursement rate that the payor will pay for the product once coverage is approved. 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 FDA-approved products for a particular indication. A decision by a third-party payor not to cover our product candidates could reduce physician utilization of our products once approved and have a material adverse effect on our sales, results of operations and financial condition. Moreover, a third-party payor's decision to provide coverage for a pharmaceutical or biologic product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. Additionally, coverage and reimbursement for products can differ significantly from payor to payor. One third-party payor's decision to cover a particular medical product or service does not ensure that other payors will also provide coverage for the medical product or service, or will provide coverage at an adequate reimbursement rate. As a result, the coverage-determination process will require us to provide scientific and clinical support for the use of our products to each payor separately and will be a time-consuming process.

In the EEA, governments influence the price of products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription products, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of pharmaceutical or biological products have been a focus in this effort. Third-party payors are increasingly challenging the prices charged for medical products and services, examining the medical necessity and reviewing the cost-effectiveness of pharmaceutical or biological products, medical devices and medical services, in addition to questioning safety and efficacy. If these third-party payors do not consider our products to be cost effective compared to other available therapies, they may not cover our products after approval, if any, or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit.

Healthcare Reform

A primary trend in the U.S. healthcare industry 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 medical products. For example, the ACA, among other things, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; introduced a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for products that are inhaled, infused, instilled, implanted or injected; extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid-managed care plans; imposed mandatory discounts for certain Medicare Part D beneficiaries as a condition for manufacturers' outpatient drugs coverage under Medicare Part D; subjected manufacturers to new annual fees based on pharmaceutical companies' share of sales to federal healthcare programs; created a new Patient Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; created the Independent Payment Advisory Board, which, once empaneled, will have authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs and biologics; and established a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending. Since its enactment, the U.S. federal government has delayed or suspended implementation of certain provisions of the ACA. In addition, there have been judicial and Congressional challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and lower reimbursement, and additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors. Moreover, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our product candidates.

Additionally, in August, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will stay in effect through 2025 unless additional action is taken by Congress. In January, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. More recently, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which have resulted in several Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical and biologic products.

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 products once approved or additional pricing pressures.

Employees

As of March 31, 2018, we had 37 employees. None of our employees is subject to a collective bargaining agreement or represented by a trade or labor union. We consider our relationship with our employees to be good.

Facilities

Our principal office is located at Fourth Floor, One Cavendish Place, London W1G 0QF, United Kingdom, where we lease approximately 4,000 square feet of office space. We lease this office space under a lease that terminates on August 16, 2025. We intend to add new facilities as we add employees, and we believe that suitable additional or substitute space will be available as needed to accommodate any such expansion of our operations.

Legal Proceedings

We are not subject to any material legal proceedings.

MANAGEMENT

Executive Officers and Directors

The following table presents information about our executive officers and directors, including their ages, as of the date of this prospectus:

Name	Age	Position
Executive Officers		
Denise Scots-Knight, Ph.D.	58	Chief Executive Officer and Director
Richard Jones	51	Chief Financial Officer and Director
Alastair MacKinnon, MBBS	47	Chief Medical Officer
John Richard	60	Head of Corporate Development
Charles Sermon	48	General Counsel
Non-Executive Directors		
Peter Fellner, Ph.D.	74	Chairman of the Board
Frank Armstrong, MBChB	61	Director
Peter Bains	60	Director
Paul Blackburn	63	Director
Anders Ekblom, M.D., Ph.D.	63	Director
Kunal Kashyap	53	Director

The current business addresses for our executive officers and directors is c/o Mereo BioPharma Group plc, Fourth Floor, One Cavendish Place, London, W1G 0QF, United Kingdom.

The following are brief biographies of our executive officers and directors:

Denise Scots-Knight, Ph.D. Dr. Scots-Knight has served as our Chief Executive Officer since July 2015 and as a member of our board of directors since our inception. From 2010 until joining Mereo, Dr. Scots-Knight was the Managing Partner of Phase4 Partners Ltd., or Phase4, a global life science venture capital firm. Dr. Scots-Knight is currently a board member of OncoMed Pharmaceuticals, Inc. and Phase4. Dr. Scots-Knight holds a B.Sc. (Hons.) and a Ph.D. from Birmingham University.

Richard Jones. Mr. Jones has served as our Chief Financial Officer and as a member of our board of directors since January 2017. From 2011 until joining Mereo, Mr. Jones was the Chief Financial Officer and Company Secretary of Shield Therapeutics plc, where he also served as a Non-Executive Director from 2010 to 2011. Mr. Jones is a qualified chartered accountant (ACA) with the Institute of Chartered Accountants in England and Wales (ICAEW) and holds a B.Eng. (Hons.) from the University of Newcastle upon Tyne.

Alastair MacKinnon, MBBS. Dr. MacKinnon has served as our Chief Medical Officer since July 2015. From 2010 until joining Mereo, Dr. MacKinnon was a Partner of Phase4, where he currently serves as a member of the Board of Directors. Dr. MacKinnon holds a B.Sc. and a MBBS from King's College London and is a Member of the Royal College of Surgeons in Edinburgh.

John Richard. Mr. Richard has served as our Head of Corporate Development since July 2015. Prior to joining Mereo, he was a consultant for Nomura, a global investment bank, and Phase4. Mr. Richard serves on the boards of Vaxart, Inc., Catalyst Biosciences, QUE Oncology, and Phase4. Mr. Richard holds a B.S. from Stanford University and an MBA from Harvard Business School.

Charles Sermon. Mr. Sermon has served as our General Counsel and Company Secretary since July 2015. From 2010 until joining Mereo, Mr. Sermon was a Partner of Phase4, where he currently

serves as a member of the Board of Directors. Mr. Sermon trained and qualified as a lawyer with Freshfields after completing the Law Society's Final Examination. Mr. Sermon holds an LL.B. (Hons.) from Hull University.

Peter Fellner, Ph.D. Dr. Fellner has been Chairman of our board of directors since July 2015. He also serves as Chairman of the board of directors of Consort Medical plc and Vernalis plc, and was Chairman of the board of directors of Ablynx nv until January 2018. Dr. Fellner was previously Chairman of the board of directors of Acambis plc until its acquisition by Sanofi Pasteur and Optos plc until its acquisition by Nikon Corporation, and Vice Chairman of Astex Pharmaceuticals Inc. until its acquisition by Otsuka Pharmaceutical Company. He also served as a Director of UCB SA and was CEO and then Chairman of Celltech Group plc. Dr. Fellner holds a B.Sc. (Hons.) from the University of Sheffield and a Ph.D. from the University of Cambridge.

Frank Armstrong, MBChB. Dr. Armstrong has served on our board of directors since July 2015. Dr. Armstrong served as Chief Executive Officer of CuraGen Corporation and Fulcrum Pharmaceuticals. Prior to that, Dr. Armstrong served as Senior Vice President at Merck Serono, Executive Vice President Product Development at Bayer AG, and Senior Vice President Medical Research at Zeneca Pharmaceuticals (now AstraZeneca). Dr. Armstrong currently serves as Non-Executive Chairman of Caldan Therapeutics Ltd., Summit Therapeutics plc, and Faron Pharmaceuticals. Dr. Armstrong holds a B.Sc. (Hons.) and MBChB from the University of Edinburgh, and is a Fellow of the Royal College of Physicians.

Peter Bains. Mr. Bains has served on our board of directors since July 2015. Mr. Bains is Representative Executive Officer and Chief Executive Officer of Sosei Group Corporation, a biotechnology company. Previously, he was Chief Executive Officer of Syngene International Ltd., or Syngene, and served as a Non-Executive Director until 2016. Mr. Bains currently serves as Non-Executive Director for Phase4 and MiNA Therapeutics Ltd. and as Non-Executive Chairman of Fermenta Biotech Ltd. Mr. Bains holds a B.Sc. (Hons.) from Sheffield University.

Paul Blackburn. Mr. Blackburn has served on our board of directors since October 2015. Mr. Blackburn was Senior Vice President Strategic Finance Projects and Financial Controller at GlaxoSmithKline. Mr. Blackburn currently serves on the Board of Directors of Syngene. Mr. Blackburn holds a B.Sc. from Warwick University.

Anders Ekblom, M.D., Ph.D. Dr. Ekblom has served on our board of directors since July 2015. Dr. Ekblom has held a number of executive positions at AstraZeneca, including Executive Vice President Global Drug Development, Executive Vice President Global Medicines Development, Global Head Clinical Development, Global Therapy Area Head, Global Head Science & Technology Integration, and Chief Executive Officer of AstraZeneca AB Sweden. He currently serves as Chairman of the Board at the Karolinska University Hospital and on the Boards of Directors of Alligator Bioscience AB, Infant Bacterial AB, and Medivir AB. Dr. Ekblom is a board-certified medical doctor and an Associate Professor at the Karolinska Institute. Dr. Ekblom holds a D.D.S., M.D. and Ph.D. from Karolinska Institutet.

Kunal Kashyap. Mr. Kashyap has served on our board of directors since July 2015. Mr. Kashyap is Chairman and Managing Director of Allegro Capital Advisors and also serves as an Independent Director of GlaxoSmithKline Consumer Healthcare Ltd and a Non-Executive Director of Phase4. Mr. Kashyap is also the Founder and was the Executive Director of Celstream Technologies Private Limited. Mr. Kashyap holds a Bachelor of Commerce from Bombay University.

In accordance with our Articles of Association, our directors serve for three-year terms. In 2018, the term for all of the members of our board of directors except for Richard Jones will expire. In 2019,

the term for Mr. Jones will expire. Our shareholders elect directors in accordance with our Articles of Association. If our shareholders do not elect a new director, then the retiring director may, if willing to serve, continue as a director. See “Description of Share Capital and Articles of Association—Articles of Association—Directors—Appointment of Directors.”

Foreign Private Issuer Exemption

As a “foreign private issuer,” as defined by the SEC, we are permitted to follow home country corporate governance practices, instead of certain corporate governance practices required by Nasdaq for U.S. domestic issuers. While we intend to follow most Nasdaq corporate governance rules, we intend to follow U.K. corporate governance practices in lieu of Nasdaq corporate governance rules as follows:

- We do not intend to follow Nasdaq Rule 5620(c) regarding quorum requirements applicable to meetings of shareholders. Such quorum requirements are not required under English 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 intend to follow Nasdaq Rule 5605(b)(2), which requires that independent directors regularly meet in executive session, where only independent directors are present. Our independent directors may choose to meet in executive session at their discretion.

Although we may rely on certain home country corporate governance practices, we must comply with Nasdaq Rule 5640 Notification of Noncompliance and Rule 5640 Voting Rights. Further, we must have an audit committee that satisfies Rule 5605(c)(3), which addresses audit committee responsibilities and authority, and that consists of committee members that meet the independence requirements of Rule 5605(c)(2)(A)(ii).

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 the Nasdaq corporate governance rules and 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 Exchange Act. They will, however, be subject to the obligations to report changes in share ownership under Section 13 of the Exchange Act and related SEC rules.

Composition of our Board of Directors

Our board of directors currently consists of eight members. Our board of directors has determined that four of our eight directors, Peter Fellner, Peter Bains, Paul Blackburn, and Anders Ekblom, do not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of director and that each of these directors is “independent” as that term is defined under the rules of Nasdaq. As a foreign private issuer, we are not required to meet the Nasdaq rule that our board be comprised of a majority of independent directors. However, we intend to comply with this requirement within 12 months of the listing of our ADSs with Nasdaq. There are no family relationships among any of our directors or senior management.

In accordance with our Articles of Association, each of our directors serves for a term of three years, and, as a result, effectively one-third of our directors retire from office at every annual general meeting of shareholders. Retiring directors are eligible for re-election and, if no other director is elected to fill his or her position and the director is willing, shall be re-elected by default. See “Description of Share Capital and Articles of Association—Articles of Association—Directors—Appointment of Directors.”

Committees of our Board of Directors

Our board of directors has four standing committees: an audit and risk committee, a remuneration committee, a nomination committee, and a research and development committee.

Audit and Risk Committee

The audit and risk committee, which consists of Paul Blackburn, Anders Ekblom, and Kunal Kashyap, assists the board in overseeing our accounting and financial reporting processes and the audits of our financial statements. Mr. Blackburn serves as Chairman of the committee. The audit and risk committee consists exclusively of members of our board who are financially literate, and Mr. Blackburn is considered an “audit committee financial expert” as defined by applicable SEC rules and has the requisite financial sophistication as defined under the applicable Nasdaq rules and regulations. Our board has determined that all of the members of the audit and risk committee satisfy the “independence” requirements set forth in Rule 10A-3 under the Exchange Act. The audit and risk committee will be governed by a charter that complies with Nasdaq rules, effective upon the effectiveness of the registration statement of which this prospectus forms a part.

The audit and risk committee's responsibilities include:

- recommending the appointment of the independent auditor to the general meeting of shareholders;
- the appointment, compensation, retention and oversight of any accounting firm engaged for the purpose of preparing or issuing an audit report or performing other audit services;
- pre-approving the audit services and non-audit services to be provided by our independent auditor before the auditor is engaged to render such services;
- evaluating the independent auditor's qualifications, performance and independence, and presenting its conclusions to the full board on at least an annual basis;
- reviewing and discussing with the executive officers, the board, and the independent auditor our financial statements and our financial reporting process; and
- approving or ratifying any related person transaction (as defined in our related person transaction policy) in accordance with our related person transaction policy.

The audit and risk committee will meet as often as one or more members of the audit and risk committee deem necessary, but in any event will meet at least four times per year. The audit and risk committee will meet at least once per year with our independent accountant, without our senior management being present.

Remuneration Committee

The remuneration committee, which consists of Frank Armstrong, Peter Bains, and Anders Ekblom, assists the board in determining senior management compensation. Dr. Ekblom serves as Chairman of the committee. Under SEC and Nasdaq rules, there are heightened independence standards for members of the remuneration committee, including a prohibition against the receipt of any compensation from us other than standard board member fees. However, foreign private issuers are not required to meet this heightened standard. Nonetheless, our board has determined that Mr. Bains and Dr. Ekblom meet this heightened standard, and we intend for all members of our remuneration committee to comply with this heightened standard within 12 months of the listing of our ADSs with Nasdaq. The remuneration committee will be governed by a charter that complies with Nasdaq rules, effective upon the effectiveness of the registration statement of which this prospectus forms a part.

The remuneration committee's responsibilities include:

- identifying, reviewing, and proposing policies relevant to senior management compensation;

- evaluating each member of senior management's performance in light of such policies and reporting to the board;
- analyzing the possible outcomes of the variable compensation components and how they may affect the compensation of senior management;
- recommending any equity long-term incentive component of each member of senior management's compensation in line with any compensation policy and reviewing our senior management compensation and benefits policies generally; and
- reviewing and assessing risks arising from our compensation policies and practices.

Nomination Committee

The nomination committee, which consists of Peter Bains, Anders Ekblom, and Peter Fellner, assists our board in identifying individuals qualified to become members of our board and senior management consistent with criteria established by our board and in developing our corporate governance principles. Dr. Fellner serves as Chairman of the nomination committee. The nomination committee will be governed by a charter that complies with Nasdaq rules, effective upon the effectiveness of the registration statement of which this prospectus forms a part.

The nomination committee's responsibilities include:

- drawing up selection criteria and appointment procedures for board members;
- reviewing and evaluating the size and composition of our board and making a proposal for a composition profile of the board at least annually;
- recommending nominees for election to our board and its corresponding committees;
- assessing the functioning of individual members of the board and senior management and reporting the results of such assessment to the board; and
- developing and recommending to the board rules governing the board, reviewing and reassessing the adequacy of such rules governing the board, and recommending any proposed changes to the board.

Research and Development Committee

The research and development committee, which consists of Frank Armstrong, Peter Bains, and Anders Ekblom, assists our senior management with oversight and guidance related to research and development matters and provides guidance and makes recommendations to our board regarding research and development matters. Dr. Armstrong serves as Chairman of the research and development committee.

The research and development committee's responsibilities include oversight of:

- our strategic development plans for products, taking into account any regulatory feedback; and
- the acquisition of new products.

In addition, the research and development committee is tasked with keeping informed of strategic issues and commercial changes affecting our development programs and potential product acquisitions.

Code of Business Conduct and Ethics and Anti-Bribery and Anti-Corruption Policy

In connection with the global offering, we adopted a Code of Business Conduct and Ethics and an Anti-Bribery and Anti-Corruption Policy, effective upon the effectiveness of the registration statement of which this prospectus forms a part, that covers a broad range of matters including the handling of conflicts of interest, compliance issues, and other corporate policies such as equal opportunity and non-discrimination standards.

Compensation

Executive Officer Remuneration

The following table sets forth the approximate remuneration paid during the years ended December 31, 2017 and 2016 to our current executive officers.

Name and Principal Position	Year	Salary (£)	Bonus(1) (£)	All Other Compensation(2) (£)	Total(3) (£)
Denise Scots-Knight, Ph.D.	2017	365,000	242,725	64,196	671,921
Chief Executive Officer	2016	340,000	166,600	56,863	563,463
Richard Jones (4)	2017	231,090	166,250	29,224	426,564
Chief Financial Officer	2016	—	—	—	—
Alastair MacKinnon, MBBS	2017	256,000	170,240	27,916	454,156
Chief Medical Officer	2016	230,000	112,700	25,071	367,771
Charles Sermon	2017	271,625	180,631	33,164	485,420
General Counsel	2016	265,000	129,850	31,847	426,697
John Richard (5)	2017	275,338	218,727	—	494,065
Head of Corporate Development	2016	259,745	158,589	—	418,334

- (1) Amount shown reflects cash bonuses awarded for achievement of performance goals in 2016 and 2017, as applicable.
- (2) Amount shown represents health benefit payments and pension contributions made by us.
- (3) Total compensation set out in this table does not include any amounts for awards under our Deferred Bonus Share Plan or the value of options to acquire our ordinary shares or awards granted to or held by current senior management, which is described in “—Equity Compensation Arrangements.”
- (4) Mr. Jones commenced employment with us in January 2017.
- (5) Mr. Richard provided services to us in 2017 under a consultancy agreement and currently provides services to us under a consultancy agreement and an employment agreement. These agreements are described in “—Executive Officer Employment and Consultancy Agreements—John Richard.”

Executive Officer Employment and Consultancy Agreements

Denise Scots-Knight, Ph.D.

We entered into an employment agreement with Dr. Scots-Knight on July 29, 2015. This agreement entitles Dr. Scots-Knight to receive an initial annual base salary of £275,000 (which was subsequently increased to £379,600 for 2018) and an opportunity to earn an annual discretionary performance-based bonus, subject to the achievement of performance goals determined in accordance with our annual bonus plan. We currently contribute to Dr. Scots-Knight's Self-Invested Personal Pension Scheme an amount equal to 15% of Dr. Scots-Knight's annual salary, provided that she contributes 4% or more of her annual salary to that scheme. In lieu of a pension contribution, we may, at Dr. Scots-Knight's request, pay a pro-rata amount equal to 10% of her base salary as additional compensation. Either party may terminate the employment agreement by giving the other party not less than 12 months' written notice, provided that we may terminate Dr. Scots-Knight at any time with immediate effect for cause or by giving written notice to Dr. Scots-Knight that we will instead pay her basic salary for any remaining notice period. Dr. Scots-Knight's employment agreement also contains restrictive covenants pursuant to which she has agreed to refrain from competing with us or soliciting our key employees for a period of six months following her termination of employment or soliciting our customers for a period of nine months following her termination of employment.

Richard Jones

We entered into an employment agreement with Mr. Jones on November 7, 2016 pursuant to which he commenced employment with us on January 28, 2017. This agreement entitles Mr. Jones to

receive an initial annual base salary of £250,000 (which was subsequently increased to £260,000 for 2018) and an opportunity to earn an annual discretionary performance-based bonus, subject to the achievement of performance goals determined in accordance with our annual bonus plan. Mr. Jones is also eligible to participate in our group personal pension scheme and we have agreed to contribute to the pension scheme an amount equal to 10% of Mr. Jones's annual salary provided that he contributes 4% or more of his annual salary to that scheme. In lieu of a pension contribution, we may, at Mr. Jones's request, pay a pro-rata amount equal to 10% of his base salary as additional compensation. Either party may terminate the employment agreement by giving the other party not less than six months' written notice, provided that we may terminate Mr. Jones at any time with immediate effect for cause or by giving written notice to Mr. Jones that we will instead pay his basic salary for any remaining notice period. Mr. Jones's employment agreement also contains restrictive covenants pursuant to which he has agreed to refrain from competing with us or soliciting our key employees for a period of six months following his termination of employment or soliciting our customers for a period of nine months following his termination of employment.

Alastair MacKinnon

We entered into an employment agreement with Dr. MacKinnon on July 29, 2015, and subsequently amended the agreement on November 24, 2017. This agreement entitles Dr. MacKinnon to receive an initial annual base salary of £210,000 (which was subsequently increased to £281,600 for 2018) and an opportunity to earn an annual discretionary performance-based bonus, subject to the achievement of performance goals determined in accordance with our annual bonus plan. Dr. MacKinnon is also eligible to participate in our group personal pension scheme and we have agreed to contribute to the pension scheme an amount equal to 10% of Dr. MacKinnon's annual salary provided that he contributes 4% or more of his annual salary to that scheme. In lieu of a pension contribution, we may, at Dr. MacKinnon's request, pay a pro-rata amount equal to 10% of his base salary as additional compensation. Either party may terminate the employment agreement by giving the other party not less than six months' written notice, provided that we may terminate Dr. MacKinnon at any time with immediate effect for cause or by giving written notice to Dr. MacKinnon that we instead pay his basic salary for any remaining notice period. Dr. MacKinnon's employment agreement also contains restrictive covenants pursuant to which he has agreed to refrain from competing with us for a period of three months following his termination of employment, soliciting our key employees for a period of six months following his termination of employment, or soliciting our customers for a period of nine months following his termination of employment.

Charles Sermon

We entered into an employment agreement with Mr. Sermon on July 29, 2015. This agreement entitles Mr. Sermon to receive an initial annual base salary of £245,000 (which was subsequently increased to £282,490 for 2018) and an opportunity to earn an annual discretionary performance-based bonus, subject to the achievement of performance goals determined in accordance with our annual bonus plan. We have agreed to contribute to Mr. Sermon's Self-Invested Personal Pension Scheme an amount equal to 10% of Mr. Sermon's annual salary provided that he contributes 4% or more of his annual salary to that scheme. In lieu of a pension contribution, we may, at Mr. Sermon's request, pay a pro-rata amount equal to 10% of his base salary as additional compensation. Either party may terminate the employment agreement by giving the other party not less than six months' written notice, provided that we may terminate Mr. Sermon at any time with immediate effect for cause or by giving written notice to Mr. Sermon that we will instead pay his basic salary for any remaining notice period. Mr. Sermon's employment agreement also contains restrictive covenants pursuant to which he has agreed to refrain from competing with us or soliciting our key employees for a period of six months following his termination of employment or soliciting our customers for a period of nine months following his termination of employment.

John Richard

We entered into a consultancy agreement with Mr. Richard on February 1, 2017, pursuant to which he provided services to us during 2017 and which has subsequently expired. Mr. Richard currently provides services to us pursuant to an employment agreement dated February 26, 2018, or the Richard Employment Agreement, and a consultancy agreement dated February 1, 2018, or the Richard Consulting Agreement.

The Richard Employment Agreement entitles Mr. Richard to receive an initial base salary of £3,900 per month and an opportunity to earn an annual discretionary performance-based bonus, subject to the achievement of performance goals determined in accordance with our annual bonus plan. Mr. Richard is also eligible to participate in our group personal pension scheme and we have agreed to contribute to the pension scheme an amount equal to 10% of Mr. Richard's annual salary provided that he contributes 4% or more of his annual salary to that scheme. In lieu of a pension contribution, we may, at Mr. Richard's request, pay a pro-rata amount equal to 10% of his base salary as additional compensation. Either party may terminate the employment agreement by giving the other party not less than six months' written notice, provided that we may terminate Mr. Richard at any time with immediate effect for cause or by giving written notice to Mr. Richard that we will instead pay his basic salary for any remaining notice period. Mr. Richard's employment agreement also contains restrictive covenants pursuant to which he has agreed to refrain from competing with us or soliciting our key employees for a period of six months following his termination of employment, or soliciting our customers for a period of nine months following his termination of employment.

Pursuant to the Richard Consulting Agreement, Mr. Richard also provides services to us as a consultant for up to 75% of his working capacity. The Richard Consulting Agreement is expected to remain in effect until January 31, 2019. The Richard Consulting Agreement entitles Mr. Richard to receive a retainer of \$25,550 per month and an opportunity to earn a one-time discretionary payment from us based upon the achievement of agreed-upon performance goals with regard to the preceding 12-month period.

Equity Compensation Arrangements

We have granted or may grant or intend to grant share options and awards under the following five equity award plans, or the Share Plans: (i) the 2015 Plan; (ii) the Share Option Plan; (iii) the LTIP; (iv) the DBSP; and (v) the Share Option Scheme for Non-Executive Directors, or the NED Plan.

The 2015 Plan

Prior to the admission of our ordinary shares to trading on AIM, or Admission, we granted options under the 2015 Plan. No further grants have been made under the 2015 Plan since Admission.

Eligibility, Awards and Administration

The 2015 Plan provides for the grant of options to executive directors, non-executive directors, employees and consultants.

Options granted under the 2015 Plan vest in accordance with the vesting schedule set out in each option holder's option agreement, in normal circumstances, between the first and fourth anniversary (or between the first and third anniversary for non-executive directors) of the vesting start date (typically the date of commencement of employment, appointment as a director, or entering into a consultancy agreement with us).

Admission did not automatically accelerate the vesting of options, and unvested options continue to vest in accordance with their original vesting schedule, subject to the rules of the 2015 Plan. The options are not subject to performance conditions other than continued service.

Options are not automatically exercisable on vesting, but upon Admission became exercisable to the extent vested. Options may generally be exercised until the day immediately preceding the tenth anniversary of the date of grant.

Options have been granted under the 2015 Plan with an exercise price ranging from £1.29 per ordinary share to £2.21 per ordinary share.

Plan Leavers

Options held by option holders who leave their office or employment will lapse immediately, unless the option holder is a Good Leaver (as defined in the plan rules). If the option holder is a Good Leaver, the option may be exercised to the extent vested at the date of cessation of services and for such period as our board of directors determines and communicates to the option holder at that time (except upon death, in which case, options may be exercised for a period of one year), after which time they will lapse.

Certain Transactions

Under the 2015 Plan, certain corporate events such as a Takeover or a Trade Sale (as defined in the plan rules) will accelerate the vesting of all unvested options upon the occurrence of such event. Options will then be exercisable for a period of 40 days thereafter, after which they will lapse.

Adjustments

In the event of any capitalization, rights issue, consolidation, subdivision, reduction or any other variation of our share capital, the number of ordinary shares subject to an option and the exercise price applying to an option may be varied in such manner as our board of directors may determine.

Amendment and Termination

Our board of directors may, at any time, amend the rules of the 2015 Plan with effect from a current, future or past date by way of a resolution, except that no amendment may be made which would abrogate or adversely affect the subsisting rights of option holders, unless consent from a majority of the affected option holders is obtained (by reference to the number of ordinary shares subject to options). However, any amendment to benefit the administration of the 2015 Plan, to take account of legislative changes, a Takeover or a Trade Sale (as defined in the plan rules) or to obtain or maintain favorable tax treatment or regulatory treatment may be made by our board of directors without the consent of option holders.

The Mereo BioPharma Group plc Share Option Plan

Our board of directors adopted the Share Option Plan on March 4, 2016, and has subsequently amended it. Except where the context indicates otherwise, references to our ordinary shares shall be deemed to include a number of ADSs representing a right to receive such ordinary shares.

Eligibility, Awards and Administration

The Share Option Plan provides for the grant of options to acquire our ordinary shares to employees and executive directors. Options may be granted to all eligible employees on commencement of employment and may be granted on a periodic basis after that. The Share Option Plan is administered by our board of directors who also set the terms and conditions of all options granted under the Share Option Plan, including any vesting and vesting acceleration conditions. Options are granted under the Share Option Plan at the discretion of our board of directors.

Vesting and Exercise

Under the Share Option Plan, our board of directors may determine the vesting schedule of an option and whether the vesting of an option will be subject to the satisfaction of a performance condition, although options are not currently granted subject to performance conditions other than continued service with us. Once an option has vested, it may be exercised during the period ending on the tenth anniversary of the date of grant, after which time it will lapse. The exercise price of an option may not be less than the greater of: (i) the market value of a share on the date of grant; or (ii) if the shares are to be subscribed, the nominal value of a share. Our board of directors may determine that an options be settled in cash or by net exercise of the option.

Limitation on Awards

No eligible employee may be granted options that, at the time they are granted, would cause the market value of shares subject to the options granted to the employee in respect of a financial year to exceed 400% of the employee's salary.

Plan Leavers

If a participant ceases to hold office or employment with us as a result of dismissal for gross misconduct, any option the participant holds, whether vested or unvested, will lapse.

If a participant ceases to hold office or employment with us for any reason other than dismissal for gross misconduct then: (i) if the option is already vested, it may be exercised within six months from the date of cessation of services if such cessation did not occur as a result of the participant's death, and within 12 months from the date of cessation of services if such cessation occurred as a result of the participant's death; and (ii) if the option is not already vested, it will vest on the normal vesting date as described above, unless our board of directors determines that the option will vest on the date of cessation of services. Where an option vests in these circumstances, any performance condition will be taken into account and, unless our board of directors determines otherwise, will be pro-rated for time.

Unless the board determines otherwise, options may not be transferred in any way and will lapse immediately on any attempt to do so, except that options may be transferred to a participant's personal representative upon death.

Certain Transactions

Under the Share Option Plan, if certain changes are made in, or events occur with respect to our ordinary shares (including any variation of share capital, demerger, delisting, special dividend, rights issue or any other event, which may, in the opinion of our board of directors affect the current or future value of our ordinary shares), the number of shares subject to an option or the exercise price of an option may be adjusted as determined by our board of directors. In addition, upon such an event, our board of directors will determine: (i) whether and to what extent options which have not yet vested will vest; and (ii) the period of time during which any vested option may be exercised.

In the event of certain corporate transactions, including a scheme of arrangement or general offer, the vesting and exercisability of all options will accelerate to the extent determined by our board of directors, after which they will be exercisable for one month (or such longer period as determined by our board of directors, but not exceeding six months), following which they will lapse. However, if there is an internal reorganization, unless our board of directors determines otherwise, an option will generally be exchanged in consideration of the grant of a new option which, as determined by our board of directors, is equivalent to the option but relates to shares in a different company (whether the acquiring company or a different company). Any option that does not vest or is not exchanged will lapse immediately.

Amendment and Termination

Our board of directors may, at any time, amend the rules of the Share Option Plan, except that no amendment may be made: (i) which would be to the material disadvantage of the existing rights of participants unless every participant who may be affected by such amendment has been invited to indicate whether he or she approves the amendment and the amendment is approved by a majority of such participants; or (ii) which would prevent the Share Option Plan from being an employees' share scheme in accordance with the Companies Act 2006. No options may be granted pursuant to the Share Option Plan after the tenth anniversary of the date of our Admission.

The Mereo BioPharma Group plc Long Term Incentive Plan

In order to further incentivize our employees and align their interests with shareholders, our board of directors adopted the LTIP on June 9, 2016 and has subsequently amended it.

Eligibility, Awards and Administration

The LTIP provides for the grant of nil-cost options, conditional awards, cash conditional awards or cash options, or, the LTIP Awards, to our employees. The shares used to satisfy the LTIP Awards are currently delivered through the Mereo BioPharma Group plc Employee Benefit Trust, which is based in Jersey.

Our board of directors may determine that the LTIP Awards are settled in cash.

Vesting and Exercise

The LTIP Awards are subject to a vesting schedule as determined by our board of directors. LTIP Awards granted to key executive directors and senior management are subject to: (i) a share price performance condition; and (ii) the achievement of strategic operational targets. If on the date a LTIP Award is due to vest or be exercisable a restriction on share dealing (as may be imposed by our share dealing code or the AIM rules) applies to the award, then the award will vest on the date on which such dealing restriction lifts.

Limitation on Awards

No eligible employee may be granted LTIP Awards that, at the time they are granted, would cause the market value of shares subject to the LTIP Awards granted to the employee in respect of a financial year to exceed 300% of the employee's salary.

The LTIP Awards may be: (i) reduced; or (ii) where the underlying shares or cash has already been transferred to the participant following vesting or exercise of the LTIP Award (as applicable), clawed back, where prior to the second anniversary of the end of the relevant performance period there has been a material misstatement of our accounts, an error in assessing a performance condition such that the LTIP Award vests to a greater extent than it would have vested, or fraudulent or material misconduct on the part of the participant.

Scheme Leavers

The LTIP Awards will usually lapse on the participant's cessation of employment or office, unless the cessation is because of death, ill health, injury or disability, or where the participant is no longer employed by us, or for any other reason at our board of directors' discretion, except where the participant is summarily dismissed, in which case any unvested LTIP Awards will usually continue until the normal vesting date, unless our board of directors determines otherwise.

Certain Transactions

Under the LTIP, if certain changes are made in or events occur with respect to our ordinary shares (including any variation of share capital, any demerger, delisting, special dividend, rights issue or other

event which may in the opinion of our board of directors, affect the current or future value of our ordinary shares), the number of shares subject to a LTIP Award, or any performance condition, may be adjusted as determined by our board of directors. In addition, upon such an event, our board of directors will determine: (i) whether and to what extent Awards which have not yet vested will vest; and (ii) the period of time during which any vested option may be exercised.

In the event of certain corporate transactions, including a general offer or a scheme of arrangement, the vesting and exercisability of all LTIP Awards will accelerate to the extent determined by our board of directors (taking into account the extent to which any performance conditions have been satisfied and usually the period of time from the date of grant to the date of the corporate transaction), and any nil-cost options will remain exercisable for one month (or such other period as determined by our board of directors), following which they will lapse. However, if there is an internal reorganization, a LTIP Award will be exchanged in consideration of the grant of a new award which, as determined by our board of directors, is equivalent to the LTIP Award but relates to shares in a different company (whether the acquiring company or a different company). Any LTIP Award that does not vest or is not exchanged will lapse immediately.

Amendment and Termination

Our board of directors may, at any time, amend the rules of the LTIP or the terms of any LTIP Award, except that no amendment may be made: (i) which would be to the material disadvantage of the existing rights of participants unless every participant who may be affected by such amendment has been invited to indicate whether he or she approves the amendment and the amendment is approved by a majority of such participants; or (ii) which would prevent the LTIP from being an employees' share scheme in accordance with the Companies Act 2006. No LTIP Awards may be granted pursuant to the LTIP after the tenth anniversary of the date of Admission.

The Mereo BioPharma Group plc Deferred Bonus Share Plan

Our board of directors adopted the DBSP on June 9, 2016 and has subsequently amended it.

Eligibility, Awards and Administration

The DBSP provides for the deferral of a percentage (currently 30%) of the annual bonuses awarded to our employees into the right to acquire shares equal in value to the amount deferred, free of charge.

Under the DBSP, conditional awards or nil-cost options, or the DBSP Awards, may only be granted to participants who have earned a bonus, pursuant to our annual bonus plan, for the financial year immediately preceding the financial year in which the grant date occurs. A DBSP Award will be granted over such number of shares as have at the grant date a market value, as determined by our board of directors, equal to the deferred bonus (the amount of bonus which is to be delivered in the form of a conditional award or a nil-cost option).

Vesting and Exercise

The DBSP Awards will generally vest three years after the date of grant and have no performance conditions or service condition. The DBSP Awards may be settled in cash if determined by our board of directors. The shares used to satisfy the DBSP Awards are currently delivered through the Mereo BioPharma Group plc Employee Benefit Trust, which is based in Jersey.

If on the date a DBSP Award is due to vest or be exercisable a restriction on share dealing (as may be imposed by our share dealing code or the AIM rules) applies to the award, then the award will vest on the date on which such dealing restriction lifts.

Once a nil-cost option has vested, it may be exercised during the period ending on the first anniversary of the date on which it vested in such manner as our board of directors determines, after which time it will lapse.

Limitation on Awards

No eligible employee may be granted DBSP Awards that, at the time they are granted, would cause the market value of shares subject to the DBSP Awards granted to the employee in respect of a financial year to exceed 100% of the employee's salary.

The DBSP Awards may, prior to the third anniversary of the grant date, be: (i) reduced; or (ii) where the underlying shares or cash have already been transferred to the participant following vesting or exercise of the DBSP Award (as applicable), clawed back, where there has been a material misstatement of our accounts, an error in assessing the information on which the bonus was determined such that the bonus was overpaid, or fraudulent or material misconduct on the part of the participant.

Certain Transactions

Under the DBSP, if certain changes are made in or events occur with respect to our ordinary shares (including any variation of share capital, any demerger, delisting, special dividend, rights issue or other event which may in the opinion of our board of directors, affect the current or future value of our ordinary shares), the number of shares subject to a DBSP Award may be adjusted as determined by our board of directors. In addition, upon such an event, our board of directors will determine: (i) whether and to what extent DBSP Awards which have not yet vested will vest; and (ii) the period of time during which any vested option may be exercised.

In the event of certain corporate transactions, including a general offer or a scheme of arrangement, the vesting and exercisability of all DBSP Awards will accelerate to the extent determined by our board of directors, after which, the DBSP Awards will be exercisable for one month (or such other period as or determined by our board of directors), following which they will lapse. However, if there is an internal reorganization, a DBSP Award will be exchanged in consideration of the grant of a new award which, as determined by our board of directors, is equivalent to the DBSP Award but relates to shares in a different company (whether the acquiring company or a different company).

Scheme Leavers

Except for where a participant is summarily dismissed (in which case the awards will be forfeited), the DBSP Awards usually will continue upon cessation of office or employment with us and vest in full on the normal vesting date as described above. Options will remain exercisable for a period of 12 months from the date of vesting.

Amendment and Termination

Our board of directors may, at any time, amend the rules of the DBSP, except that no amendment may be made: (i) which would be to the material disadvantage of the existing rights of participants unless every participant who may be affected by such amendment has been invited to indicate whether he or she approves of the amendment and the amendment is approved by a majority of such participants; or (ii) which would prevent the DBSP from being an employees' share scheme in accordance with the Companies Act 2006.

No DBSP Awards may be granted pursuant to the DBSP after the tenth anniversary of the date of Admission.

The Mereo BioPharma Group plc Share Option Scheme for Non-Executive Directors

Our board of directors adopted the NED Plan on March 20, 2018. Except where the context indicates otherwise, references to our ordinary shares shall be deemed to include a number of ADSs representing the right to receive such ordinary shares.

Eligibility, Awards and Administration

The NED Plan provides for the grant of options to acquire our ordinary shares to non-executive directors. The NED Plan is administered by our board of directors who also set the terms and conditions of all options granted under the NED Plan, including any vesting and vesting acceleration conditions. Options are granted under the NED Plan at the discretion of our board of directors.

Vesting and Exercise

Under the NED Plan, our board of directors may determine the vesting schedule of the option. Once an option has vested, it may be exercised during the period ending on the tenth anniversary of the date of grant, after which time it will lapse. The exercise price of an option may not be less than the greater of: (i) the market value of a share on the date of grant; or (ii) if the shares are to be subscribed, the nominal value of a share. Our board of directors may determine that options be settled in cash or by cashless exercise of the option.

Plan Leavers

If a participant ceases to hold office with us as a result of dismissal for gross misconduct, any option the participant holds, whether vested or unvested, will lapse. If a participant ceases to hold office with us for any reason other than dismissal for gross misconduct then: (i) if the option is already vested, it may be exercised within six months from the date of cessation of services if such cessation did not occur as a result of the participant's death, and within 12 months from the date of cessation of services if such cessation occurred as a result of the participant's death; and (ii) if the option is not already vested, it will vest on the option's normal vesting date, unless our board of directors determines that the option will vest on the date of cessation of services. Where an option vests in these circumstances, options will be pro-rated for time, unless the Board decides otherwise. Options may not be transferred in any way and will lapse immediately on any attempt to do so, except that options may be transferred to a participant's personal representative upon death.

Certain Transactions

Under the NED Plan, if certain changes are made in, or events occur with respect to our ordinary shares (including any variation of share capital, demerger, delisting, special dividend, rights issue or any other event, which may, in the opinion of our board of directors affect the current or future value of our ordinary shares), the number of shares subject to an option or the exercise price of an option may be adjusted as determined by our board of directors. In addition, upon such an event, our board of directors will determine: (i) whether and to what extent options which have not yet vested will vest; and (ii) the period of time during which any vested option may be exercised.

In the event of certain corporate transactions, including a scheme of arrangement or general offer, the vesting and exercisability of all options will accelerate to the extent determined by our board of directors, after which they will be exercisable for one month (or such longer period as determined by our board of directors, but not exceeding six months), following which they will lapse. However, if there is an internal reorganization, unless our board of directors determines otherwise, an option will generally be exchanged in consideration of the grant of a new option which, as determined by our board of directors, is equivalent to the option but relates to shares in a different company (whether the acquiring company or a different company). Any option that does not vest or is not exchanged will lapse immediately.

Amendment and Termination

Our board of directors may, at any time, amend the rules of the NED Plan, except that no amendment may be made which would be to the material disadvantage of the existing rights of

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participants unless every participant who may be affected by such amendment has been invited to indicate whether he or she approves the amendment and the amendment is approved by a majority of such participants. No options may be granted pursuant to the NED Plan after the tenth anniversary of the date of its adoption.

The following table summarizes: (i) the outstanding number of options and awards under the equity incentive plans; and (ii) the number of shares granted to directors, executive officers, and non-executive directors, as of March 31, 2018:

Name	Ordinary Shares	Ordinary Shares Underlying Options	Exercise Price Per Ordinary Share (£)	Grant Date	Expiration Date
Denise Scots-Knight, Ph.D.	844,199	1,544,745 461,538 25,319 N/A	1.29 nil nil N/A	September 25, 2015 June 9, 2016 April 4, 2017 N/A	September 25, 2025 June 9, 2026 April 4, 2021 N/A
Richard Jones	—	650,000 185,950	3.02 nil	April 4, 2017 April 4, 2017	April 4, 2027 June 9, 2026
Alastair MacKinnon	425,974	772,371 234,162 17,127 N/A	1.29 nil nil N/A	September 25, 2015 June 9, 2016 April 4, 2017 N/A	September 25, 2025 June 9, 2026 April 4, 2021 N/A
John Richard	249,658	772,371 50,000 N/A	1.29 2.21 N/A	September 25, 2015 June 1, 2016 N/A	September 25, 2025 June 1, 2026 N/A
Charles Sermon	524,504	772,371 269,796 19,734 N/A	1.29 nil nil N/A	September 25, 2015 June 9, 2016 April 4, 2017 N/A	September 25, 2025 June 9, 2026 April 4, 2021 N/A
Peter Fellner	10,000	1,692,673 N/A	1.29 N/A	September 29, 2015 N/A	September 29, 2025 N/A
Frank Armstrong	256,444	216,264 N/A N/A	1.29 N/A N/A	September 29, 2015 N/A N/A	September 29, 2025 N/A N/A
Peter Bains	107,906	710,583 N/A	1.29 N/A	September 29, 2015 N/A	September 29, 2025 N/A
Paul Blackburn	22,624	236,974 N/A	1.84 N/A	May 11, 2016 N/A	May 11, 2026 N/A
Anders Ekblom	93,002	216,264 N/A	1.29 N/A	September 29, 2015 N/A	September 29, 2025 N/A
Kunal Kashyap	1,497,735	216,264 N/A	1.29 N/A	September 29, 2015 N/A	September 29, 2025 N/A

Incentive Award Arrangements

In connection with the global offering, our board of directors has approved one-time incentive awards, effective upon the effectiveness of the registration statement of which this prospectus forms a part, to our current executive officers, to incentivize future performance and recognize their service and significant efforts for our business. These awards are in the form of option grants under the Share Option Plan in the following amounts: Dr. Scots-Knight: 460,000 shares subject to the option;

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Mr. Jones: 250,000 shares subject to the option; Dr. MacKinnon: 200,000 shares subject to the option; Mr. Sermon: 200,000 shares subject to the option; and Mr. Richard: 200,000 shares subject to the option. The options will have a per share exercise price equal to the offering price of our ordinary shares in the European private placement and will vest over three years following the date of grant, subject to continued employment on the applicable vesting date.

Our board of directors has also approved one-time incentive awards, effective upon the effectiveness of the registration statement of which this prospectus forms a part, to each of the following non-executive directors: Frank Armstrong, Peter Bains, Paul Blackburn, Anders Ekblom, Peter Fellner, and Kunal Kashyap. Each award is in the form of an option grant under the NED Plan with respect to 20,000 shares. The options will have a per share exercise price equal to the offering price of our ordinary shares in the European private placement and will vest as to one-third of the shares subject to the option, on the first anniversary of the date of grant, and as to the remainder of the shares subject to the option, in 24 equal monthly installments thereafter, subject to continued service on the applicable vesting date.

Following the global offering, we currently expect to make grants of incentive awards under our Share Plans representing an aggregate of 4% of our share capital on an annual basis to our employees and non-executive directors. The terms, allocation and amounts of these awards will be determined by our board of directors.

Non-Employee Directors Remuneration

The following table sets forth the remuneration paid during 2017 to the current non-employee directors, all of which was in the form of annual fees:

Name	Annual Fees (£)
Frank Armstrong	56,000
Peter Bains	44,000
Paul Blackburn	48,000
Anders Ekblom	48,000
Peter Fellner	100,000
Kunal Kashyap	40,000

Non-Employee Director Service Contracts

The remuneration of the non-executive directors is determined by our board as a whole, based on a review of current practices in other companies. We have entered into service contracts with our directors for their services, which are subject to a three-month termination period. There are no arrangements under which any non-executive director is entitled to receive compensation upon the early termination of his appointment.

Pension, Retirement or Similar Benefits

We operate a defined contribution pension scheme which is available to all employees. We make payments of up to 10% of basic salary for executives (up to 15% for our Chief Executive Officer) into any pension scheme or similar arrangement as the participating executive may reasonably request (or a payment in lieu thereof). Such payments are not counted for the purposes of determining bonuses or awards under the LTIP. The total amount set aside or accrued by us to provide pension, retirement or similar benefits to our current directors and our senior management with respect to 2017 was £130,622, which represents contributions made by us in 2017 in respect of a defined contribution scheme.

Employees

As of December 31, 2017 and 2016, we had 31 and 24 employees, respectively. All of our employees were based in the United Kingdom. All of our employees were engaged in either general and administrative or research and development functions. None of our employees are covered by a collective bargaining agreement.

Insurance and Indemnification

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 ensure such persons against certain liabilities. We have entered into a deed of indemnity with each of our directors and we expect to enter into a new deed of indemnity with each of our directors and executive officers in connection with the global offering.

Insofar as indemnification of liabilities arising under the Securities Act may be permitted to our board, executive officers, or persons controlling us pursuant to the forgoing provisions, we have been informed that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

PRINCIPAL SHAREHOLDERS

The following table sets forth information relating to the beneficial ownership of our ordinary shares as of March 31, 2018 by:

- each person, or group of affiliated persons, known by us to own beneficially 3% or more of our outstanding ordinary shares; and
- each member of our board of directors and each of our other executive officers.

The number of ordinary shares beneficially owned by each entity, person, board member, or executive officer is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any shares over which the individual has sole or shared voting power or investment power as well as any shares that the individual has the right to acquire within 60 days of March 31, 2018 through the exercise of any option, warrant or other right. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all ordinary shares held by that person.

The percentage of ordinary shares beneficially owned before the offering is computed on the basis of 71,094,974 ordinary shares outstanding as of March 31, 2018. Ordinary shares that a person has the right to acquire within 60 days of March 31, 2018 are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, except with respect to the percentage ownership of all board members and executive officers as a group. Unless otherwise indicated below, the address for each beneficial owner listed is c/o Mereo BioPharma Group plc, Fourth Floor, One Cavendish Place, London W1G 0QF, United Kingdom.

	Number of Ordinary Shares Beneficially Owned	Percentage of Ordinary Shares Beneficially Owned	
<u>Name and address of beneficial owner</u>	<u>Before Offering</u>	<u>Before Offering</u>	<u>After Offering</u>
3% or Greater Shareholders:			
Woodford Investment Management(1)	29,843,946	42.0%	34.3%
Invesco Asset Management(2)	19,149,176	26.9	22.0
Novartis Pharma AG(3)	13,887,000	19.5	18.0
Hargreave Hale(4)	2,870,000	4.0	3.3
Executive Officers and Directors:			
Denise Scots-Knight, Ph.D.	844,199	1.2	*
Richard Jones	—	—	—
Alastair MacKinnon, MBBS	425,974	*	*
John Richard	249,658	*	*
Charles Sermon	524,504	*	*
Peter Fellner, Ph.D.	10,000	*	*
Frank Armstrong, MBChB	249,658	*	*
Peter Bains	107,906	*	*
Paul Blackburn	22,624	*	*
Anders Ekblom, M.D., Ph.D.	93,002	*	*
Kunal Kashyap	1,497,735	2.1	1.7

* Indicates beneficial ownership of less than 1% of the total outstanding ordinary shares.

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- (1) Consists of (i) 16,853,667 shares of common stock held LF Woodford Equity Income Fund, a sub fund of CF Woodford Investment Fund, or WEIF, (ii) 2,023,636 ordinary shares held by Omnis Income & Growth Fund, a sub fund of Omnis Portfolio Investments ICVC, or OIGF, (iii) 1,070,770 shares held by Old Mutual Woodford Equity Income Fund, or OMWEIF, and (iv) 9,895,873 ordinary shares of common stock held by Woodford Patient Capital Trust, Plc, or WPCT. Woodford Investment Management Limited acts as agent for and on behalf of WEIF, OIGF, OMWEIF, and WPCT, each as a discretionary managed client. Woodford Investment Management Limited has the power to direct the vote and disposition of the common stock held by WEIF, OIGF, OMWEIF and WPCT. Accordingly, Woodford Investment Management Limited may be deemed to be the beneficial owner of these ordinary shares. Neil Woodford is Head of Investments for Woodford Investment Management Limited and may be deemed to share beneficial ownership of these ordinary shares with Woodford Investment Management Limited. Mr. Woodford expressly disclaims beneficial ownership of these shares, except to the extent of any pecuniary interest therein. Beneficial ownership information is based on information known to us and a Form TR 1 provided to us on November 6, 2017. The address of Woodford Investment Management Limited is 9400 Garsington Road, Oxford, OX4 2HN, United Kingdom.
- (2) The share holdings of Invesco Asset Management consist of (i) 13,529,377 ordinary shares beneficially owned by Invesco Perpetual High Income Fund; (ii) 501,678 ordinary shares beneficially owned by Invesco Perpetual Income Fund; and (iii) 5,118,121 ordinary shares beneficially owned by Invesco Perpetual UK Growth Fund. Beneficial ownership information is based on information known to us and a Form TR 1 provided to us on April 28, 2017. The address of Invesco Asset Management Limited is 30 Finsbury Square, London EC2A 1AG, United Kingdom.
- (3) Consists of 13,767,841 ordinary shares held by Novartis Pharma AG ("Novartis") and 119,159 ordinary shares that Novartis is able to acquire pursuant to the Novartis Notes within 60 days of March 31, 2018 before the offering. Under the terms of the Novartis Notes, Novartis may only convert its notes into our ordinary shares if, following such conversion, it owns no more than 19.5% of the aggregate voting power of our company. As a result after giving effect to the offering, Novartis is able to acquire up to an additional 1,777,242 ordinary shares pursuant to the Novartis Notes within 60 days of March 31, 2018. Novartis AG is the publicly owned parent company of Novartis and may be deemed to beneficially own the ordinary shares held by Novartis. Beneficial ownership information is based on information known to us and a Form TR 1 provided to us on April 28, 2017. The address of Novartis AG is Lichtstrasse 35, 4056 Basel, Switzerland.
- (4) Consists of 1,250,000 ordinary shares held by Marlborough Special Situations Fund and 1,620,000 ordinary shares held by Marlborough UK Micro Cap Growth Fund, for which Hargreave Hale acts as manager. Beneficial ownership information is based on information known to us.

To our knowledge, and other than changes in percentage ownership as a result of the shares issued in connection with our initial public offering in the United Kingdom, there has been no significant change in the percentage ownership held by the major shareholders listed above in the last three years, except as discussed under the heading "Related Party Transactions."

RELATED PARTY TRANSACTIONS

The following is a description of related party transactions we have entered into with the beneficial owners of 3% or more of our ordinary shares, which are our only voting securities, and senior management and members of our board of directors, since our incorporation.

Subscription Agreement

On July 28, 2015, we entered into a subscription agreement for ordinary shares, or the Subscription Agreement, with Invesco Perpetual High Income Fund, Woodford Patient Capital Trust plc and LF Woodford Equity Income Fund, or, collectively, the Existing Investors, and Novartis. Under the Subscription Agreement, we initially issued 10,869,566 ordinary shares to the Existing Investors at a price per ordinary share of £1.84 for total aggregate cash proceeds of £20.0 million, and 3,849,000 ordinary shares to Novartis in connection with the asset purchase agreements described under “—Other Transactions with Novartis.”

The Subscription Agreement provided for us to draw down additional investments from the Existing Investors. The Subscription Agreement also obligated us, upon the issuance of additional ordinary shares, to issue to Novartis the number of ordinary shares required to maintain Novartis’ percentage ownership of us at 19.5%, with the maximum aggregate number of ordinary shares that may be issued to Novartis under the Subscription Agreement set at 14,000,000. On June 9, 2016, we issued an additional 30,727,361 ordinary shares to the Existing Investors pursuant to the drawdown and 8,697,480 ordinary shares to Novartis to maintain its percentage ownership following the drawdown and an additional private placement of our ordinary shares, for aggregate cash proceeds to us of £72.6 million. In accordance with its terms, the Subscription Agreement was terminated upon the admission of our ordinary shares to trading on AIM on June 9, 2016. In lieu of the remaining ordinary shares that we were obligated to issue to Novartis under the Subscription Agreement, Novartis is entitled to receive additional shares upon conversion of the convertible notes issued to Novartis on June 3, 2016. See “—Other Transactions with Novartis—Novartis Notes.”

Other Transactions with Novartis

On July 28, 2015, we entered into asset purchase agreements with Novartis to purchase each of BPS-804, BCT-197, and BGS-649. See “Business—Material Agreements—Novartis Agreements.” As consideration, we issued 3,849,000 ordinary shares to Novartis.

Novartis Notes

On June 3, 2016, we issued 3,463,563 Novartis Notes to Novartis, for aggregate proceeds to us of £3.5 million. The Novartis Notes bear interest at 4% per annum and accruing daily. Novartis may at any time convert all or some of the Novartis Notes into our ordinary shares at a conversion price of £2.21 per ordinary share as long as, following such conversion, Novartis holds no more than 19.5% of the aggregate voting rights of our company. In addition, upon the conversion of any Novartis Notes, Novartis is entitled to receive a number of Bonus Shares equal to the number of shares into which such Novartis Notes are converted multiplied by 0.93, up to 1,453,520 Bonus Shares in aggregate. To the extent any of the Novartis Notes remain outstanding on March 2, 2021, we are obligated to pay Novartis the principal amount of such outstanding Novartis Notes together with any accrued interest.

On April 6, 2017, Novartis delivered to us a notice of conversion with respect to £1,398,552 aggregate principal amount of Novartis Notes. Pursuant to such notice, on April 26, 2017, £1,398,552 aggregate principal amount of Novartis Notes was converted into 632,829 fully paid ordinary shares. Additionally, in connection with such conversion, we issued 588,532 Bonus Shares to Novartis.

As of the date of this prospectus, the outstanding principal and accrued interest of the Novartis Notes is £2,267,883.

Supply Payments

In 2016, we paid Novartis a total of £968,219. In 2017, we paid Novartis a total of £4,610,106 for the manufacture and supply of clinical trial material.

Novartis Board Observer Rights

Pursuant to our Articles of Association, for as long as Novartis holds not less than one percent of our issued share capital, Novartis may appoint one observer who may attend, but not participate or vote in, any meeting of our board of directors.

Transactions with Our Executive Officers and Directors

Frank Armstrong, a member of our board of directors, is a director of Dr. Frank M Armstrong Consulting Ltd., or Armstrong Consulting. In 2015, we paid Armstrong Consulting a total of £120,412 for assistance with diligence activities, advisory services and reimbursement of travel costs.

Dr. Denise Scots-Knight, Dr. Alastair MacKinnon, Charles Sermon, John Richard, Kunal Kashyap, and Peter Bains are directors of Phase4. In 2015, we paid Phase4 a total of £458,359 for reimbursement of pre-establishment third-party consultancy services and for office and travel costs.

We have entered into employment agreements or consultancy agreements with certain of our executive officers. See “Management—Compensation—Executive Officer Employment and Consultancy Agreements.”

Indemnity Agreements

We have entered into deeds of indemnity with each of our directors and we expect to enter into a new deed of indemnity with each of our directors and executive officers in connection with the global offering. See “Management—Insurance and Indemnification.”

Related Person Transaction Policy

Our board of directors has adopted a written related person transaction policy, to be effective immediately upon the effectiveness of the registration statement of which this prospectus forms a part, setting forth the policies and procedures for the review and approval or ratification of related person transactions. This policy will cover, any transaction or proposed transactions between us and a related person that are material to us or the related person, including without limitation, purchases of goods or services by or from the related person or entities in which the related person has a material interest, indebtedness, guarantees of indebtedness and employment by us of a related person. In reviewing and approving any such transactions, our audit and risk committee is tasked to consider all relevant facts and circumstances, including, but not limited to, whether the transaction is on terms comparable to those that could be obtained in an arm's length transaction and the extent of the related person's interest in the transaction. All of the transactions described in this section occurred prior to the adoption of this policy.

DESCRIPTION OF SHARE CAPITAL AND ARTICLES OF ASSOCIATION

General

We were incorporated as a private limited company with the legal name Mereo BioPharma Group Limited under the laws of England and Wales on March 10, 2015 with the company number 09481161. On June 3, 2016, we were re-registered as a public limited company with the legal name Mereo BioPharma Group plc. Our registered office is 4th Floor, One Cavendish Place, London, W1G 0QF, United Kingdom. The principal legislation under which we operate and our ordinary shares are issued is the U.K. Companies Act 2006.

Share Capital

As of March 31, 2018, our issued share capital was £213,285. The nominal value of our ordinary shares is £0.003 per ordinary share. Each issued ordinary share is fully paid.

Options

As of March 31, 2018, there were options to purchase 11,916,424 ordinary shares outstanding with a weighted average exercise price of £1.42 per ordinary share. The options generally lapse after 10 years from the date of the grant.

Novartis Notes

On June 3, 2016, we issued 3,463,563 Novartis Notes to Novartis. As of the date of this prospectus, the outstanding principal and accrued interest on the Novartis Notes was £2,267,883, which may be converted into 1,026,191 ordinary shares at a conversion price of £2.21 per ordinary share at any time until they mature. In connection with any such conversion, we are also obligated to issue a number of Bonus Shares equal to the number of shares into which the Novartis Notes are converted multiplied by 0.93, up to a maximum of 1,453,520 Bonus Shares. To date, we have issued 588,532 Bonus Shares. The Novartis Notes mature on March 2, 2021, at which time we will be obligated to pay any outstanding principal together with any accrued interest.

Ordinary Shares

The following summarizes the rights of holders of our ordinary shares:

- each holder of our ordinary shares is entitled to one vote per ordinary share at a meeting of shareholders (provided that certain shareholders each have their votes on a poll limited to 19.5% of the total voting share capital and any votes which would have otherwise been exercisable by them shall be deemed to be held and exercisable by the other shareholders, other than those and certain other shareholders, on a pro rata basis);
- the holders of the ordinary shares shall be entitled to receive notice of, attend, speak, and vote at our general meetings; and
- holders of our ordinary shares are entitled to receive such dividends as are recommended by our directors and declared by our shareholders.

Registered Shares

We are required by the U.K. Companies Act 2006 to keep a register of our shareholders. Under English law, the ordinary shares are deemed to be issued when the name of the shareholder is entered in our share register. The share register therefore is prima facie evidence of the identity of our shareholders, and the shares that they hold. The share register generally provides limited, or no, information regarding the ultimate beneficial owners of our ordinary shares. Our share register is maintained by our registrar, Link Asset Services.

Holders of our ADSs will not be treated as shareholders and their names will therefore not be entered in our share register. The depositary, the custodian or their nominees will be the holder of the ordinary shares underlying our ADSs. For discussion on our ADSs and ADS holder rights see “Description of American Depositary Shares” in this prospectus. Holders of our ADSs have a right to receive the ordinary shares underlying their ADSs as discussed in “Description of American Depositary Shares” in this prospectus.

Under the U.K. Companies Act 2006, we must enter an allotment of ordinary shares in our share register as soon as practicable and in any event within two months of the allotment. We will perform all procedures necessary to update the share register to reflect the ordinary shares being sold in the global offering, including updating the share register with the number of ordinary shares to be issued to the depositary upon the closing of the U.S. offering. We also are required by the U.K. Companies Act 2006 to register a transfer of ordinary shares (or give the transferee notice of and reasons for refusal) as soon as practicable and in any event within two months of receiving notice of the transfer.

We, any of our shareholders or any other affected person may apply to the court for rectification of the share register if:

- the name of any person, without sufficient cause, is wrongly entered in or omitted from our register of members; or
- there is a default or unnecessary delay in entering on the register the fact of any person having ceased to be a member or on which we have a lien, provided that such refusal does not prevent dealings in the shares taking place on an open and proper basis.

Preemptive Rights

English law generally provides shareholders with preemptive rights when new shares are issued for cash; however, it is possible for the articles of association, or shareholders in a general meeting, to exclude preemptive rights. Such an exclusion of preemptive rights may be for a maximum period of up to five years from the date of adoption of the articles of association, if the exclusion is contained in the articles of association, or from the date of the shareholder resolution, if the exclusion is by shareholder resolution. In either case, this exclusion would need to be renewed by our shareholders upon its expiration (i.e., at least every five years). On June 2, 2016, our shareholders approved the exclusion of preemptive rights for a period of five years from the date of the approval in respect of the allotment of up to a maximum amount of £350,000 of ordinary shares of £0.003 each, which exclusion will need to be renewed upon expiration (i.e., at least every five years) to remain effective, but may be sought more frequently for additional five-year terms (or any shorter period).

Articles of Association

The following is a description of our Articles of Association.

Shares and Rights Attaching to Them

Objects

The objects of our company are unrestricted.

Share Rights

Subject to any special rights attaching to shares already in issue, our shares may be issued with or have attached to them any rights or restrictions as we may resolve by ordinary resolution of the shareholders or failing such determination, as the board may determine.

Voting Rights

Without prejudice to any special rights, privileges or restrictions as to voting rights attached to any shares forming part of our share capital from time to time, the voting rights attaching to shares are as follows:

- on a show of hands, every shareholder who (being an individual) is present in person and (being a corporation) is present by a duly authorized representative shall have one vote;
- on a show of hands, each proxy present in person has one vote for and one vote against a resolution if the proxy has been duly appointed by more than one shareholder and the proxy has been instructed by one or more of those shareholders to vote for the resolution and by one or more other of those shareholders to vote against it;
- on a show of hands, each proxy present in person has one vote for and one vote against a resolution if the proxy has been duly appointed by more than one shareholder entitled to vote on the resolution and either: (1) the proxy has been instructed by one or more of those shareholders to vote for the resolution and has been given any discretion by one or more other of those shareholders to vote and the proxy exercises that discretion to vote against it; or (2) the proxy has been instructed by one or more of those shareholders to vote against the resolution and has been given any discretion by one or more other of those shareholders to vote and the proxy exercises that discretion to vote for it; or
- on a poll every shareholder who is present in person or by proxy shall have one vote for each share of which he is the holder, provided that certain shareholders each have their votes limited to 19.5% of the total voting share capital and any votes which would have otherwise been exercisable by them shall be deemed to be held and exercisable by the other shareholders, other than those and certain other shareholders, on a pro rata basis.

At any general meeting a resolution put to the vote of the meeting shall be decided on a show of hands unless a poll is demanded. Subject to the provisions of the U.K. Companies Act 2006, as described in "Differences in Corporate Law—Voting Rights" in this prospectus, a poll may be demanded by:

- the chairman of the meeting;
- the directors;
- two or more persons having the right to vote on the resolution; or
- a person or persons representing not less than 10% of the total voting rights of all shareholders having the right to vote on the resolution.

Restrictions on Voting

No shareholder shall be entitled to vote at any general meeting in respect of any share held by him unless all sums payable by him in respect of that share have been paid.

The board may from time to time make calls upon the shareholders in respect of any money unpaid on their shares and each shareholder shall (subject to at least 14 days' notice specifying when and how the payment is to be made) pay at the time or times so specified the amount called on his shares.

Dividends

We may by ordinary resolution of shareholders declare dividends out of profits available for distribution in accordance with the respective rights of shareholders but no such dividend shall exceed the amount recommended by the directors. The board may from time to time pay shareholders such interim dividends as appear to the board to be justified by our financial position but, if at any time, our share capital is divided into different classes the board may not pay such interim dividends in respect of those shares which confer on the holders thereof deferred or non-preferential rights with regard to dividends if, at the time of payment, any preferential dividend is in arrears.

Subject to any special rights attaching to or the terms of issue of any share, all dividends shall be declared and paid according to the amounts paid up on the shares and shall be apportioned and paid pro rata according to the amounts paid up on the shares during any part or parts of the period in respect of which the dividend is paid.

No dividend or other moneys payable by us on or in respect of any share shall bear interest against us unless otherwise provided by the rights attached to the share or the provisions of another agreement between the shareholder and us. Any dividend unclaimed after a period of 12 years from the date such dividend became due for payment shall be forfeited and cease to remain owing.

Dividends may be declared or paid in any currency and the board may decide the rate of exchange for any currency conversions that may be required, and how any costs involved are to be met, in relation to the currency of any dividend.

Any general meeting declaring a dividend may by ordinary resolution of shareholders, upon the recommendation of the board, direct payment or satisfaction of such dividend wholly or in part by the distribution of non-cash assets of equivalent value, including shares or other securities in any company.

The directors may, if authorized by an ordinary resolution of shareholders, offer any holders of ordinary shares the right to elect to receive in lieu of a dividend, or part of a dividend, an allotment of ordinary shares credited as fully paid up.

Change of Control

There is no specific provision in our Articles that would have the effect of delaying, deferring, or preventing a change of control.

Distributions on Winding Up

If we are in liquidation, the liquidator may, if authorized by a special resolution of shareholders and any other authority required at law, divide among shareholders (excluding us to the extent we are a shareholder by virtue only of holding treasury shares) in specie or in kind the whole or any part of our assets (whether or not the assets consist of property of one kind or consist of properties of different kinds and the liquidator may for such purpose set such value as the liquidator deems fair upon any one or more class or classes of property and may determine how such division shall be carried out as between the shareholders or different classes of shareholders), or vest the whole or any part of such assets in trustees upon such trusts for the benefit of the shareholders as the liquidator determines (and the liquidation of the Company may be closed and the Company dissolved), but no shareholder shall be compelled to accept any shares or other assets upon which there is any liability or potential liability.

Variation of Rights

All or any of the rights and privileges attached to any class of shares issued may be varied or abrogated only with the consent in writing of the holders of not less than three-fourths in nominal value of the issued shares of that class (excluding any shares held as treasury shares) or by special resolution passed at a separate general meeting of the holders of such shares, subject to the other provisions of the U.K. Companies Act 2006 and the terms of their issue. The U.K. Companies Act 2006 also provides a right to object to the variation of the share capital by the shareholders who did not vote in favor of the variation. Should 15% or more of the shareholders of the issued shares in question apply to the court to have the variation cancelled, the variation shall have no effect unless and until it is confirmed by the court.

Alteration to Share Capital

We may, by ordinary resolution of shareholders, consolidate all or any of our share capital into shares of larger amount than our existing shares, or sub-divide our shares or any of them into shares of a smaller amount. We may, by special resolution of shareholders, confirmed by the court, reduce our

share capital or any capital redemption reserve or any share premium account in any manner authorized by the U.K. Companies Act 2006. We may redeem or purchase all or any of our shares as described in “—Other U.K. Law Considerations—Purchase of Own Shares.”

Preemption Rights

In certain circumstances, our shareholders may have statutory preemption rights under the U.K. Companies Act 2006 in respect of the allotment of new shares as described in “—Preemptive Rights” and “—Differences in Corporate Law—Pre-emptive Rights” in this prospectus.

Transfer of Shares

Any shareholder holding shares in certificated form may transfer all or any of his shares by an instrument of transfer in any usual form or any other form approved by the board. Any written instrument of transfer shall be signed by or on behalf of the transferor and (in the case of a partly paid share) the transferee.

In the case of uncertificated shares, the directors may take such action as they consider appropriate to achieve a transfer. The Uncertificated Securities Regulations 2001 permit shares to be issued and held in uncertificated form and transferred by means of a computer based system.

The board may decline to register any transfer of any share:

- which is not a fully paid share;
- where the transfer is not lodged at our registered office or such other place as the directors have appointed;
- where the transfer is not accompanied by the share certificate to which it relates, or such other evidence as the board may reasonably require to show the transferor's right to make the transfer, or evidence of the right of someone other than the transferor to make the transfer on the transferor's behalf;
- where the transfer is in respect of more than one class of share; and
- where the number of joint holders to whom the share is to be transferred exceeds four.

If the board declines to register a transfer, it must return to the transferee the instrument of transfer together with notice of the refusal, unless the board suspects that the proposed transfer may be fraudulent.

CREST

To be traded on AIM, securities must be able to be transferred and settled through the CREST system. CREST is a computerized paperless share transfer and settlement system which allows securities to be transferred by electronic means, without the need for a written instrument of transfer. The Articles are consistent with CREST membership and, amongst other things, allow for the holding and transfer of shares in uncertificated form.

Shareholder Meetings

Annual General Meetings

In accordance with the U.K. Companies Act 2006, we are required in each year to hold an annual general meeting in addition to any other general meetings in that year and to specify the meeting as such in the notice convening it. The annual general meeting shall be convened whenever and wherever the board sees fit, subject to the requirements of the U.K. Companies Act 2006, as described in “—Differences in Corporate Law—Annual General Meeting” and “—Differences in Corporate Law—Notice of General Meetings” in this prospectus.

Notice of General Meetings

The arrangements for the calling of general meetings are described in “—Differences in Corporate Law—Notice of General Meetings” in this prospectus.

Quorum of General Meetings

No business shall be transacted at any general meeting unless a quorum is present. At least two shareholders present in person or by proxy and entitled to vote shall be a quorum for all purposes.

Class Meetings

The provisions in the Articles relating to general meetings apply to every separate general meeting of the holders of a class of shares.

Directors

Number of Directors

We may not have less than two directors on the board of directors and not more than nine. We may, by ordinary resolution of the shareholders, vary the minimum and maximum number of directors from time to time.

Appointment of Directors

Subject to the provisions of the Articles, we may, by ordinary resolution of the shareholders or a decision of the directors, elect any person to be a director, either to fill a casual vacancy or as an addition to the existing board, provided the total number of directors does not exceed the maximum number fixed by or in accordance with the Articles. However, any person that is not a director retiring from the existing board must be recommended by the board or the person must have confirmed in writing to the Company their willingness to be elected as a director not later than seven days before the general meeting at which the relevant resolution is proposed.

Any director appointed by the board will hold office only until the next following annual general meeting at which they must retire. In addition, all directors must retire at the third annual general meeting following the annual general meeting at which such director was elected or last re-elected. Such directors are eligible for re-election at the annual general meeting at which they retire

The shareholders may, at the meeting at which a director retires, fill the vacated office by electing a person and in default the retiring director shall, if willing to continue to act, be deemed to have been re-elected, unless at such meeting it is expressly resolved not to fill such vacated office or unless a resolution for the re-election of such director shall have been put to the meeting and lost.

Directors' Interests

If a situation arises in which a director has, or can have, a direct or indirect interest that conflicts, or possibly may conflict, with our interests (other than a situation that cannot reasonably be regarded as likely to give rise to a conflict of interest or a conflict of interest arising in relation to a transaction or arrangement with the Company), the board may authorize in accordance with the U.K. Companies Act 2006 the director's interest and the continuing performance by the relevant director of his duties as a director on such terms as the board may determine.

A director shall not be accountable to us for any benefit which he derives from or in connection with a relationship involving a conflict of interest or possible conflict of interest which has been authorized by the directors or by the Company in a general meeting and any such transaction or arrangement shall not be liable to be avoided on the grounds of any such benefit.

Subject to the requirements under sections 175, 177 and 182 of the U.K. Companies Act 2006, a director shall declare the nature and extent of such conflicts.

A director may participate in the decision-making process and count in the quorum and vote on a proposed decision of the board which is concerned with such director's interests (subject to any restrictions imposed by the other directors when providing such consent) if such director has declared the nature and extent of any interest of his and provided a majority of the other directors consent, or if one of the following situations applies:

- the director's interest arises solely through an interest in shares, debentures or other securities of or otherwise in or through the Company;
- an ordinary resolution of the Company permits the director to count in the quorum and vote on the proposed decision;
- the director's interest cannot reasonably be regarded as likely to give rise to a material conflict of interest;
- the conflict of interest arises from one of the following:
 - a guarantee, security or indemnity given, or to be given, by or to the director in respect of an obligation incurred by or on behalf of the Company or any of its subsidiaries;
 - a subscription, or agreement to subscribe, for shares or other securities of the Company or any of its subsidiaries, or to underwrite, sub-underwrite or guarantee an offer of any such shares or securities by the Company or any of its subsidiaries for subscription, purchase or exchange;
 - arrangements pursuant to which benefits are made available to employees and directors, or former employees and directors, of the Company or any of its subsidiaries which do not provide special benefits for directors or former directors;
 - the purchase or maintenance of insurance which the Company is empowered to purchase or maintain for directors or officers;
 - the giving to the director of an indemnity against liabilities incurred or to be incurred by the director in the execution and discharge of his duties;
 - the provision of funds to the director to meet expenditure incurred or to be incurred by the director in defending criminal or civil proceedings against him or in connection with any application under certain provisions of the U.K. Companies Act 2006 or otherwise enabling him to avoid incurring that expenditure; or
 - proposals concerning another company in which the director is interested directly or indirectly (whether as officer, shareholder or otherwise), if the director and any other persons connected with him do not to his knowledge hold an interest in shares representing 1% or more of the issued shares of any class of the equity share capital of that company (or of any third company through which his or their interest is derived) or of the voting rights available to shareholders of the relevant company.

A director shall not be counted in the quorum present at a meeting in relation to a resolution on which he is not entitled to vote.

If a question arises at a meeting of the board or of a committee of the board as to the right of a director to vote or be counted in the quorum, and such question is not resolved by his voluntarily agreeing to abstain from voting, the question shall be determined by a resolution of the board or such committee (with such director being excluded from voting on the resolution).

Directors' Fees and Remuneration

Each of the directors is entitled to remuneration as determined by the board for their service as directors and other services undertaken for the Company.

Each director may be paid his reasonable expenses in connection with such director's attendance at meetings of the board or committees of the board or general meetings or separate meetings of the holders class of shares or of debentures, or otherwise in connection with the exercise of powers and the discharge of responsibilities in relation to the Company.

Indemnity

Every director, officer or former director or officer of our group may be indemnified against all costs, charges, losses, expenses and liabilities incurred by him in connection with any negligence, default, breach of duty, or breach of trust by him in relation to us or in connection with our activities as a trustee of an occupational pension scheme, in the actual or purported exercise of his powers or duties or otherwise as our officer, to the extent permitted under the U.K. Companies Act 2006.

Novartis Observer

For as long as Novartis holds not less than one percent of our issued share capital, Novartis may appoint one observer who may attend, but not participate or vote in, any meeting of our board of directors.

Other U.K. Law Considerations

Notification of Voting Rights

A shareholder in a public company incorporated in the United Kingdom whose shares are admitted to trading on AIM is required pursuant to Chapter 5 of the Disclosure Guidance and Transparency Rules of the U.K. Financial Conduct Authority to notify us of the percentage of his voting rights if the percentage of voting rights which he holds as a shareholder or through his direct or indirect holding of financial instruments (or a combination of such holdings) reaches, exceeds, or falls below 3%, 4%, 5%, and each 1% threshold thereafter up to 100% as a result of an acquisition or disposal of shares or financial instruments.

Mandatory Purchases and Acquisitions

Pursuant to Sections 979 to 991 of the U.K. Companies Act 2006, where a takeover offer has been made for us and the offeror has acquired or unconditionally contracted to acquire not less than 90% in value of the shares to which the offer relates and not less than 90% of the voting rights carried by those shares, the offeror may give notice to the holder of any shares to which the offer relates which the offeror has not acquired or unconditionally contracted to acquire that he wishes to acquire, and is entitled to so acquire, those shares on the same terms as the general offer. The offeror would do so by sending a notice to the outstanding minority shareholders telling them that it will compulsorily acquire their shares. Such notice must be sent within three months of the last day on which the offer can be accepted in the prescribed manner. The squeeze-out of the minority shareholders can be completed at the end of six weeks from the date the notice has been given, subject to the minority shareholders failing to successfully lodge an application to the court to prevent such squeeze-out any time prior to the end of those six weeks following which the offeror can execute a transfer of the outstanding shares in its favor and pay the consideration to us, which would hold the consideration on trust for the outstanding minority shareholders. The consideration offered to the outstanding minority shareholders whose shares are compulsorily acquired under the U.K. Companies Act 2006 must, in general, be the same as the consideration that was available under the takeover offer.

Sell Out

The U.K. Companies Act 2006 also gives our minority shareholders a right to be bought out in certain circumstances by an offeror who has made a takeover offer for all of our shares. The holder of shares to which the offer relates, and who has not otherwise accepted the offer, may require the offeror to acquire his shares if, prior to the expiry of the acceptance period for such offer, (i) the offeror has acquired or unconditionally agreed to acquire not less than 90% in value of the voting shares, and (ii) not less than 90% of the voting rights carried by those shares. The offeror may impose a time limit on the rights of minority shareholders to be bought out that is not less than three months after the end

of the acceptance period. If a shareholder exercises his rights to be bought out, the offeror is required to acquire those shares on the terms of this offer or on such other terms as may be agreed.

Disclosure of Interest in Shares

Pursuant to Part 22 of the U.K. Companies Act 2006, we are empowered to give notice in writing to any person whom we know or have reasonable cause to believe to be interested in our shares, or to have been so interested at any time during the three years immediately preceding the date on which the notice is issued requiring such persons, within a reasonable time to disclose to us particulars of that person's interest and (so far as is within his knowledge) particulars of any other interest that subsists or subsisted in those shares.

Under our Articles, if a person defaults in supplying us with the required particulars in relation to the shares in question, or default shares, within the prescribed period, the directors may by notice direct that:

- in respect of the default shares, the relevant shareholder shall not be entitled to vote (either in person or by proxy) at any general meeting or to exercise any other right conferred by a shareholding in relation to general meetings;
- where the default shares represent at least 0.25% of their class, (a) any dividend or other money payable in respect of the default shares shall be retained by us without liability to pay interest and/or (b) no transfers by the relevant shareholder of any default shares may be registered (unless the shareholder himself is not in default and the shareholder provides a certificate, in a form satisfactory to the directors, to the effect that after due and careful enquiry the shareholder is satisfied that none of the shares to be transferred are default shares); and
- any shares held by the relevant shareholder in uncertificated form shall be converted into certificated form and that shareholder shall not after that be entitled to convert all or any shares held by him into uncertificated form (except with the authority of the directors) unless the shareholder himself is not in default and the shares which the shareholder wishes to convert are part only of the shareholder's holding and the shareholder provides a certificate, in a form satisfactory to the directors, to the effect that after due and careful enquiry the shareholder is satisfied that none of the shares to be converted into uncertificated form are default shares.

Purchase of Own Shares

Under English law, a limited company may only purchase its own shares out of the distributable profits of the company or the proceeds of a fresh issue of shares made for the purpose of financing the purchase, provided that they are not restricted from doing so by their articles. A limited company may not purchase its own shares if, as a result of the purchase, there would no longer be any issued shares of the company other than redeemable shares or shares held as treasury shares. Shares must be fully paid in order to be repurchased.

Subject to the above, we may purchase our own shares in the manner prescribed below. We may make a market purchase of our own fully paid shares pursuant to an ordinary resolution of shareholders. The resolution authorizing the purchase must:

- specify the maximum number of shares authorized to be acquired;
- determine the maximum and minimum prices that may be paid for the shares; and
- specify a date, not being later than five years after the passing of the resolution, on which the authority to purchase is to expire.

We may purchase our own fully paid shares otherwise than on a recognized investment exchange pursuant to a purchase contract authorized by resolution of shareholders before the purchase takes place. Any authority will not be effective if any shareholder from whom we propose to purchase shares

votes on the resolution and the resolution would not have been passed if he had not done so. The resolution authorizing the purchase must specify a date, not being later than five years after the passing of the resolution, on which the authority to purchase is to expire.

Distributions and Dividends

Under the U.K. Companies Act 2006, before a company can lawfully make a distribution or dividend, it must ensure that it has sufficient distributable reserves (on a non-consolidated basis). The basic rule is that a company's profits available for the purpose of making a distribution are its accumulated, realized profits, so far as not previously utilized by distribution or capitalization, less its accumulated, realized losses, so far as not previously written off in a reduction or reorganization of capital duly made. The requirement to have sufficient distributable reserves before a distribution or dividend can be paid applies to us and to each of our subsidiaries that has been incorporated under English law.

It is not sufficient that we, as a public company, have made a distributable profit for the purpose of making a distribution. An additional capital maintenance requirement is imposed on us to ensure that the net worth of the company is at least equal to the amount of its capital. A public company can only make a distribution:

- if, at the time that the distribution is made, the amount of its net assets (that is, the total excess of assets over liabilities) is not less than the total of its called up share capital and undistributable reserves; and
- if, and to the extent that, the distribution itself, at the time that it is made, does not reduce the amount of the net assets to less than that total.

City Code on Takeovers and Mergers

As a public company incorporated in England and Wales with our registered office in England and Wales which has shares admitted to AIM, we are subject to the U.K. City Code on Takeovers and Mergers, or the City Code, which is issued and administered by the U.K. Panel on Takeovers and Mergers, or the Panel. The City Code provides a framework within which takeovers of companies subject to it are conducted. In particular, the City Code contains certain rules in respect of mandatory offers. Under Rule 9 of the City Code, if a person:

- acquires an interest in our shares which, when taken together with shares in which he or persons acting in concert with him are interested, carries 30% or more of the voting rights of our shares; or
- who, together with persons acting in concert with him, is interested in shares that in the aggregate carry not less than 30% and not more than 50% of the voting rights of our shares, and such persons, or any person acting in concert with him, acquires additional interests in shares that increase the percentage of shares carrying voting rights in which that person is interested,

the acquirer and depending on the circumstances, its concert parties, would be required (except with the consent of the Panel) to make a cash offer for our outstanding shares at a price not less than the highest price paid for any interests in the shares by the acquirer or its concert parties during the previous 12 months.

Exchange Controls

There are no governmental laws, decrees, regulations or other legislation in the United Kingdom that may affect the import or export of capital, including the availability of cash and cash equivalents for use by us, or that may affect the remittance of dividends, interest, or other payments by us to non-resident holders of our ordinary shares or ADSs, other than withholding tax requirements. There is no limitation imposed by English law or in the Articles on the right of non-residents to hold or vote shares.

Differences in Corporate Law

The applicable provisions of the U.K. Companies Act 2006 differ from laws applicable to U.S. corporations and their shareholders. Set forth below is a summary of certain differences between the provisions of the U.K. Companies Act 2006 applicable to us and the General Corporation Law of the State of Delaware relating to shareholders' rights and protections. This summary is not intended to be a complete discussion of the respective rights and it is qualified in its entirety by reference to Delaware law and English law.

	England and Wales	Delaware
Number of Directors	Under the U.K. Companies Act 2006, a public limited company must have at least two directors and the number of directors may be fixed by or in the manner provided in a company's articles of association.	Under Delaware law, a corporation must have at least one director and the number of directors shall be fixed by or in the manner provided in the bylaws.
Removal of Directors	Under the U.K. Companies Act 2006, shareholders may remove a director without cause by an ordinary resolution (which is passed by a simple majority of those voting in person or by proxy at a general meeting) irrespective of any provisions of any service contract the director has with the company, provided 28 clear days' notice of the resolution has been given to the company and its shareholders. On receipt of notice of an intended resolution to remove a director, the company must forthwith send a copy of the notice to the director concerned. Certain other procedural requirements under the U.K. Companies Act 2006 must also be followed such as allowing the director to make representations against his or her removal either at the meeting or in writing.	Under Delaware law, any director or the entire board of directors may be removed, with or without cause, by the holders of a majority of the shares then entitled to vote at an election of directors, except (a) unless the certificate of incorporation provides otherwise, in the case of a corporation whose board of directors is classified, shareholders may effect such removal only for cause, or (b) in the case of a corporation having cumulative voting, if less than the entire board of directors is to be removed, no director may be removed without cause if the votes cast against his removal would be sufficient to elect him if then cumulatively voted at an election of the entire board of directors, or, if there are classes of directors, at an election of the class of directors of which he is a part.
Vacancies on the Board of Directors	Under English law, the procedure by which directors, other than a company's initial directors, are appointed is generally set out in a company's articles of association, provided that where two or more persons are appointed as directors of a public limited company by resolution of the shareholders, resolutions appointing each director must be voted on individually.	Under Delaware law, vacancies and newly created directorships may be filled by a majority of the directors then in office (even though less than a quorum) or by a sole remaining director unless (a) otherwise provided in the certificate of incorporation or by-laws of the corporation or (b) the certificate of incorporation directs that a particular class of stock is to elect such director, in which case a majority of the other directors elected by such class, or a sole remaining director elected by such class, will fill such vacancy.

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	England and Wales	Delaware
Annual General Meeting	Under the U.K. Companies Act 2006, a public limited company must hold an annual general meeting in each six-month period following the company's annual accounting reference date.	Under Delaware law, the annual meeting of stockholders shall be held at such place, on such date and at such time as may be designated from time to time by the board of directors or as provided in the certificate of incorporation or by the bylaws.
General Meeting	Under the U.K. Companies Act 2006, a general meeting of the shareholders of a public limited company may be called by the directors. Shareholders holding at least 5% of the paid-up capital of the company carrying voting rights at general meetings (excluding any paid up capital held as treasury shares) can require the directors to call a general meeting and, if the directors fail to do so within a certain period, may themselves convene a general meeting.	Under Delaware law, special meetings of the stockholders may be called by the board of directors or by such person or persons as may be authorized by the certificate of incorporation or by the bylaws.
Notice of General Meetings	Under the U.K. Companies Act 2006, 21 clear days' notice must be given for an annual general meeting and any resolutions to be proposed at the meeting. Subject to a company's articles of association providing for a longer period, at least 14 clear days' notice is required for any other general meeting. In addition, certain matters, such as the removal of directors or auditors, require special notice, which is 28 clear days' notice. The shareholders of a company may in all cases consent to a shorter notice period, the proportion of shareholders' consent required being 100% of those entitled to attend and vote in the case of an annual general meeting and, in the case of any other general meeting, a majority in number of the members having a right to attend and vote at the meeting, being a majority who together hold not less than 95% in nominal value of the shares giving a right to attend and vote at the meeting.	Under Delaware law, unless otherwise provided in the certificate of incorporation or bylaws, written notice of any meeting of the stockholders must be given to each stockholder entitled to vote at the meeting not less than ten nor more than 60 days before the date of the meeting and shall specify the place, date, hour, and purpose or purposes of the meeting.

	England and Wales	Delaware
Proxy	Under the U.K. Companies Act 2006, at any meeting of shareholders, a shareholder may designate another person to attend, speak and vote at the meeting on their behalf by proxy.	Under Delaware law, at any meeting of stockholders, a stockholder may designate another person to act for such stockholder by proxy, but no such proxy shall be voted or acted upon after three years from its date, unless the proxy provides for a longer period. A director of a Delaware corporation may not issue a proxy representing the director's voting rights as a director.
Pre-emptive Rights	Under the U.K. Companies Act 2006, "equity securities", being (i) shares in the company other than shares that, with respect to dividends and capital, carry a right to participate only up to a specified amount in a distribution ("ordinary shares") or (ii) rights to subscribe for, or to convert securities into, ordinary shares, proposed to be allotted for cash must be offered first to the existing equity shareholders in the company in proportion to the respective nominal value of their holdings, unless an exception applies or a special resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise in each case in accordance with the provisions of the U.K. Companies Act 2006.	Under Delaware law, shareholders have no preemptive rights to subscribe to additional issues of stock or to any security convertible into such stock unless, and except to the extent that, such rights are expressly provided for in the certificate of incorporation.
Authority to Allot	Under the U.K. Companies Act 2006, the directors of a company must not allot shares or grant of rights to subscribe for or to convert any security into shares unless an exception applies or an ordinary resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise in each case in accordance with the provisions of the U.K. Companies Act 2006.	Under Delaware law, if the corporation's charter or certificate of incorporation so provides, the board of directors has the power to authorize the issuance of stock. It may authorize capital stock to be issued for consideration consisting of cash, any tangible or intangible property or any benefit to the corporation or any combination thereof. It may determine the amount of such consideration by approving a formula. In the absence of actual fraud in the transaction, the judgment of the directors as to the value of such consideration is conclusive.
Liability of Directors and Officers	Under the U.K. Companies Act 2006, any provision, whether contained in a company's articles of association or any contract or otherwise, that purports to exempt a director of a company, to any extent, from any liability that would	Under Delaware law, a corporation's certificate of incorporation may include a provision eliminating or limiting the personal liability of a director to the corporation and its stockholders for damages arising from a breach of

	England and Wales	Delaware
	<p>otherwise attach to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company is void.</p> <p>Any provision by which a company directly or indirectly provides an indemnity, to any extent, for a director of the company or of an associated company against any liability attaching to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company of which he is a director is also void except as permitted by the U.K. Companies Act 2006, which provides exceptions for the company to (a) purchase and maintain insurance against such liability; (b) provide a “qualifying third party indemnity” (being an indemnity against liability incurred by the director to a person other than the company or an associated company or criminal proceedings in which he is convicted); and (c) provide a “qualifying pension scheme indemnity” (being an indemnity against liability incurred in connection with the company’s activities as trustee of an occupational pension plan).</p>	<p>fiduciary duty as a director. However, no provision can limit the liability of a director for:</p> <ul style="list-style-type: none"> any breach of the director’s duty of loyalty to the corporation or its stockholders; acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law; <ul style="list-style-type: none"> intentional or negligent payment of unlawful dividends or stock purchases or redemptions; or any transaction from which the director derives an improper personal benefit.
Voting Rights	<p>Under English law, unless a poll is demanded by the shareholders of a company or is required by the chairman of the meeting or the company’s articles of association, shareholders shall vote on all resolutions on a show of hands. Under the U.K. Companies Act 2006, a poll may be demanded by (a) not fewer than five shareholders having the right to vote on the resolution; (b) any shareholder(s) representing not less than 10% of the total voting rights of all the shareholders having the right to vote on the resolution (excluding any voting rights attaching to treasury shares); or (c) any shareholder(s) holding shares in the company conferring a right to vote on the resolution (excluding any voting rights attaching to treasury shares) being shares on which an aggregate sum has been paid up equal to not less than 10% of the</p>	<p>Delaware law provides that, unless otherwise provided in the certificate of incorporation, each stockholder is entitled to one vote for each share of capital stock held by such stockholder.</p>

	England and Wales	Delaware
	<p>total sum paid up on all the shares conferring that right. A company's articles of association may provide more extensive rights for shareholders to call a poll.</p> <p>Under English law, an ordinary resolution is passed on a show of hands if it is approved by a simple majority (more than 50%) of the votes cast by shareholders present (in person or by proxy) and entitled to vote. If a poll is demanded, an ordinary resolution is passed if it is approved by holders representing a simple majority of the total voting rights of shareholders present, in person or by proxy, who, being entitled to vote, vote on the resolution. Special resolutions require the affirmative vote of not less than 75% of the votes cast by shareholders present (in person or by proxy) at the meeting. If a poll is demanded, a special resolution is passed if it is approved by holders representing not less than 75% of the total voting rights of shareholders present (in person or by proxy) who (being entitled to vote) vote on the resolutions.</p>	
Shareholder Vote on Certain Transactions	<p>The U.K. Companies Act 2006 provides for schemes of arrangement, which are arrangements or compromises between a company and any class of shareholders or creditors and used in certain types of reconstructions, amalgamations, capital reorganizations, or takeovers. These arrangements require:</p> <ul style="list-style-type: none"> the approval at a shareholders' or creditors' meeting convened by order of the court, of a majority in number of shareholders or creditors representing 75% in value of the capital held by, or debt owed to, the class of shareholders or creditors, or class thereof present and voting, either in person or by proxy; and the approval of the court. 	<p>Generally, under Delaware law, unless the certificate of incorporation provides for the vote of a larger portion of the stock, completion of a merger, consolidation, sale, lease or exchange of all or substantially all of a corporation's assets or dissolution requires:</p> <ul style="list-style-type: none"> the approval of the board of directors; and approval by the vote of the holders of a majority of the outstanding stock or, if the certificate of incorporation provides for more or less than one vote per share, a majority of the votes of the outstanding stock of a corporation entitled to vote on the matter.

	England and Wales	Delaware
Standard of Conduct for Directors	<p>Under English law, a director owes various statutory and fiduciary duties to the company, including:</p> <ul style="list-style-type: none"> ■ to act in the way he considers, in good faith, would be most likely to promote the success of the company for the benefit of its members as a whole; ■ to avoid a situation in which he has, or can have, a direct or indirect interest that conflicts, or possibly conflicts, with the interests of the company; ■ to act in accordance with the company's constitution and only exercise his powers for the purposes for which they are conferred; <ul style="list-style-type: none"> ■ to exercise independent judgment; ■ to exercise reasonable care, skill, and diligence; ■ not to accept benefits from a third party conferred by reason of his being a director or doing, or not doing, anything as a director; and ■ a duty to declare any interest that he has, whether directly or indirectly, in a proposed or existing transaction or arrangement with the company. 	<p>Delaware law does not contain specific provisions setting forth the standard of conduct of a director. The scope of the fiduciary duties of directors is generally determined by the courts of the State of Delaware. In general, directors have a duty to act without self-interest, on a well-informed basis and in a manner they reasonably believe to be in the best interest of the stockholders.</p> <p>Directors of a Delaware corporation owe fiduciary duties of care and loyalty to the corporation and to its shareholders. The duty of care generally requires that a director act in good faith, with the care that an ordinarily prudent person would exercise under similar circumstances. Under this duty, a director must inform himself of all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director act in a manner he reasonably believes to be in the best interests of the corporation. He must not use his corporate position for personal gain or advantage. In general, but subject to certain exceptions, actions of a director are presumed to have been made on an informed basis, in good faith and in the honest belief that the action taken was in the best interests of the corporation. However, this presumption may be rebutted by evidence of a breach of one of the fiduciary duties. Delaware courts have also imposed a heightened standard of conduct upon directors of a Delaware corporation who take any action designed to defeat a threatened change in control of the corporation.</p> <p>In addition, under Delaware law, when the board of directors of a Delaware corporation approves the sale or break-up of a corporation, the board of directors may, in certain circumstances, have a duty to obtain the highest value reasonably available to the shareholders.</p>

	England and Wales	Delaware
Stockholder Suits	<p>Under English law, generally, the company, rather than its shareholders, is the proper claimant in an action in respect of a wrong done to the company or where there is an irregularity in the company's internal management. Notwithstanding this general position, the U.K. Companies Act 2006 provides that (i) a court may allow a shareholder to bring a derivative claim (that is, an action in respect of and on behalf of the company) in respect of a cause of action arising from a director's negligence, default, breach of duty or breach of trust and (ii) a shareholder may bring a claim for a court order where the company's affairs have been or are being conducted in a manner that is unfairly prejudicial to some of its shareholders.</p>	<p>Under Delaware law, a stockholder may initiate a derivative action to enforce a right of a corporation if the corporation fails to enforce the right itself. The complaint must:</p> <ul style="list-style-type: none">▪ state that the plaintiff was a stockholder at the time of the transaction of which the plaintiff complains or that the plaintiffs shares thereafter devolved on the plaintiff by operation of law; and▪ allege with particularity the efforts made by the plaintiff to obtain the action the plaintiff desires from the directors and the reasons for the plaintiff's failure to obtain the action; or▪ state the reasons for not making the effort. <p>Additionally, the plaintiff must remain a stockholder through the duration of the derivative suit. The action will not be dismissed or compromised without the approval of the Delaware Court of Chancery.</p>

DESCRIPTION OF AMERICAN DEPOSITARY SHARES

American Depositary Shares

Citibank, N.A., or Citibank, has agreed to act as the depositary for the ADSs. Citibank's depositary offices are located at 388 Greenwich Street, New York, New York 10013. ADSs represent ownership interests in securities that are on deposit with the depositary. ADSs may be represented by certificates that are commonly known as American Depositary Receipts, or ADRs. The depositary typically appoints a custodian to safekeep the securities on deposit. In this case, the custodian is Citibank, N.A., London Branch, located at 25 Canada Square, Canary Wharf, London, E14 5LB, United Kingdom.

We have appointed Citibank as depositary pursuant to a deposit agreement. A copy of the deposit agreement will be on file with the SEC under cover of a registration statement on Form F-6. You may obtain a copy of the deposit agreement from the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549 and from the SEC's website (www.sec.gov). Please refer to registration number 333-223883 when retrieving such copy.

We are providing you with a summary description of the material terms of the ADSs and of your material rights as an owner of ADSs. Please remember that summaries by their nature lack the precision of the information summarized and that the rights and obligations of an owner of ADSs will be determined by reference to the terms of the deposit agreement and not by this summary. We urge you to review the deposit agreement in its entirety.

Each ADS represents the right to receive, and to exercise the beneficial ownership interests in, four ordinary shares that are on deposit with the depositary and/or custodian. An ADS also represents the right to receive, and to exercise the beneficial interests in, any other property received by the depositary or the custodian on behalf of the owner of the ADS but that has not been distributed to the owners of ADSs because of legal restrictions or practical considerations. We and the depositary may agree to change the ADS-to-Share ratio by amending the deposit agreement. This amendment may give rise to, or change, the depositary fees payable by ADS owners. The custodian, the depositary and their respective nominees will hold all deposited property for the benefit of the holders and beneficial owners of ADSs. The deposited property does not constitute the proprietary assets of the depositary, the custodian or their nominees. Beneficial ownership in the deposited property will under the terms of the deposit agreement be vested in the beneficial owners of the ADSs. The depositary, the custodian and their respective nominees will be the record holders of the deposited property represented by the ADSs for the benefit of the holders and beneficial owners of the corresponding ADSs. A beneficial owner of ADSs may or may not be the holder of ADSs. Beneficial owners of ADSs will be able to receive, and to exercise beneficial ownership interests in, the deposited property only through the registered holders of the ADSs, the registered holders of the ADSs (on behalf of the applicable ADS owners) only through the depositary, and the depositary (on behalf of the owners of the corresponding ADSs) directly, or indirectly, through the custodian or their respective nominees, in each case upon the terms of the deposit agreement.

If you become an owner of ADSs, you will become a party to the deposit agreement and therefore will be bound to its terms and to the terms of any ADR that represents your ADSs. The deposit agreement and the ADR specify our rights and obligations as well as your rights and obligations as owner of ADSs and those of the depositary. As an ADS holder you appoint the depositary to act on your behalf in certain circumstances. The deposit agreement and the ADRs are governed by New York law. However, our obligations to the holders of ordinary shares will continue to be governed by the laws of England and Wales, which may be different from the laws in the United States.

In addition, applicable laws and regulations may require you to satisfy reporting requirements and obtain regulatory approvals in certain circumstances. You are solely responsible for complying with

such reporting requirements and obtaining such approvals. Neither the depositary, the custodian, us or any of their or our respective agents or affiliates shall be required to take any actions whatsoever on your behalf to satisfy such reporting requirements or obtain such regulatory approvals under applicable laws and regulations.

As an owner of ADSs, we will not treat you as one of our shareholders and you will not have direct shareholder rights. The depositary will hold on your behalf the shareholder rights attached to the ordinary shares underlying your ADSs. As an owner of ADSs you will be able to exercise the shareholders rights for the ordinary shares represented by your ADSs through the depositary only to the extent contemplated in the deposit agreement. To exercise any shareholder rights not contemplated in the deposit agreement you will, as an ADS owner, need to arrange for the cancellation of your ADSs and become a direct shareholder.

As an owner of ADSs, you may hold your ADSs either by means of an ADR registered in your name, through a brokerage or safekeeping account, or through an account established by the depositary in your name reflecting the registration of uncertificated ADSs directly on the books of the depositary (commonly referred to as the direct registration system or DRS). The direct registration system reflects the uncertificated (book-entry) registration of ownership of ADSs by the depositary. Under the direct registration system, ownership of ADSs is evidenced by periodic statements issued by the depositary to the holders of the ADSs. The direct registration system includes automated transfers between the depositary and The Depository Trust Company, or DTC, the central book-entry clearing and settlement system for equity securities in the United States. If you decide to hold your ADSs through your brokerage or safekeeping account, you must rely on the procedures of your broker or bank to assert your rights as ADS owner. Banks and brokers typically hold securities such as the ADSs through clearing and settlement systems such as DTC. The procedures of such clearing and settlement systems may limit your ability to exercise your rights as an owner of ADSs. Please consult with your broker or bank if you have any questions concerning these limitations and procedures. All ADSs held through DTC will be registered in the name of a nominee of DTC. This summary description assumes you have opted to own the ADSs directly by means of an ADS registered in your name and, as such, we will refer to you as the “holder.” When we refer to “you,” we assume the reader owns ADSs and will own ADSs at the relevant time.

The registration of the ordinary shares in the name of the depositary or the custodian shall, to the maximum extent permitted by applicable law, vest in the depositary or the custodian the record ownership in the applicable ordinary shares with the beneficial ownership rights and interests in such ordinary shares being at all times vested with the beneficial owners of the ADSs representing the ordinary shares. The depositary or the custodian shall at all times be entitled to exercise the beneficial ownership rights in all deposited property, in each case only on behalf of the holders and beneficial owners of the ADSs representing the deposited property.

Dividends and Other Distributions

As a holder of ADSs, you generally have the right to receive the distributions we make on the securities deposited with the custodian. Your receipt of these distributions may be limited, however, by practical considerations and legal limitations. Holders of ADSs will receive such distributions under the terms of the deposit agreement in proportion to the number of ADSs held as of the specified record date, after deduction the applicable fees, taxes, and expenses.

Distributions of Cash

Whenever we make a cash distribution for the securities on deposit with the custodian, we will deposit the funds with the custodian. Upon receipt of confirmation of the deposit of the requisite funds, the depositary will arrange for the funds to be converted into U.S. dollars and for the distribution of the U.S. dollars to the holders, subject to the laws and regulations of England and Wales.

The conversion into U.S. dollars will take place only if practicable and if the U.S. dollars are transferable to the United States. The depositary will apply the same method for distributing the proceeds of the sale of any property (such as undistributed rights) held by the custodian in respect of securities on deposit.

The distribution of cash will be made net of the fees, expenses, taxes, and governmental charges payable by holders under the terms of the deposit agreement. The depositary will hold any cash amounts it is unable to distribute in a non-interest bearing account for the benefit of the applicable holders and beneficial owners of ADSs until the distribution can be effected or the funds that the depositary holds must be escheated as unclaimed property in accordance with the laws of the relevant states of the United States.

Distributions of Shares

Whenever we make a free distribution of ordinary shares for the securities on deposit with the custodian, we will deposit the applicable number of ordinary shares with the custodian. Upon receipt of confirmation of such deposit, the depositary will either distribute to holders new ADSs representing the ordinary shares deposited or modify the ADS-to-ordinary shares ratio, in which case each ADS you hold will represent rights and interests in the additional ordinary shares so deposited. Only whole new ADSs will be distributed. Fractional entitlements will be sold and the proceeds of such sale will be distributed as in the case of a cash distribution.

The distribution of new ADSs or the modification of the ADS-to-ordinary shares ratio upon a distribution of ordinary shares will be made net of the fees, expenses, taxes, and governmental charges payable by holders under the terms of the deposit agreement. In order to pay such taxes or governmental charges, the depositary may sell all or a portion of the new ordinary shares so distributed.

No such distribution of new ADSs will be made if it would violate a law (e.g., the U.S. securities laws) or if it is not operationally practicable. If the depositary does not distribute new ADSs as described above, it may sell the ordinary shares received upon the terms described in the deposit agreement and will distribute the proceeds of the sale as in the case of a distribution of cash.

Distributions of Rights

Whenever we intend to distribute rights to purchase additional ordinary shares, we will give prior notice to the depositary and we will assist the depositary in determining whether it is lawful and reasonably practicable to distribute rights to purchase additional ADSs to holders.

The depositary will establish procedures to distribute rights to purchase additional ADSs to holders and to enable such holders to exercise such rights if it is lawful and reasonably practicable to make the rights available to holders of ADSs, and if we provide all of the documentation contemplated in the deposit agreement (such as opinions to address the lawfulness of the transaction). You may have to pay fees, expenses, taxes and other governmental charges to subscribe for the new ADSs upon the exercise of your rights. The depositary is not obligated to establish procedures to facilitate the distribution and exercise by holders of rights to purchase new ordinary shares other than in the form of ADSs.

The depositary will *not* distribute the rights to you if:

- we do not timely request that the rights be distributed to you or we request that the rights not be distributed to you; or
- we fail to deliver satisfactory documents to the depositary; or
- it is not reasonably practicable to distribute the rights.

The depositary will sell the rights that are not exercised or not distributed if such sale is lawful and reasonably practicable. The proceeds of such sale will be distributed to holders as in the case of a cash distribution. If the depositary is unable to sell the rights, it will allow the rights to lapse.

Elective Distributions

Whenever we intend to distribute a dividend payable at the election of shareholders either in cash or in additional shares, we will give prior notice thereof to the depositary and will indicate whether we wish the elective distribution to be made available to you. In such case, we will assist the depositary in determining whether such distribution is lawful and reasonably practicable.

The depositary will make the election available to you only if it is reasonably practicable and if we have provided all of the documentation contemplated in the deposit agreement. In such case, the depositary will establish procedures to enable you to elect to receive either cash or additional ADSs, in each case as described in the deposit agreement.

If the election is not made available to you, you will receive either cash or additional ADSs, depending on what a shareholder in England and Wales would receive upon failing to make an election, as more fully described in the deposit agreement.

Other Distributions

Whenever we intend to distribute property other than cash, ordinary shares, or rights to purchase additional ordinary shares, we will notify the depositary in advance and will indicate whether we wish such distribution to be made to you. If so, we will assist the depositary in determining whether such distribution to holders is lawful and reasonably practicable.

If it is reasonably practicable to distribute such property to you and if we provide all of the documentation contemplated in the deposit agreement, the depositary will distribute the property to the holders in a manner it deems practicable.

The distribution will be made net of fees, expenses, taxes, and governmental charges payable by holders under the terms of the deposit agreement. In order to pay such taxes and governmental charges, the depositary may sell all or a portion of the property received.

The depositary will *not* distribute the property to you and will sell the property if:

- we do not request that the property be distributed to you or if we ask that the property not be distributed to you; or
- we do not deliver satisfactory documents to the depositary; or
- the depositary determines that all or a portion of the distribution to you is not reasonably practicable.

The proceeds of such a sale will be distributed to holders as in the case of a cash distribution.

Redemption

Whenever we decide to redeem any of the securities on deposit with the custodian, we will notify the depositary in advance. If it is practicable and if we provide all of the documentation contemplated in the deposit agreement, the depositary will provide notice of the redemption to the holders.

The custodian will be instructed to surrender the shares being redeemed against payment of the applicable redemption price. The depositary will convert the redemption funds received into U.S. dollars upon the terms of the deposit agreement and will establish procedures to enable holders to

receive the net proceeds from the redemption upon surrender of their ADSs to the depositary. You may have to pay fees, expenses, taxes, and other governmental charges upon the redemption of your ADSs. If less than all ADSs are being redeemed, the ADSs to be retired will be selected by lot or on a *pro rata* basis, as the depositary may determine.

Changes Affecting Ordinary Shares

The ordinary shares held on deposit for your ADSs may change from time to time. For example, there may be a change in nominal or par value, split-up, cancellation, consolidation, or any other reclassification of such ordinary shares or a recapitalization, reorganization, merger, consolidation, or sale of assets of the Company.

If any such change were to occur, your ADSs would, to the extent permitted by law, represent the right to receive the property received or exchanged in respect of the ordinary shares held on deposit. The depositary may in such circumstances deliver new ADSs to you, amend the deposit agreement, the ADRs and the applicable registration statement(s) on Form F-6, call for the exchange of your existing ADSs for new ADSs and take any other actions that are appropriate to reflect as to the ADSs the change affecting the Shares. If the depositary may not lawfully distribute such property to you, the depositary may sell such property and distribute the net proceeds to you as in the case of a cash distribution.

Issuance of ADSs upon Deposit of Ordinary Shares

Upon completion of the U.S. offering, the ordinary shares being offered pursuant to this prospectus will be deposited by us with the custodian. Upon receipt of confirmation of such deposit, the depositary will issue ADSs to the underwriters named in this prospectus.

After the closing of this offer, the depositary may create ADSs on your behalf if you or your broker deposit ordinary shares with the custodian. The depositary will deliver these ADSs to the person you indicate only after you pay any applicable issuance fees and any charges and taxes payable for the transfer of the ordinary shares to the custodian. Your ability to deposit ordinary shares and receive ADSs may be limited by the legal considerations in the United States and England and Wales applicable at the time of deposit.

The issuance of ADSs may be delayed until the depositary or the custodian receives confirmation that all required approvals have been given and that the ordinary shares have been duly transferred to the custodian. The depositary will only issue ADSs in whole numbers.

When you make a deposit of ordinary shares, you will be responsible for transferring good and valid title to the depositary. As such, you will be deemed to represent and warrant that:

- the ordinary shares are duly authorized, validly issued, fully paid, non-assessable, and legally obtained;
- all preemptive (and similar) rights, if any, with respect to such ordinary shares have been validly waived or exercised;
- you are duly authorized to deposit the ordinary shares;
- the ordinary shares presented for deposit are free and clear of any lien, encumbrance, security interest, charge, mortgage, or adverse claim, and are not, and the ADSs issuable upon such deposit will not be, “restricted securities” (as defined in the deposit agreement); and
- the ordinary shares presented for deposit have not been stripped of any rights or entitlements.

If any of the representations or warranties are incorrect in any way, we and the depositary may, at your cost and expense, take any and all actions necessary to correct the consequences of the misrepresentations.

Transfer, Combination and Split Up of ADRs

As an ADR holder, you will be entitled to transfer, combine, or split up your ADRs and the ADSs evidenced thereby. For transfers of ADRs, you will have to surrender the ADRs to be transferred to the depositary and also must:

- ensure that the surrendered ADR is properly endorsed or otherwise in proper form for transfer;
- provide such proof of identity and genuineness of signatures as the depositary deems appropriate;
- provide any transfer stamps required by the State of New York or the United States; and
- pay all applicable fees, charges, expenses, taxes, and other government charges payable by ADR holders pursuant to the terms of the deposit agreement, upon the transfer of ADRs.

To have your ADRs either combined or split up, you must surrender the ADRs in question to the depositary with your request to have them combined or split up, and you must pay all applicable fees, charges, and expenses payable by ADR holders, pursuant to the terms of the deposit agreement, upon a combination or split up of ADRs.

Withdrawal of Ordinary Shares Upon Cancellation of ADSs

As a holder, you will be entitled to present your ADSs to the depositary for cancellation and then receive the corresponding number of underlying ordinary shares at the custodian's offices. Your ability to withdraw the ordinary shares held in respect of the ADSs may be limited by the legal considerations in the United States and England and Wales applicable at the time of withdrawal. In order to withdraw the ordinary shares represented by your ADSs, you will be required to pay to the depositary the fees for cancellation of ADSs and any charges and taxes payable upon the transfer of the ordinary shares. You assume the risk for delivery of all funds and securities upon withdrawal. Once canceled, the ADSs will not have any rights under the deposit agreement.

If you hold ADSs registered in your name, the depositary may ask you to provide proof of identity and genuineness of any signature and such other documents as the depositary may deem appropriate before it will cancel your ADSs. The withdrawal of the ordinary shares represented by your ADSs may be delayed until the depositary receives satisfactory evidence of compliance with all applicable laws and regulations. Please keep in mind that the depositary will only accept ADSs for cancellation that represent a whole number of securities on deposit.

You will have the right to withdraw the securities represented by your ADSs at any time subject only to:

- temporary delays that may arise because (i) the transfer books for the ordinary shares or ADSs are closed, or (ii) ordinary shares are immobilized on account of a shareholders' meeting or a payment of dividends;
- obligations to pay fees, taxes, and similar charges; and/or
- restrictions imposed because of laws or regulations applicable to ADSs or the withdrawal of securities on deposit.

The deposit agreement may not be modified to impair your right to withdraw the securities represented by your ADSs except to comply with mandatory provisions of law.

Voting Rights

As a holder, you generally have the right under the deposit agreement to instruct the depositary to exercise the voting rights for the ordinary shares represented by your ADSs. The voting rights of holders of ordinary shares are described in "Description of Share Capital and Articles of Association—Articles of Association" in this prospectus.

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At our request, the depositary will distribute to you any notice of shareholders' meeting received from us together with information explaining how to instruct the depositary to exercise the voting rights of the securities represented by ADSs.

If the depositary timely receives voting instructions from a holder of ADSs, it will endeavor to vote the securities (in person or by proxy) represented by the holder's ADSs as follows:

- *In the event of voting by show of hands*, the depositary will vote (or cause the custodian to vote) all ordinary held on deposit at that time in accordance with the voting instructions received from a majority of holders of ADSs who provide timely voting instructions.
- *In the event of voting by poll*, the depositary will vote (or cause the custodian to vote) the ordinary shares held on deposit in accordance with the voting instructions received from the holders of ADSs. The depositary will give a discretionary proxy to a person designated by the Company to vote any ordinary shares held on deposit for which voting instructions were not received from the holders of ADSs, unless the Company informs the depositary that (a) the Company does not wish such proxy to be given, (b) substantial opposition exists, or (c) the rights of holders of ADSs may be adversely affected.

Securities for which no voting instructions have been received will not be voted (except as otherwise contemplated herein). Please note that the ability of the depositary to carry out voting instructions may be limited by practical and legal limitations and the terms of the securities on deposit. We cannot assure you that you will receive voting materials in time to enable you to return voting instructions to the depositary in a timely manner.

Fees and Charges

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

Service	Fee
Issuance of ADSs (e.g., an issuance of ADS upon a deposit of ordinary shares or upon a change in the ADS(s)-to-ordinary shares ratio), excluding ADS issuances as a result of distributions of ordinary shares	Up to \$.05 per ADS issued
Cancellation of ADSs (e.g., a cancellation of ADSs for delivery of deposited property or upon a change in the ADS(s)-to-ordinary shares ratio)	Up to \$.05 per ADS cancelled
Distribution of cash dividends or other cash distributions (e.g., upon a sale of rights and other entitlements)	Up to \$.05 per ADS held
Distribution of ADSs pursuant to (i) stock dividends or other free stock distributions, or (ii) exercise of rights to purchase additional ADSs	Up to \$.05 per ADS held
Distribution of securities other than ADSs or rights to purchase additional ADSs (e.g., upon a spin-off)	Up to \$.05 per ADS held
ADS Services	Up to \$.05 per ADS held on the applicable record date(s) established by the depositary

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

- taxes (including applicable interest and penalties) and other governmental charges;
- the registration fees as may from time to time be in effect for the registration of ordinary shares on the share register and applicable to transfers of ordinary shares to or from the name of the custodian, the depositary, or any nominees upon the making of deposits and withdrawals, respectively;

- certain cable, telex, and facsimile transmission and delivery expenses;
- the expenses and charges incurred by the depositary in the conversion of foreign currency;
- the fees and expenses incurred by the depositary in connection with compliance with exchange control regulations and other regulatory requirements applicable to ordinary shares, ADSs, and ADRs; and
- the fees and expenses incurred by the depositary, the custodian, or any nominee in connection with the servicing or delivery of deposited property.

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

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

Amendments and Termination

We may agree with the depositary to modify the deposit agreement at any time without your consent. We undertake to give holders 30 days' prior notice of any modifications that would materially prejudice any of their substantial rights under the deposit agreement. We will not consider to be materially prejudicial to your substantial rights any modifications or supplements that are reasonably necessary for the ADSs to be registered under the Securities Act or to be eligible for book-entry settlement, in each case without imposing or increasing the fees and charges you are required to pay. In addition, we may not be able to provide you with prior notice of any modifications or supplements that are required to accommodate compliance with applicable provisions of law.

You will be bound by the modifications to the deposit agreement if you continue to hold your ADSs after the modifications to the deposit agreement become effective. The deposit agreement cannot be amended to prevent you from withdrawing the ordinary shares represented by your ADSs (except as permitted by law).

We have the right to direct the depositary to terminate the deposit agreement. Similarly, the depositary may in certain circumstances on its own initiative terminate the deposit agreement. In either case, the depositary must give notice to the holders at least 30 days before termination. Until termination, your rights under the deposit agreement will be unaffected.

Termination

After termination, the depositary will continue to collect distributions received (but will not distribute any such property until you request the cancellation of your ADSs) and may sell the securities held on deposit. After the sale, the depositary will hold the proceeds from such sale and any other funds then held for the holders of ADSs in a non-interest bearing account. At that point, the depositary will have no further obligations to holders other than to account for the funds then held for the holders of ADSs still outstanding (after deduction of applicable fees, taxes and expenses).

In connection with the termination of the deposit agreement, the depositary may, independently and without the need for any action by us, make available to holders a means to withdraw the ordinary shares and other deposited securities represented by their ADSs and to direct the deposit of such ordinary shares and other deposited securities into an unsponsored American depositary shares program established by the depositary, upon such terms and conditions as the depositary may deem reasonably appropriate, subject however, in each case, to satisfaction of the applicable registration requirements by the unsponsored American depositary shares program under the Securities Act, and to receipt by the depositary of payment of the applicable fees and charges of, and reimbursement of the applicable expenses incurred by, the depositary.

Books of Depositary

The depositary will maintain ADS holder records at its depositary office. You may inspect such records at such office during regular business hours but solely for the purpose of communicating with other holders in the interest of business matters relating to the ADSs and the deposit agreement.

The depositary will maintain in New York facilities to record and process the issuance, cancellation, combination, split-up, and transfer of ADSs. These facilities may be closed from time to time, to the extent not prohibited by law.

Transmission of Notices, Reports and Proxy Soliciting Material

The depositary will make available for your inspection at its office all communications that it receives from us as a holder of deposited securities that we make generally available to holders of deposited securities. Subject to the terms of the deposit agreement, the depositary will send you copies of those communications or otherwise make those communications available to you if we ask it to.

Limitations on Obligations and Liabilities

The deposit agreement limits our obligations and the depositary's obligations to you. Please note the following:

- We and the depositary are obligated only to take the actions specifically stated in the deposit agreement without negligence or bad faith.
- The depositary disclaims any liability for any failure to carry out voting instructions, for any manner in which a vote is cast or for the effect of any vote, provided it acts in good faith and in accordance with the terms of the deposit agreement.
- The depositary disclaims any liability for any failure to determine the lawfulness or practicality of any action, for the content of any document forwarded to you on our behalf or for the

accuracy of any translation of such a document, for the investment risks associated with investing in ordinary shares, for the validity or worth of the ordinary shares, for any tax consequences that result from the ownership of ADSs, for the credit-worthiness of any third party, for allowing any rights to lapse under the terms of the deposit agreement, for the timeliness of any of our notices, or for our failure to give notice.

- We and the depositary will not be obligated to perform any act that is inconsistent with the terms of the deposit agreement.
- We and the depositary disclaim any liability if we or the depositary are prevented or forbidden from or subject to any civil or criminal penalty or restraint on account of, or delayed in, doing or performing any act or thing required by the terms of the deposit agreement, by reason of any provision, present or future of any law or regulation, or by reason of present or future provision of any provision of our Articles of Association, or any provision of or governing the securities on deposit, or by reason of any act of God or war or other circumstances beyond our control.
- We and the depositary disclaim any liability by reason of any exercise of, or failure to exercise, any discretion provided for in the deposit agreement or in our Articles of Association or in any provisions of or governing the securities on deposit.
- We and the depositary further disclaim any liability for any action or inaction in reliance on the advice or information received from legal counsel, accountants, any person presenting Shares for deposit, any holder of ADSs or authorized representatives thereof, or any other person believed by either of us in good faith to be competent to give such advice or information.
- We and the depositary also disclaim liability for the inability by a holder to benefit from any distribution, offering, right or other benefit that is made available to holders of ordinary shares but is not, under the terms of the deposit agreement, made available to you.
- We and the depositary may rely without any liability upon any written notice, request or other document believed to be genuine and to have been signed or presented by the proper parties.
- We and the depositary also disclaim liability for any consequential or punitive damages for any breach of the terms of the deposit agreement.
- No disclaimer of any Securities Act liability is intended by any provision of the deposit agreement.

Pre-Release Transactions

Subject to the terms and conditions of the deposit agreement, the depositary may issue to broker/dealers ADSs before receiving a deposit of ordinary shares or release ordinary shares to broker/dealers before receiving ADSs for cancellation. These transactions are commonly referred to as “pre-release transactions,” and are entered into between the depositary and the applicable broker/dealer. The deposit agreement limits the aggregate size of pre-release transactions (not to exceed 30% of the ordinary shares on deposit in the aggregate, but such limit may be changed or disregarded from time to time as the depositary deems appropriate) and imposes a number of conditions on such transactions (e.g., the need to receive collateral, the type of collateral required, the representations required from brokers, etc.). The depositary may retain the compensation received from the pre-release transactions.

Taxes

You will be responsible for the taxes and other governmental charges payable on the ADSs and the securities represented by the ADSs. We, the depositary and the custodian may deduct from any distribution the taxes and governmental charges payable by holders and may sell any and all property on deposit to pay the taxes and governmental charges payable by holders. You will be liable for any deficiency if the sale proceeds do not cover the taxes that are due.

The depositary may refuse to issue ADSs; to deliver, transfer, split, and combine ADRs; or to release securities on deposit until all taxes and charges are paid by the applicable holder. The

depository and the custodian may take reasonable administrative actions to obtain tax refunds and reduced tax withholding for any distributions on your behalf. However, you may be required to provide to the depository and to the custodian proof of taxpayer status and residence and such other information as the depository and the custodian may require to fulfill legal obligations. You are required to indemnify us, the depository and the custodian for any claims with respect to taxes based on any tax benefit obtained for you.

Foreign Currency Conversion

The depository will arrange for the conversion of all foreign currency received into U.S. dollars if such conversion is practical, and it will distribute the U.S. dollars in accordance with the terms of the deposit agreement. You may have to pay fees and expenses incurred in converting foreign currency, such as fees and expenses incurred in complying with currency exchange controls and other governmental requirements.

If the conversion of foreign currency is not practical or lawful, or if any required approvals are denied or not obtainable at a reasonable cost or within a reasonable period, the depository may take the following actions in its discretion:

- Convert the foreign currency to the extent practical and lawful and distribute the U.S. dollars to the holders for whom the conversion and distribution is lawful and practical.
- Distribute the foreign currency to holders for whom the distribution is lawful and practical.
- Hold the foreign currency (without liability for interest) for the applicable holders.

Governing Law/Waiver of Jury Trial

The deposit agreement and the ADRs will be interpreted in accordance with the laws of the State of New York. The rights of holders of ordinary shares (including ordinary shares represented by ADSs) is governed by the laws of England and Wales.

AS A PARTY TO THE DEPOSIT AGREEMENT, YOU WAIVE YOUR RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING AGAINST US AND/OR THE DEPOSITORY ARISING OUT OF THE DEPOSIT AGREEMENT OR THE ADRs.

ORDINARY SHARES AND ADSs ELIGIBLE FOR FUTURE SALE

Prior to the U.S. offering, there has been no market for our ADSs. Future sales of substantial amounts of our ADSs or ordinary shares in the public market, or the perception that such sales may occur, could adversely affect prevailing market prices of our ADSs or ordinary shares.

Based on the number of our ordinary shares outstanding as of March 31, 2018, upon the closing of the global offering, we will have 2,838,021 ADSs outstanding, representing 11,352,084 ordinary shares, and 86,987,891 ordinary shares outstanding (including ordinary shares in the form of ADSs), or, if the underwriters exercise in full their option to purchase an additional 425,703 ADSs in the U.S. offering, 88,690,703 ordinary shares (including ordinary shares in the form of ADSs). The ordinary shares and ADSs sold in the global offering will be freely tradable without restriction or further registration under the Securities Act of 1933, as amended, or the Securities Act, except for any ordinary shares or ADSs purchased by our “affiliates,” as that term is defined in Rule 144 under the Securities Act, whose sale would be subject to the Rule 144 resale restrictions described below other than the holding period requirement. We expect at least 17,799,887 of our ordinary shares outstanding after the global offering will be subject to the contractual 180-day lock-up period described below.

Rule 144

In general, a person who has beneficially owned our unregistered ordinary shares for at least six months would be entitled to sell such shares pursuant to Rule 144 of the Securities Act, provided that (i) such person is not deemed to have been one of our affiliates at the time of, or at any time during the 90 days preceding, a sale and (ii) we are subject to Exchange Act periodic reporting requirements for at least 90 days before the sale.

Persons who are our affiliates at the time of, or any time during the 90 days preceding, a sale of our ordinary shares or ADSs, are subject to additional restrictions, as follows:

- in the case of a sale of our unregistered ordinary shares, such persons must have beneficially owned such shares for at least six months; and
- such person may sell within any three month period only a number of our securities that does not exceed the greater of either of the following:
 - 1% of the number of our ordinary shares then outstanding, which will equal approximately 869,878 ordinary shares immediately after the global offering, assuming no exercise of the underwriters' options to purchase additional ADSs; or
 - the average weekly trading volume of our ordinary shares in the form of ADSs on the Nasdaq Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale;

provided, in each case, that we are subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale. Such sales by non-affiliates and affiliates must also comply with the manner of sale, current public information and notice provisions of Rule 144 to the extent applicable.

Rule 701

In general, under Rule 701 under the Securities Act, any of our employees, board members, senior management, consultants or advisors who purchases ordinary shares from us in connection with a compensatory share or option plan or other written agreement before the effective date of the registration statement of which this prospectus forms a part, or the effective date, is entitled to resell such shares 90 days after the effective date in reliance on Rule 144, without having to comply with the holding period requirements or other restrictions contained in Rule 701.

The SEC has indicated that Rule 701 will apply to typical share options granted by an issuer before it becomes subject to the reporting requirements of the Exchange Act, along with the shares acquired upon exercise of such options, including exercises after the date of this prospectus. Securities issued in reliance on Rule 701 are restricted securities and, subject to the lock-up restrictions described below, beginning 90 days after the date of this prospectus, may be sold by persons other than “affiliates,” as defined in Rule 144, subject only to the manner of sale provisions of Rule 144 and by affiliates under Rule 144 without compliance with the holding period requirement.

Regulation S

Regulation S provides generally that sales made in offshore transactions are not subject to the registration or prospectus-delivery requirements of the Securities Act.

Lock-up Agreements

All of our board members and executive officers and certain other holders of our ordinary shares and other securities have agreed, subject to certain exceptions, not to offer, sell, assign, transfer, pledge, contract to sell, or otherwise dispose of or announce the intention to otherwise dispose of, or enter into any swap, hedge or similar agreement or arrangement that transfers, in whole or in part, the economic risk of ownership of, directly or indirectly, our ADSs or ordinary shares or securities convertible into or exchangeable or exercisable for our ADSs or ordinary shares for a period of 180 days after the date of this prospectus, without the prior written consent of Cowen and Company, LLC and BMO Capital Markets Corp. See “Underwriting.”

MATERIAL TAX CONSIDERATIONS

U.S. Federal Income Taxation

The following is a description of the material U.S. federal income tax consequences to the U.S. Holders (as defined below) of owning and disposing of our ordinary shares or ADSs. It is not a comprehensive description of all tax considerations that may be relevant to a particular person's decision to acquire our ordinary shares or ADSs. This discussion applies only to a U.S. Holder that holds our ordinary shares or ADSs as a capital asset for tax purposes (generally, property held for investment). In addition, it does not describe all of the tax consequences that may be relevant in light of a U.S. Holder's particular circumstances, including non-U.S. tax consequences, state and local tax consequences, estate tax consequences, alternative minimum tax consequences, the potential application of the Medicare contribution tax, and tax consequences applicable to U.S. Holders subject to special rules, such as:

- banks, insurance companies, and certain other financial institutions;
- U.S. expatriates and certain former citizens or long term residents of the United States;
- dealers or traders in securities who use a mark to market method of tax accounting;
- persons holding ordinary shares or ADSs as part of a hedging transaction, "straddle," wash sale, conversion transaction or integrated transaction or persons entering into a constructive sale with respect to ordinary shares or ADSs;
- persons whose "functional currency" for U.S. federal income tax purposes is not the U.S. dollar;
- brokers, dealers or traders in securities, commodities or currencies;
- tax exempt entities or government organizations;
- S corporations, partnerships, or other entities or arrangements classified as partnerships for U.S. federal income tax purposes;
- regulated investment companies or real estate investment trusts;
- persons who acquired our ordinary shares or ADSs pursuant to the exercise of any employee stock option or otherwise as compensation;
- persons subject to special tax accounting rules as a result of any item of gross income with respect to the ADSs being taken into account in an applicable financial statement;
- persons that own or are deemed to own ten percent or more of our shares, measured by vote or by value; and
- persons holding our ordinary shares or ADSs in connection with a trade or business, permanent establishment, or fixed base outside the United States.

If an entity that is classified as a partnership for U.S. federal income tax purposes holds ordinary shares or ADSs, the U.S. federal income tax treatment of a partner will generally depend on the status of the partner and the activities of the partnership. Partnerships owning ordinary shares or ADSs and partners in such partnerships are encouraged to consult their tax advisers as to the particular U.S. federal income tax consequences of owning and disposing of our ordinary shares or ADSs.

The discussion is based on the Internal Revenue Code of 1986, as amended, or the Code, administrative pronouncements, judicial decisions, final, temporary and proposed Treasury Regulations, and the income tax treaty between the United Kingdom and the United States, or the Treaty, all as of the date hereof, changes to any of which may affect the tax consequences described herein—possibly with retroactive effect.

A “U.S. Holder” is a holder who, for U.S. federal income tax purposes, is a beneficial owner of ordinary shares or ADSs who is eligible for the benefits of the Treaty and is:

- (1) a citizen or individual resident of the United States;
- (2) a corporation, or other entity taxable as a corporation, created or organized in or under the laws of the United States, any state therein or the District of Columbia;
- (3) an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- (4) a trust (A) that is subject to the primary supervision of a court within the United States and one or more United States persons as described in Code Section 7701(a)(30) have the authority to control all substantial decisions of the trust or (B) any trust that has a valid election in effect under applicable United States Treasury Regulations to be treated the as a U.S. person.

U.S. Holders are encouraged to consult their tax advisers concerning the U.S. federal, state, local and foreign tax consequences of owning and disposing of ordinary shares or ADSs in their particular circumstances.

The discussion below assumes that the representations contained in the deposit agreement are true and that the obligations in the deposit agreement and any related agreement will be complied with in accordance with their terms. Generally, a holder of an ADS should be treated for U.S. federal income tax purposes as owning the ordinary shares represented by the ADS. Accordingly, no gain or loss will be recognized upon an exchange of ADSs for ordinary shares. The U.S. Treasury has expressed concerns that intermediaries in the chain of ownership between the holder of an ADS and the issuer of the security underlying the ADS may be taking actions that are inconsistent with the beneficial ownership of the underlying security. Accordingly the consequences described below may not apply if, as a result of actions taken by intermediaries in the chain of ownership between the holders of ADSs and our Company, the holders of our ADSs are not properly treated as beneficial owners of the underlying ordinary shares.

Passive Foreign Investment Company Rules

Because we do not expect to earn revenue from our business operations during the current taxable year, and because our sole source of income currently is interest on bank accounts held by us, we believe we will likely be a PFIC for the current taxable year. A non U.S. corporation will be classified as a PFIC for any taxable year in which, after applying certain look through rules, either:

- at least 75% of its gross income is passive income (such as interest income); or
- at least 50% of its gross assets (determined on the basis of a quarterly average) is attributable to assets that produce passive income or are held for the production of passive income.

We will be treated as owning our proportionate share of the assets and earning our proportionate share of the income of any other corporation, the equity of which we own, directly or indirectly, 25% or more (by value).

A separate determination must be made after the close of each taxable year as to whether we are a PFIC for that year. As a result, our PFIC status may change. While it is possible we may not meet the PFIC test described above once we start generating substantial revenue from our business operations, the analysis is factual and it is possible we may continue to be a PFIC for future years. In particular, the total value of our assets for purposes of the asset test generally will be calculated using the market price of the ordinary shares or ADSs, which may fluctuate considerably. Fluctuations in the market price of the ordinary shares or ADSs may result in our being a PFIC for any taxable year.

If we are classified as a PFIC in any year with respect to which a U.S. Holder owns the ordinary shares or ADSs, we will continue to be subject to the PFIC rules discussed below with respect to such U.S. Holder in all succeeding years during which the U.S. Holder owns the ordinary shares or ADSs, regardless of whether we continue to meet the tests described above unless (1) we cease to be a PFIC and the U.S. Holder has made a “deemed sale” election under the PFIC rules, or (2) the U.S. Holder makes a QEF Election (defined and discussed further below) with respect to all taxable years in which we are a PFIC. If you make a deemed sale election, you will be deemed to have sold the ordinary shares or ADSs you hold at their fair market value and any gain from such deemed sale would be subject to the “excess distribution” rules described further below. After the deemed sale election, so long as we do not become a PFIC in a subsequent taxable year, your ordinary shares or ADSs with respect to which you made such election will not be treated as shares in a PFIC and you will not be subject to the rules described below with respect to any “excess distribution” you receive from us or any gain from an actual sale or other disposition of the ordinary shares or ADSs. U.S. Holders should consult their tax advisors as to the possibility and consequences of making a deemed sale election if we cease to be a PFIC and such election becomes available.

If the U.S. Holder makes a QEF Election in the first year in the U.S. Holder’s holding period in which we are a PFIC, or a Pedigreed Election, then the U.S. Holder may make the QEF Election by simply filing the appropriate documents at the time the U.S. Holder files its tax return for such first year (as discussed further below). If a Pedigreed Election is made, and we no longer qualify as a PFIC in a subsequent year, normal Code rules and not the PFIC rules will apply. If a U.S. shareholder makes a QEF Election that is not a Pedigreed Election (i.e., it is made after the first year during which the company is a PFIC and the U.S. shareholder holds shares of the company), the QEF rules apply prospectively but do not apply to years prior to the year in which the QEF first becomes effective.

For each taxable year we are treated as a PFIC with respect to you, you will be subject to special tax rules with respect to any “excess distribution” you receive and any gain you recognize from a sale or other disposition (including a pledge) of ordinary shares or ADSs, unless you make a QEF Election or a mark to market election as discussed further below. Distributions you receive in a taxable year that are greater than 125% of the average annual distributions you received during the shorter of the three preceding taxable years or your holding period for the ordinary shares or ADSs will be treated as an excess distribution. Under these special tax rules:

- the excess distribution or gain will be allocated ratably over your holding period for the ordinary shares or ADSs;
- the amount allocated to the current taxable year, and any taxable year prior to the first taxable year in which we became a PFIC, will be treated as ordinary income; and
- the amount allocated to each other year will be subject to the highest tax rate in effect for that year and the interest charge generally applicable to underpayments of tax will be imposed on the resulting tax attributable to each such year.

The tax liability for amounts allocated to years prior to the year of disposition or “excess distribution” cannot be offset by any net operating losses for such years, and gains (but not losses) realized on the sale of the ordinary shares or ADSs cannot be treated as capital, even if you hold the ordinary shares or ADSs as capital assets.

If we are a PFIC, to the extent any of our subsidiaries are also PFICs or we make direct or indirect equity investments in other entities that are PFICs, you may be deemed to own shares in such lower-tier PFICs that are directly or indirectly owned by us in that proportion which the value of the ADSs you own bears to the value of all of our ADSs. A U.S. Holder will generally be subject to similar rules to those described above with respect to distributions we receive from, and our dispositions of the stock

of, any of our direct or indirect subsidiaries that also are PFICs, as if such distributions were indirectly received by, and/or dispositions were indirectly carried out by, such U.S. Holder. It is possible that one or more of our subsidiaries may be treated as a lower-tier PFIC. U.S. Holders should consult their tax advisors regarding the application of the PFIC rules to our subsidiaries and the adverse tax consequences that may result from such U.S. Holder's deemed ownership interests in any lower-tier PFICs.

U.S. Holders can avoid the interest charge on excess distributions or gain relating to the ordinary shares or ADSs by making a mark to market election with respect to the ordinary shares or ADSs, provided that the ordinary shares or ADSs are "marketable." Ordinary shares or ADSs will be marketable if they are "regularly traded" on certain U.S. stock exchanges or on a foreign stock exchange that meets certain conditions. For these purposes, the ordinary shares or ADSs will be considered regularly traded during any calendar year during which they are traded, other than in de minimis quantities, on at least 15 days during each calendar quarter. In addition, if we initiate a public offering of ADSs in the fourth quarter of a calendar year, the ADSs will be considered regularly traded if the ADSs are traded other than in de minimis quantities, on the greater of 1/6 of the days remaining in the quarter in which the offering occurs, or 5 days. Any trades that have as their principal purpose meeting this requirement will be disregarded. Our ADSs will be listed on the Nasdaq, which is a qualified exchange for these purposes. Consequently, if our ADSs remain listed on the Nasdaq and are regularly traded, and you are a holder of ADSs, we expect the mark to market election would be available to you if we are a PFIC (which we believe likely for the current year). It is unclear whether our ordinary shares would be considered "marketable" for purposes of these rules and, therefore, whether you would be able to make a mark-to-market election with respect to our ordinary shares. Each U.S. Holder should consult its tax advisor as to the whether a mark to market election is available or advisable with respect to the ordinary shares or ADSs.

A U.S. Holder that makes a valid mark to market election with respect to ordinary shares or ADSs must include in ordinary income for each year an amount equal to the excess, if any, of the fair market value of the ordinary shares or ADSs (as applicable) at the close of the taxable year over the U.S. Holder's adjusted tax basis in such ordinary shares or ADSs (as applicable). An electing holder may also claim an ordinary loss deduction for the excess, if any, of the U.S. Holder's adjusted basis in the ordinary shares or ADSs (as applicable) over the fair market value of the ordinary shares or ADSs (as applicable) at the close of the taxable year, but this deduction is allowable only to the extent of any net mark to market gains for prior years. If a mark-to-market election applies, gains from an actual sale or other disposition of the ordinary shares or ADSs (as applicable) will be treated as ordinary income, and any losses incurred on a sale or other disposition will be treated as an ordinary loss to the extent of any net mark to market gains for prior years. Once made, the mark-to-market election cannot be revoked without the consent of the IRS unless the ordinary shares or ADSs with respect to which the election was made cease to be marketable.

However, a mark to market election generally cannot be made for equity interests in any lower tier PFICs that we own, unless shares of such lower tier PFIC are themselves "marketable." It is possible that one or more of our subsidiaries will be treated as a lower-tier PFIC and shares in any such subsidiary would not be considered marketable for this purpose. As a result, even if a U.S. Holder validly makes a mark to market election with respect to our ordinary shares or ADSs, the U.S. Holder may continue to be subject to the general "excess distribution" PFIC rules (described above) with respect to its indirect interest in any of our investments that are treated as an equity interest in a PFIC for U.S. federal income tax purposes. U.S. Holders should consult their tax advisors as to the availability and desirability of a mark to market election, as well as the impact of such election on indirect interests in any lower tier PFICs.

Alternatively, a U.S. Holder can make an election, if we provide the necessary information, to treat us and each lower tier PFIC as a qualified electing fund, or a QEF Election, in the first taxable year we (and our relevant subsidiaries) are treated as a PFIC with respect to the holder. If such election remains in place while we and any lower tier PFIC subsidiaries are PFICs, we and our subsidiaries will not be treated as PFICs with respect to such U.S. Holder when we cease to be a PFIC. To make the QEF Election for each PFIC, a U.S. Holder must attach a separate properly completed IRS Form 8621 for each PFIC to the holder's timely filed U.S. federal income tax return. We will provide the information necessary for a U.S. Holder to make a QEF Election with respect to us and will cause each lower tier PFIC which we control to provide such information with respect to such lower tier PFIC.

If a U.S. Holder makes a QEF Election with respect to a PFIC, the holder will be currently taxable on its pro rata share of the PFIC's ordinary earnings and net capital gain (at ordinary income and capital gain rates, respectively) for each taxable year that the entity is classified as a PFIC. If a U.S. Holder makes a QEF Election with respect to us, any distributions paid by us out of our earnings and profits that were previously included in the holder's income under the QEF Election would not be taxable to the holder. A U.S. Holder will increase its tax basis in its ordinary shares or ADSs by an amount equal to any income included under the QEF Election and will decrease its tax basis by any amount distributed on the ordinary shares or ADSs that is not included in the holder's income. In addition, a U.S. Holder will recognize capital gain or loss on the disposition of ordinary shares or ADSs in an amount equal to the difference between the amount realized and the holder's adjusted tax basis in the ordinary shares or ADSs. U.S. Holders should note that if they make QEF Elections with respect to us and our subsidiaries that are treated as lower tier PFICs, they may be required to pay U.S. federal income tax with respect to their ordinary shares or ADSs for any taxable year significantly in excess of any cash distributions received on the ordinary shares or ADSs for such taxable year. U.S. Holders should consult their tax advisors regarding making QEF Elections in their particular circumstances.

Unless otherwise provided by the U.S. Treasury, each U.S. shareholder of a PFIC is required to file an annual report containing such information as the U.S. Treasury may require. A U.S. Holder's failure to file the annual report will cause the statute of limitations for such U.S. Holder's U.S. federal income tax return to remain open with regard to the items required to be included in such report until three years after the U.S. Holder files the annual report, and, unless such failure is due to reasonable cause and not willful neglect, the statute of limitations for the U.S. Holder's entire U.S. federal income tax return will remain open during such period. U.S. Holders should consult their tax advisors regarding the requirements of filing such information returns under these rules.

Calculation of Basis in the Ordinary Shares or ADSs

A U.S. Holder's initial tax basis in the ordinary shares or ADSs will generally equal the cost of such ordinary shares. If a U.S. Holder used foreign currency to purchase the ordinary shares or ADSs, the cost of the ordinary shares or ADSs will be the U.S. dollar value of the foreign currency purchase price on the date of purchase, translated at the spot rate of exchange on that date.

Taxation of Distributions

Subject to the discussion above under "—Passive Foreign Investment Company Rules," distributions paid on ordinary shares or ADSs, other than certain pro rata distributions of ordinary shares or ADSs, will generally be treated as dividends to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). Because we do not calculate our earnings and profits under U.S. federal income tax principles, we expect that distributions generally will be reported to U.S. Holders as dividends. Subject to applicable limitations, dividends paid to certain non-corporate U.S. Holders may be taxable at preferential rates applicable to "qualified dividend income." However, the qualified dividend income treatment will not apply if we are

treated as a PFIC in the year the dividend is paid or in the preceding year. The amount of a dividend will include any amounts withheld by us in respect of United Kingdom income taxes. The amount of the dividend will be treated as foreign source dividend income to U.S. Holders and will not be eligible for the dividends received deduction generally available to U.S. corporations under the Code. Dividends will generally be included in a U.S. Holder's income on the date of the U.S. Holder's actual or constructive receipt of the dividend. The amount of any dividend income paid in foreign currency will be the U.S. dollar amount calculated by reference to the exchange rate in effect on the date of actual or constructive receipt, regardless of whether the payment is in fact converted into U.S. dollars. If the dividend is converted into U.S. dollars on the date of receipt, a U.S. Holder should not be required to recognize foreign currency gain or loss in respect of the dividend income. A U.S. Holder may have foreign currency gain or loss if the dividend is converted into U.S. dollars after the date of receipt. Such gain or loss would generally be treated as U.S. source ordinary income or loss. The amount of any distribution of property other than cash (and other than certain pro rata distributions of ordinary shares or ADSs or rights to acquire ordinary shares or ADSs) will be the fair market value of such property on the date of distribution. Amounts, if any, not treated as dividend income will constitute a return of capital and will first be applied to reduce a U.S. Holder's tax basis in its ordinary shares or ADSs, but not below zero, and then any excess will be treated as a gain realized on a sale or other disposition of ordinary shares or ADSs.

For foreign tax credit purposes, our dividends will generally be treated as passive category income. Subject to applicable limitations, some of which vary depending upon the U.S. Holder's particular circumstances, any United Kingdom income taxes withheld from dividends on ordinary shares or ADSs at a rate not exceeding the rate provided by the Treaty will be creditable against the U.S. Holder's U.S. federal income tax liability. The rules governing foreign tax credits are complex and U.S. Holders should consult their tax advisers regarding the creditability of foreign taxes in their particular circumstances. In lieu of claiming a foreign tax credit, U.S. Holders may, at their election, deduct foreign taxes, including any United Kingdom income tax, in computing their taxable income, subject to generally applicable limitations under U.S. law. An election to deduct foreign taxes instead of claiming foreign tax credits applies to all foreign taxes paid or accrued in the taxable year.

Sale or Other Taxable Disposition of Ordinary Shares and ADSs

Subject to the discussion above under “—Passive Foreign Investment Company Rules,” gain or loss realized on the sale or other taxable disposition of ordinary shares or ADSs will be capital gain or loss, and will be long term capital gain or loss if the U.S. Holder held the ordinary shares or ADSs for more than one year. The amount of the gain or loss will equal the difference between the U.S. Holder's tax basis in the ordinary shares or ADSs disposed of and the amount realized on the disposition, in each case as determined in U.S. dollars. This gain or loss will generally be U.S. source gain or loss for foreign tax credit purposes. The deductibility of capital losses is subject to limitations.

If the consideration received by a U.S. Holder is not paid in U.S. dollars, the amount realized will be the U.S. dollar value of the payment received determined by reference to the spot rate of exchange on the date of the sale or other disposition. However, if the ordinary shares or ADSs are treated as traded on an “established securities market” and you are either a cash basis taxpayer or an accrual basis taxpayer that has made a special election (which must be applied consistently from year to year and cannot be changed without the consent of the IRS), you will determine the U.S. dollar value of the amount realized in a non U.S. dollar currency by translating the amount received at the spot rate of exchange on the settlement date of the sale. If you are an accrual basis taxpayer that is not eligible to or does not elect to determine the amount realized using the spot rate on the settlement date, you will recognize foreign currency gain or loss to the extent of any difference between the U.S. dollar amount realized on the date of sale or disposition and the U.S. dollar value of the currency received at the spot rate on the settlement date.

WE STRONGLY URGE YOU TO CONSULT YOUR TAX ADVISOR REGARDING THE IMPACT OF OUR PFIC STATUS ON YOUR INVESTMENT IN THE ORDINARY SHARES OR ADSs AS WELL AS THE APPLICATION OF THE PFIC RULES TO YOUR INVESTMENT IN THE ORDINARY SHARES OR ADSs.

Information Reporting and Backup Withholding

Payments of dividends and sales proceeds that are made within the United States or through certain U.S. related financial intermediaries generally are subject to information reporting, and may be subject to backup withholding, unless (i) the U.S. Holder is a corporation or other exempt recipient or (ii) in the case of backup withholding, the U.S. Holder provides a correct taxpayer identification number and certifies that it is not subject to backup withholding.

Backup withholding is not an additional tax. The amount of any backup withholding from a payment to a U.S. Holder will be allowed as a credit against the holder's U.S. federal income tax liability and may entitle it to a refund, provided that the required information is timely furnished to the IRS.

Transfer Reporting Requirements

A U.S. Holder (including a U.S. tax-exempt entity) that acquires equity of a non-U.S. corporation may be required to file a Form 926, or a similar form, with the IRS reporting the payment of the offering price if (i) such person owned, directly or by attribution, immediately after the transfer at least 10.0% by vote or value of the corporation or (ii) if the transfer, when aggregated with all transfers made by such person (or any related person) within the preceding 12 month period, exceeds USD 100,000. Substantial penalties may be imposed upon a U.S. Holder that fails to comply. Also, in the event a U.S. Holder does not file IRS Form 926, the statute of limitations on the assessment and collection of U.S. federal income taxes of such U.S. Holder for the related tax year may not close until three years after the date the required information is filed. Each U.S. Holder should consult its own tax advisor as to the possible obligation to file Form 926. U.S. Holders should consult their tax advisers regarding the applicability of this requirement to their acquisition of our ordinary shares.

Information with Respect to Foreign Financial Assets

Certain U.S. Holders who are individuals (and, under proposed regulations, certain entities) may be required to report information relating to the ordinary shares or ADSs, subject to certain exceptions (including an exception for ordinary shares or ADSs held in accounts maintained by certain U.S. financial institutions). U.S. Holders should consult their tax advisers regarding their reporting obligations with respect to their ownership and disposition of the ordinary shares or ADSs.

FATCA

Provisions under Sections 1471 through 1474 of the Code and applicable U.S. Treasury Regulations commonly referred to as "FATCA" generally impose 30% withholding on certain "withholdable payments" and, in the future, may impose such withholding on "foreign passthru payments" made by a "foreign financial institution" (each as defined in the Code) that has entered into an agreement with the IRS to perform certain diligence and reporting obligations with respect to the foreign financial institution's U.S.-owned accounts. The United States has entered into intergovernmental agreements with the United Kingdom and other jurisdictions that modify the FATCA withholding regime. It is not yet clear how these intergovernmental agreements will address foreign passthru payments and whether such intergovernmental agreements may relieve foreign financial institutions of any obligation to withhold on foreign passthru payments. Prospective investors should consult their tax advisors regarding the potential impact of FATCA, or any intergovernmental agreement or non-U.S. legislation implementing FATCA, on their investment in the ordinary shares.

United Kingdom Taxation

The following paragraphs are intended as a general guide to current U.K. tax law and HM Revenue & Customs published practice applying as at the date of this prospectus (both of which are subject to change at any time, possibly with retrospective effect) relating to the holding of ordinary shares or ADSs. They do not constitute legal or tax advice and do not purport to be a complete analysis of all U.K. tax considerations relating to the holding of ordinary shares or ADSs. They are written on the basis that the Company is and remains solely resident in the U.K. for tax purposes and will therefore be subject to the U.K. tax regime and not the U.S. tax regime save as set out above under “—U.S. Federal Income Taxation.” They relate only to persons who are absolute beneficial owners of ordinary shares or ADSs (and where the ordinary shares or ADSs are not held through an Individual Savings Account or a Self-Invested Personal Pension) and who are resident for tax purposes in (and only in) the U.K., or U.K. Holders (except to the extent that the position of non-U.K. resident persons is expressly referred to). These paragraphs assume that a holder of ADSs is the beneficial owner of the underlying ordinary shares and any dividends paid in respect of the underlying ordinary shares (where the dividends are regarded for U.K. purposes as that person's own income) for U.K. direct tax purposes.

These paragraphs may not relate to certain classes of U.K. Holders, such as (but not limited to):

- persons who are connected with the Company;
- financial institutions;
- insurance companies;
- charities or tax-exempt organizations;
- collective investment schemes;
- pension schemes;
- brokers or dealers in securities or persons who hold ordinary shares or ADSs otherwise than as an investment;
- persons who have (or are deemed to have) acquired their ordinary shares or ADSs by virtue of an office or employment or who are or have been officers or employees of the Company or any of its affiliates; and
- individuals who are subject to U.K. taxation on a remittance basis.

THESE PARAGRAPHS DO NOT DESCRIBE ALL OF THE CIRCUMSTANCES IN WHICH HOLDERS OF ORDINARY SHARES OR ADSs MAY BENEFIT FROM AN EXEMPTION OR RELIEF FROM U.K. TAXATION. IT IS RECOMMENDED THAT ALL HOLDERS OF ORDINARY SHARES OR ADSs OBTAIN THEIR OWN TAX ADVICE AS TO THE CONSEQUENCES OF THE ACQUISITION, OWNERSHIP, AND DISPOSAL OF THE ORDINARY SHARES OR ADSs IN THEIR OWN PARTICULAR CIRCUMSTANCES. IN PARTICULAR, NON-U.K. RESIDENT OR DOMICILED PERSONS ARE ADVISED TO CONSIDER THE POTENTIAL IMPACT OF ANY RELEVANT DOUBLE TAX AGREEMENTS.

Dividends

Withholding Tax

Dividends paid by the Company will not be subject to any withholding or deduction for or on account of U.K. tax, irrespective of the residence or particular circumstances of the holders of ordinary shares or ADSs.

Income Tax

An individual U.K. Holder may, depending on his or her particular circumstances, be subject to U.K. tax on dividends received from the Company. An individual holder of ordinary shares or ADSs

who is not resident for tax purposes in the U.K. should not be chargeable to U.K. income tax on dividends received from the Company unless he or she carries on (whether solely or in partnership) any trade, profession, or vocation in the U.K. through a branch or agency to which the ordinary shares or ADSs are attributable (subject to certain exceptions for trading through independent agents, such as some brokers and investment managers).

All individual U.K. Holders will receive a tax-free allowance of £5,000 per annum (reducing to £2,000 for dividends received on or after 6 April 2018). Dividend income in excess of this tax-free allowance will be charged at 7.5% for basic rate taxpayers, 32.5% for higher rate taxpayers, and 38.1% for additional rate taxpayers. Dividend income is treated as the top slice of the total income chargeable to U.K. income tax.

Corporation Tax

Corporate U.K. Holders should not be subject to U.K. corporation tax on any dividend received from the Company so long as the dividends qualify for exemption, which is likely to be the case, provided the dividends fall within an exempt class and certain conditions are met (including anti-avoidance conditions).

Chargeable Gains

A disposal or deemed disposal of ordinary shares or ADSs by a U.K. Holder may, depending on the U.K. Holder's circumstances and subject to any available exemptions or reliefs, give rise to a chargeable gain or an allowable loss for the purposes of U.K. capital gains tax and corporation tax on chargeable gains.

If an individual U.K. Holder who is subject to U.K. income tax at either the higher or the additional rate becomes liable to U.K. capital gains tax on the disposal of ordinary shares or ADSs, the current applicable rate would be 20%. For an individual U.K. Holder who is subject to U.K. income tax at the basic rate and liable to U.K. capital gains tax on such disposal, the current applicable rate would be 10%, save to the extent that any capital gains exceed the unused basic rate tax band. In that case, the current rate applicable to the excess would be 20%.

If a corporate U.K. Holder becomes liable to U.K. corporation tax on the disposal of ordinary shares or ADSs, the main rate of U.K. corporation tax (currently 19%) would apply. An indexation allowance may be available to such a holder to give an additional deduction based on the indexation of its base cost in the shares by reference to U.K. retail price inflation over its holding period (but note that, in respect of disposals on or after 1 January 2018, the U.K. Government announced plans in the Autumn Budget 2017 to freeze indexation allowance at the amount that would be due based on the retail price index for December 2017). An indexation allowance can only reduce a gain on a future disposal, and cannot create a loss.

A holder of ordinary shares or ADSs which is not resident for tax purposes in the U.K. should not normally be liable to U.K. capital gains tax or corporation tax on chargeable gains on a disposal of ordinary shares or ADSs. However, an individual holder of ordinary shares or ADSs who has ceased to be resident for tax purposes in the U.K. for a period of less than five years and who disposes of ordinary shares or ADSs during that period may be liable on his or her return to the U.K. to U.K. tax on any capital gain realized (subject to any available exemption or relief).

Any gains or losses in respect of currency fluctuations relating to the ordinary shares or ADSs would be brought into account on the disposal.

Stamp Duty and Stamp Duty Reserve Tax

The discussion below relates to holders of ordinary shares or ADSs wherever resident.

Transfer of Ordinary Shares

Neither U.K. stamp duty nor stamp duty and reserve tax, or SDRT, should arise on transfers of ordinary shares on AIM (including instruments transferring ordinary shares or agreement to transfer ordinary shares) based on the following assumptions:

- that the ordinary shares are admitted to trading on AIM but are not listed on any market (with the term “listed” being construed in accordance with section 99A of the U.K. Finance Act 1986); and
- that AIM continues to be accepted as a “recognised growth market” (as construed in accordance with section 99A of the U.K. Finance Act 1986).

In the event that either of the above assumptions does not apply, transfers of, or agreements to transfer, ordinary shares may give rise to U.K. stamp duty or SDRT in certain circumstances.

Transfers of ADSs

No U.K. stamp duty will in practice be payable on a written instrument transferring an ADS or on a written agreement to transfer an ADS, provided that the instrument of transfer or the agreement to transfer is executed and remains at all times outside the U.K. Where these conditions are not met, the transfer of, or agreement to transfer, an ADS could, depending on the circumstances, attract a charge to U.K. stamp duty at the rate of 0.5% (rounded up to the nearest £5) of the value of the consideration.

No SDRT will be payable in respect of agreement to transfer an ADS.

UNDERWRITING

We and the underwriters for the global offering named below have entered into an underwriting agreement with respect to the ADSs and ordinary shares being offered. Subject to the terms and conditions of the underwriting agreement, each underwriter has severally agreed to purchase from us the number of ADSs and ordinary shares set forth opposite its name below. Cowen and Company, LLC, 599 Lexington Avenue, New York, New York 10022; BMO Capital Markets Corp., 3 Times Square, New York, New York 10036; and RBC Capital Markets, LLC, 3 World Financial Center, 200 Vesey Street, New York, New York 10281, are the representatives of the underwriters.

<u>Underwriters</u>	<u>Number of ADSs</u>	<u>Number of Ordinary Shares</u>
Cowen and Company, LLC		
BMO Capital Markets Corp.		
RBC Capital Markets, LLC		
JMP Securities LLC		
Cantor Fitzgerald Europe		
Total	<u>2,838,021</u>	<u>4,540,833</u>

The underwriting agreement provides that the obligations of the underwriters are subject to certain conditions precedent and that the underwriters have agreed, severally and not jointly, to purchase all of the ADSs and ordinary shares sold under the underwriting agreement if any of these ADSs or ordinary shares are purchased, other than those ADSs covered by the overallotment option described below. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against specified liabilities, including liabilities under the Securities Act and to contribute to payments the underwriters may be required to make in respect thereof.

The underwriters are offering the ADSs and ordinary shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel and other conditions specified in the underwriting agreement. The underwriters reserve the right to withdraw, cancel, or modify offers to the public and to reject orders in whole or in part.

Option to Purchase Additional ADSs. We have granted to the underwriters an option to purchase up to 425,703 additional ADSs at the public offering price per ADS, less the underwriting discounts and commissions. This option is exercisable for a period of 30 days after the date of the pricing of the global offering. The underwriters may exercise this option solely for the purpose of covering overallotments, if any, made in connection with the sale of ADSs offered hereby. To the extent that the underwriters exercise this option, the underwriters will purchase additional ADSs from us in approximately the same proportion as shown in the table above.

Discounts and Commissions. The following table shows the public offering price, underwriting discounts and commissions and proceeds, before expenses to us. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional ADSs.

We estimate that the total expenses of the global offering payable by us, excluding underwriting discounts and commissions, will be approximately \$3.1 million. We have also agreed to reimburse the underwriters for certain expenses, including up to an aggregate of \$35,000 in connection with the

clearance of the global offering with the Financial Industry Regulatory Authority, or FINRA, as set forth in the underwriting agreement.

	Per ADS	Per Share	Total	
			Without Overallotment	With Overallotment
Offering price	\$	£	\$	\$
Underwriting discounts and commissions	\$	£	\$	\$
Proceeds, before expenses, to Mereo	\$	£	\$	\$

The underwriters propose to offer the ADSs and ordinary shares at the offering prices set forth on the cover of this prospectus. The underwriters may offer the ADSs and ordinary shares to securities dealers at the public offering prices less a concession not in excess of \$ per ADS and £ per ordinary share. If all of the ADSs and ordinary shares are not sold at the relevant offering price, the underwriters may change the initial public offering price per ADS and the offering price per ordinary share and other selling terms. Sales of ADSs made outside of the United States may be made by affiliates of certain of the underwriters. Certain of the underwriters may sell ADSs or ordinary shares through one or more of their affiliates as selling agents.

Discretionary Accounts. The underwriters do not intend to confirm sales of the ADSs or ordinary shares to any accounts over which they have discretionary authority.

Market Information. Prior to the global offering, there has been no public market for the ADSs. Our ordinary shares have been listed on the AIM under the symbol “MPH” since June 9, 2016. The initial public offering price for the ADSs and the ordinary shares offered in this offering will be determined by negotiations between us and the representatives of the underwriters taking into account the most recent closing price of our ordinary shares on the AIM prior to the pricing date and prevailing market conditions. In addition, factors to be considered in these negotiations will include:

- the history of, and prospects for, our company and the industry in which we compete;
- our past and present financial information, assessment of our management, its past and present operations, and the prospects for, and timing of, our future revenues;
- the present state of our development; and
- the foregoing factors in relation to market values and various valuation measures of other companies engaged in activities similar to ours.

An active trading market for the ADSs may not develop. It is also possible that after the global offering, the ADSs will not trade in the public market at or above the initial public offering price.

We applied to list the ADSs on the Nasdaq Global Market under the trading symbol “MREO.”

Stabilization. In connection with the global offering, the underwriters may engage in stabilizing transactions, overallotment transactions, syndicate covering transactions, penalty bids and purchases to cover positions created by short sales.

- Stabilizing transactions permit bids to purchase ADSs or ordinary shares so long as the stabilizing bids do not exceed a specified maximum, and are engaged in for the purpose of preventing or retarding a decline in the market price of the ADSs or ordinary shares while the global offering is in progress.
- Overallotment transactions involve sales by the underwriters of ADSs in excess of the number of ADSs the underwriters are obligated to purchase. This creates a syndicate short position

which may be either a covered short position or a naked short position. In a covered short position, the number of ADSs overallocated by the underwriters is not greater than the number of ADSs that they may purchase in the overallocation option. In a naked short position, the number of ADSs involved is greater than the number of ADSs in the overallocation option. The underwriters may close out any short position by exercising their overallocation option and/or purchasing ADSs in the open market.

- Syndicate covering transactions involve purchases of ADSs in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of ADSs to close out the short position, the underwriters will consider, among other things, the price of ADSs available for purchase in the open market as compared with the price at which they may purchase ADSs through exercise of the overallocation option. If the underwriters sell more ADSs than could be covered by exercise of the overallocation option and, therefore, have a naked short position, the position can be closed out only by buying ADSs in the open market. A naked short position is more likely to be created if the underwriters are concerned that after pricing there could be downward pressure on the price of the ADSs in the open market that could adversely affect investors who purchase in the global offering.
- Penalty bids permit the representatives to reclaim a selling concession from a syndicate member when the ADSs or ordinary shares originally sold by that syndicate member are purchased in stabilizing or syndicate covering transactions to cover syndicate short positions.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of the ADSs or ordinary shares or preventing or retarding a decline in the market price of the ADSs or ordinary shares. As a result, the price of the ADSs and ordinary shares in the open market may be higher than it would otherwise be in the absence of these transactions. Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of the ADSs or ordinary shares. These transactions may be effected on the Nasdaq Global Market, in the over-the-counter market or otherwise and, if commenced, may be discontinued at any time.

Passive Market Making. In connection with this offering, underwriters may engage in passive market making transactions in the ADSs on the Nasdaq Global Market in accordance with Rule 103 of Regulation M under the Exchange Act during a period before the commencement of offers or sales of ADSs and extending through the completion of the distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

Lock-Up Agreements. Pursuant to certain "lock-up" agreements, we and our executive officers, directors and certain of our other shareholders, have agreed, subject to certain exceptions, not to offer, sell, assign, transfer, pledge, contract to sell, or otherwise dispose of or announce the intention to otherwise dispose of, or enter into any swap, hedge or similar agreement or arrangement that transfers, in whole or in part, the economic risk of ownership of, directly or indirectly, or engage in any short selling of, or make any demand or request for or exercise any right with respect to the registration of, or file with the SEC a registration statement under the Securities Act relating to, our ADSs or ordinary shares or securities convertible into or exchangeable or exercisable for our ADSs or ordinary shares without the prior written consent of Cowen and Company, LLC and BMO Capital Markets Corp. for a period of 180 days after the date of the pricing of the global offering.

This lock-up provision applies to ADSs, ordinary shares and securities convertible into or exchangeable or exercisable for ADSs or ordinary shares. It also applies to ADSs or ordinary shares owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition. The exceptions permit us, among other things

and subject to restrictions, to: (a) issue ADSs, ordinary shares or options pursuant to employee benefit incentive or share option plans, and file a registration statement to register the offer and sale of such securities or (b) issue ADSs or ordinary shares upon the conversion of outstanding securities or the exercise of outstanding options, or warrants or convertible debt securities. The exceptions permit parties to the “lock-up” agreements, among other things and subject to restrictions, to: (a) make certain gifts; (b) if the party is a corporation, partnership, limited liability company or other business entity, make transfers to any shareholders, partners, members of, or owners of similar equity interests in, the party, or to an affiliate of the party, if such transfer is not for value; (c) make transfers of our ADSs or ordinary shares acquired in the open market after the global offering; (d) if the party is a corporation, partnership, limited liability company or other business entity, make transfers in connection with the sale or transfer of all of the party’s capital stock, partnership interests, membership interests or other similar equity interests, as the case may be, or all or substantially all of the party’s assets, in any such case not undertaken for the purpose of avoiding the restrictions imposed by the “lock-up” agreement; (d) make certain transfers by operation of law; (e) make transfers of ADSs or ordinary shares acquired in the open market following the global offering; and (f) participate in tenders involving the acquisition of all of our outstanding ordinary shares. In addition, the lock-up provision will not restrict broker-dealers from engaging in market making and similar activities conducted in the ordinary course of their business.

Cowen and Company, LLC and BMO Capital Markets Corp., in their sole discretion, may release our ADS or ordinary shares and other securities subject to the lock-up agreements described above in whole or in part at any time. When determining whether or not to release our ADSs or ordinary shares and other securities from lock-up agreements, Cowen and Company, LLC and BMO Capital Markets Corp. will consider, among other factors, the holder’s reasons for requesting the release, the number of ADSs or ordinary shares for which the release is being requested, and market conditions at the time of the request. In the event of such a release or waiver for one of our directors or officers, Cowen and Company, LLC and BMO Capital Markets Corp. shall provide us with notice of the impending release or waiver at least three business days before the effective date of such release or waiver and we will announce the impending release or waiver by issuing a press release at least two business days before the effective date of the release or waiver.

Electronic Offer, Sale and Distribution of ADSs and Ordinary Shares. A prospectus in electronic format may be made available on the websites maintained by one or more of the underwriters or selling group members, if any, participating in the global offering and one or more of the underwriters participating in the global offering may distribute prospectuses electronically. The representatives may agree to allocate a number of ADSs or ordinary shares to underwriters for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters that will make internet distributions on the same basis as other allocations. Other than the prospectus in electronic format, the information on these websites is not part of this prospectus or the registration statement of which this prospectus forms a part, has not been approved or endorsed by us or any underwriter in its capacity as underwriter, and should not be relied upon by investors.

Other Relationships. Certain of the underwriters and their affiliates have provided, and may in the future provide, various investment banking, commercial banking, and other financial services for us and our affiliates for which they have received, and may in the future receive, customary fees.

Selling Restrictions

No action has been taken in any jurisdiction except the United States that would permit a public offering of the ADSs or ordinary shares, or the possession, circulation, or distribution of this prospectus or any other material relating to us or the ADSs or ordinary shares in any jurisdiction where action for that purpose is required. Accordingly, neither the ADSs nor ordinary shares may not be offered or sold, directly or indirectly, and neither this prospectus nor any other offering material or advertisements in

connection with the ADSs and ordinary shares may be distributed or published, in or from any country or jurisdiction except in compliance with any applicable rules and regulations of any such country or jurisdiction.

Canada. The ADSs and ordinary shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the ADSs or ordinary shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, *provided* that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with the global offering.

United Kingdom. Each of the underwriters has represented and agreed that:

- it has not made or will not make an offer of the securities to the public in the United Kingdom within the meaning of section 102B of the Financial Services and Markets Act 2000 (as amended), or FSMA, except to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities or otherwise in circumstances which do not require the publication by us of a prospectus pursuant to the Prospectus Rules of the U.K. Financial Conduct Authority;
- it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of section 21 of FSMA) to persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that also are (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, or the Order, and/or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the Order and other persons to whom it may lawfully be communicated (each such person being referred to as a "relevant person"); and
- it has complied with and will comply with all applicable provisions of FSMA with respect to anything done by it in relation to the securities in, from or otherwise involving the United Kingdom.

In the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at, relevant persons. This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents. Any investment or investment activity to which this prospectus relates is available only to relevant persons and will be engaged in only with relevant persons.

Switzerland. The securities will not be offered, directly or indirectly, to the public in Switzerland and this prospectus does not constitute a public offering prospectus as that term is understood pursuant to article 652a or 1156 of the Swiss Federal Code of Obligations.

European Economic Area. In relation to each member state of the European Economic Area which has implemented the Prospectus Directive, or each referred as a Relevant Member State, an offer to the public of any ADSs or ordinary shares which are the subject of the global offering contemplated by this prospectus may not be made in that Relevant Member State except that an offer to the public in that Relevant Member State of any ADSs or ordinary shares may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

- to any legal entity which is a “qualified investor” as defined in the Prospectus Directive;
- to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the underwriters or the underwriters nominated by us for any such offer; or
- in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of ADSs or ordinary shares shall require us or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person located in a Relevant Member State to whom any offer of ADSs or ordinary shares is made or who receives any communication in respect of an offer of ADSs or ordinary shares, or who initially acquires any ADSs or ordinary shares will be deemed to have represented, warranted, acknowledged and agreed to and with each of the underwriters and us that (1) it is a “qualified investor” within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive; and (2) in the case of any ADSs or ordinary shares acquired by it as a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, the ADSs or ordinary shares acquired by it in the offer have not been acquired on behalf of, nor have they been acquired with a view to their offer or resale to, persons in any Relevant Member State other than qualified investors, as that term is defined in the Prospectus Directive, or in circumstances in which the prior consent of the underwriters or the underwriters nominated by us has been given to the offer or resale; or where ADSs or ordinary shares have been acquired by it on behalf of persons in any Relevant Member State other than qualified investors, the offer of those ADSs or ordinary shares to it is not treated under the Prospectus Directive as having been made to such persons.

The Company, the underwriters and their respective affiliates will rely upon the truth and accuracy of the foregoing representations, warranties, acknowledgments and agreements.

This prospectus has been prepared on the basis that any offer of ADSs or ordinary shares in any Relevant Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of securities. Accordingly any person making or intending to make an offer in that Relevant Member State of ADSs or ordinary shares which are the subject of the offering contemplated in this prospectus may only do so in circumstances in which no obligation arises for us or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither us nor the underwriters have authorized, nor do they authorize, the making of any offer of ADSs or ordinary shares in circumstances in which an obligation arises for the Company or the underwriters to publish a prospectus for such offer.

For the purposes of this provision, the expressions “offer ADSs to the public” in relation to our ADSs and “offer ordinary shares to the public” in relation to our ordinary shares in any Relevant

Member State means the communication in any form and by any means of sufficient information on the terms of the offer and our ADSs or ordinary shares to be offered so as to enable an investor to decide to purchase or subscribe to our ADSs or ordinary shares, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State, and the expression "Prospectus Directive" means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

Solely for the purposes of the product governance requirements contained within: (a) EU Directive 2014/65/EU on markets in financial instruments, as amended, or MiFID II; (b) Articles 9 and 10 of Commission Delegated Directive (EU) 2017/593 supplementing MiFID II; and (c) local implementing measures, together, the MiFID II Product Governance Requirements, and disclaiming all and any liability, whether arising in tort, contract or otherwise, which any "manufacturer" (for the purposes of the MiFID II Product Governance Requirements) may otherwise have with respect thereto, the ADSs and ordinary shares have been subject to a product approval process, which has determined that such securities are: (i) compatible with an end target market of retail investors and investors who meet the criteria of professional clients and eligible counterparties, each as defined in MiFID II; and (ii) eligible for distribution through all distribution channels as are permitted by MiFID II, or the Target Market Assessment. Notwithstanding the Target Market Assessment, "distributors" (for the purposes of the MiFID II Product Governance Requirements) should note that: the price of ADSs and ordinary shares may decline and investors could lose all or part of their investment; the ADSs and ordinary shares offer no guaranteed income and no capital protection; and an investment in ADSs and ordinary shares is compatible only with investors who do not need a guaranteed income or capital protection, who (either alone or in conjunction with an appropriate financial or other adviser) are capable of evaluating the merits and risks of such an investment and who have sufficient resources to be able to bear any losses that may result therefrom. The Target Market Assessment is without prejudice to the requirements of any contractual, legal or regulatory selling restrictions in relation to the offering.

For the avoidance of doubt, the Target Market Assessment does not constitute: (a) an assessment of suitability or appropriateness for the purposes of MiFID II; or (b) a recommendation to any investor or group of investors to invest in, or purchase, or take any other action whatsoever with respect to ADSs or the ordinary shares.

Each distributor is responsible for undertaking its own target market assessment in respect of the ADSs and the ordinary shares and determining appropriate distribution channels.

Israel. In the State of Israel this prospectus shall not be regarded as an offer to the public to purchase securities under the Israeli Securities Law, 5728 – 1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728 – 1968, including, inter alia, if: (i) the offer is made, distributed, or directed to not more than 35 investors, subject to certain conditions, or the Addressed Investors; or (ii) the offer is made, distributed, or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728 – 1968, subject to certain conditions, the Qualified Investors. The Qualified Investors shall not be taken into account in the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. We have not and will not take any action that would require us to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728 – 1968. We have not and will not distribute this prospectus or make, distribute, or direct an offer to subscribe for our securities to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728 – 1968. In particular, we may request, as a condition to be offered our securities, that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728 – 1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728 – 1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728 – 1968 and the regulations promulgated thereunder in connection with the offer to be issued securities; (iv) that the securities that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728 – 1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728 – 1968; and (v) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor's name, address, and passport number or Israeli identification number.

Hong Kong. The contents of this document have not been reviewed or approved by any regulatory authority in Hong Kong. This document does not constitute an offer or invitation to the public in Hong Kong to acquire securities. Accordingly, unless permitted by the securities laws of Hong Kong, no person may issue or have in its possession for the purposes of issue, this document or any advertisement, invitation or document relating to the securities, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong other than in relation to shares which are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" (as such term is defined in the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong, or SFO) and the subsidiary legislation made thereunder); or in circumstances which do not result in this document being a "prospectus" as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32, Laws of Hong Kong, or CO); or which do not constitute an offer or an invitation to the public for the purposes of the SFO or the CO. The offer of the shares is personal to the person to whom this document has been delivered, and a subscription for shares will only be accepted from such person. No person to whom a copy of this document is issued may issue, circulate, or distribute this document in Hong Kong, or make or give a copy of this document to any other person. You are advised to exercise caution in relation to the offer. If you are in any doubt about any of the contents of this document, you should obtain independent professional advice.

Singapore. This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the ADSs or ordinary shares may not be circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor pursuant to Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or SFA, (ii) to a relevant person (as defined in Section 275(2) of the SFA), or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the ADSs or ordinary shares are subscribed or purchased pursuant to an offer made in reliance on Section 275 of the SFA by a relevant person which is:

- (a) a corporation (which is not an accredited investor) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

- (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor;

shares, debentures, and units of shares and debentures of that corporation, or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferable for six months after that corporation or that trust has acquired the shares under Section 275 except:

(1) to an institutional investor or to a relevant person (as defined in Section 275(2) of the SFA), or any person pursuant to Section 275(1A) of the SFA (in the case of that corporation) or Section 276(4)(i)(B) of the SFA (in the case of that trust);

(2) where no consideration is or will be given for the transfer; or

(3) where the transfer is by operation of law.

EXPENSES OF THE OFFERING

We estimate that our expenses in connection with the global offering, other than underwriting discounts and commissions, will be as follows:

Expenses	Amount
Securities and Exchange Commission registration fee	\$ 10,022
FINRA filing fee	12,575
The Nasdaq listing fee	150,000
AIM admission fee	22,940
Printing and engraving expenses	500,000
Legal fees and expenses	1,627,402
Accounting fees and expenses	511,004
Miscellaneous costs	266,057
Total	<u>\$ 3,100,000</u>

All amounts in the table are estimates except the SEC registration fee, the Nasdaq listing fee, and the FINRA filing fee. We will pay all of the expenses of the global offering.

LEGAL MATTERS

The validity of our ADSs and ordinary shares and certain other matters of English law and U.S. federal law will be passed upon for us by Latham & Watkins LLP. Cooley LLP is serving as legal counsel for the underwriters in connection with the global offering with respect to matters of English law and U.S. federal law.

EXPERTS

The consolidated financial statements of Mereo BioPharma Group plc at December 31, 2016 and 2017, and for each of the two years in the period ended December 31, 2017, appearing in this Prospectus and Registration Statement have been audited by Ernst & Young LLP, an independent registered public accounting firm, as set forth in their report thereon appearing elsewhere herein, and are included in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

The registered business address of Ernst & Young LLP is Apex Plaza, Reading RG1 1YE, United Kingdom.

SERVICE OF PROCESS AND ENFORCEMENT OF LIABILITIES

We are incorporated and currently existing under the laws of England and Wales. In addition, most of our directors and officers reside outside of the United States and most of the assets of our subsidiaries are located outside of the United States. As a result, it may be difficult for investors to effect service of process on us or those persons in the United States or to enforce in the United States judgments obtained in United States courts against us or those persons based on the civil liability or other provisions of the United States securities laws or other laws.

In addition, uncertainty exists as to whether the courts of England and Wales would:

- recognize or enforce judgments of United States courts obtained against us or our directors or officers predicated upon the civil liabilities provisions of the securities laws of the United States or any state in the United States; or
- entertain original actions brought in England and Wales against us or our directors or officers predicated upon the securities laws of the United States or any state in the United States.

We have been advised by Latham & Watkins LLP that there is currently no treaty between (i) the United States and (ii) England and Wales providing for reciprocal recognition and enforcement of judgments of United States courts in civil and commercial matters (although the United States and the United Kingdom are both parties to the New York Convention on the Recognition and Enforcement of Foreign Arbitral Awards) and that a final judgment for the payment of money rendered by any general or state court in the United States based on civil liability, whether or not predicated solely upon the United States securities laws, would not be automatically enforceable in England and Wales. We have also been advised by Latham & Watkins LLP that any final and conclusive monetary judgment for a definite sum obtained against us in United States courts would be treated by the courts of England and Wales as a cause of action in itself and sued upon as a debt at common law so that no retrial of the issues would be necessary, provided that:

- the relevant U.S. court had jurisdiction over the original proceedings according to English conflicts of laws principles at the time when proceedings were initiated;
- England and Wales courts had jurisdiction over the matter on enforcement and we either submitted to such jurisdiction or were resident or carrying on business within such jurisdiction and were duly served with process;
- the U.S. judgment was final and conclusive on the merits in the sense of being final and unalterable in the court that pronounced it and being for a definite sum of money;
- the judgment given by the courts was not in respect of penalties, taxes, fines, or similar fiscal or revenue obligations (or otherwise based on a U.S. law that an English court considers to relate to a penal, revenue or other public law);
- the judgment was not procured by fraud;
- the judgment was not obtained following a breach of a jurisdictional or arbitration clause, unless with the agreement of the defendant or the defendant's subsequent submission to the jurisdiction of the court;
- recognition or enforcement of the judgment in England and Wales would not be contrary to public policy or the Human Rights Act 1998;
- the proceedings pursuant to which judgment was obtained were not contrary to natural justice;
- the U.S. judgment was not arrived at by doubling, trebling, or otherwise multiplying a sum assessed as compensation for the loss or damages sustained and not being otherwise in breach of Section 5 of the UK Protection of Trading Interests Act 1980, or is a judgment based on measures designated by the Secretary of State under Section 1 of that Act;

- there is not a prior decision of an English court or the court of another jurisdiction on the issues in question between the same parties; and
- the English enforcement proceedings were commenced within the limitation period.

Whether these requirements are met in respect of a judgment based upon the civil liability provisions of the United States securities laws, including whether the award of monetary damages under such laws would constitute a penalty, is an issue for the court making such decision.

Subject to the foregoing, investors may be able to enforce in England and Wales judgments in civil and commercial matters that have been obtained from U.S. federal or state courts. Nevertheless, we cannot assure you that those judgments will be recognized or enforceable in England and Wales.

If an English court gives judgment for the sum payable under a U.S. judgment, the English judgment will be enforceable by methods generally available for this purpose. These methods generally permit the English court discretion to prescribe the manner of enforcement. In addition, it may not be possible to obtain an English judgment or to enforce that judgment if the judgment debtor is or becomes subject to any insolvency or similar proceedings, or if the judgment debtor has any set-off or counterclaim against the judgment creditor. Also note that, in any enforcement proceedings, the judgment debtor may raise any counterclaim that could have been brought if the action had been originally brought in England unless the subject of the counterclaim was in issue and denied in the U.S. proceedings.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement (including amendments and exhibits to the registration statement) on Form F-1 under the Securities Act. This prospectus, which is part of the registration statement, does not contain all of the information set forth in the registration statement and the exhibits and schedules to the registration statement. For further information, we refer you to the registration statement and the exhibits and schedules filed as part of the registration statement. If a document has been filed as an exhibit to the registration statement, we refer you to the copy of the document that has been filed. Each statement in this prospectus relating to a document filed as an exhibit is qualified in all respects by the filed exhibit.

Upon completion of the U.S. offering, we will become subject to the informational requirements of the Exchange Act. Accordingly, we will be required to file reports and other information with the SEC, including annual reports on Form 20-F and reports on Form 6-K. You may inspect and copy reports and other information filed with the SEC at the Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Information on the operation of the Public Reference Room may be obtained by calling the SEC at 1-800-SEC-0330. In addition, the SEC maintains an Internet website that contains reports and other information about issuers, like us, that file electronically with the SEC. The address of that website is www.sec.gov.

As a foreign private issuer, we are exempt under the Exchange Act from, among other things, the rules prescribing the furnishing and content of proxy statements, and our board members, executive officers, and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we will not be required under the Exchange Act to file periodic reports and financial statements with the SEC as frequently or as promptly as U.S. companies whose securities are registered under the Exchange Act.

We will send our transfer agent a copy of all notices of our general meetings of shareholders and other reports, communications, and information that are made generally available to shareholders. The transfer agent has agreed to mail to all shareholders a notice containing the information (or a summary of the information) contained in any notice of a meeting of our shareholders received by the transfer agent and will make available to all shareholders such notices and all such other reports and communications received by the transfer agent.

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Report of Independent Registered Public Accounting Firm

The Shareholders and Board of Directors of Mereo BioPharma Group plc

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Mereo BioPharma Group plc (the “Company”) as of December 31, 2017 and 2016, and the related consolidated statements of comprehensive loss, changes in equity, and cash flows for each of the two years in the period ended December 31, 2017, and 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 at December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2017, in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the 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 the Company's internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2015
Reading, United Kingdom
February 27, 2018

**Consolidated statement of comprehensive loss
for the years ended December 31, 2016 and 2017**

	<u>Notes</u>	Year ended December 31, 2016 £	Year ended December 31, 2017 £
Research and development expenses		(24,562,502)	(34,606,649)
General and administrative expenses		(11,616,816)	(10,697,194)
Operating loss		(36,179,318)	(45,303,843)
Finance income	7	374,906	826,855
Finance charge	7	(179,765)	(1,089,925)
Net foreign exchange gain/(loss)		2,262,626	(1,384,225)
Net loss before tax		(33,721,551)	(46,951,138)
Taxation	9	5,331,271	8,152,084
Loss attributable to equity holders of the Company		(28,390,280)	(38,799,054)
Total comprehensive loss for the year, attributable to the equity holders of the Company		(28,390,280)	(38,799,054)
Basic and diluted loss per share	10	(0.63)	(0.56)

The accompanying notes form an integral part of these consolidated financial statements.

**Consolidated balance sheet
as at December 31, 2016 and 2017**

	Notes	December 31, 2016 £	December 31, 2017 £
Assets			
Non-current assets			
Property, plant and equipment	11	173,869	153,361
Intangible assets	12	25,812,941	33,005,229
		<u>25,986,810</u>	<u>33,158,590</u>
Current assets			
Prepayments		1,102,146	1,970,781
R&D tax credits	9	5,331,271	8,152,084
Other receivables	14	767,009	509,350
Short-term investments	16	—	2,500,000
Cash and short-term deposits	15	53,577,571	50,044,672
		<u>60,777,997</u>	<u>63,176,887</u>
Total assets		<u>86,764,807</u>	<u>96,335,477</u>
Equity and liabilities			
Equity			
Issued capital	17	193,022	213,285
Share premium	17	99,975,399	118,226,956
Other capital reserves	17	12,667,562	16,359,169
Other reserves	17	7,000,000	7,000,000
Accumulated loss		<u>(40,579,241)</u>	<u>(79,315,920)</u>
Total equity		<u>79,256,742</u>	<u>62,483,490</u>
Non-current liabilities			
Provisions	19	1,172,420	4,075,386
Interest bearing loans and borrowings	18	3,126,526	18,812,511
Warrant Liability	20	—	1,346,484
		<u>4,298,946</u>	<u>24,234,381</u>
Current liabilities			
Trade and other payables	21	1,121,107	3,024,026
Accruals		2,088,012	4,379,774
Provisions	19	—	274,000
Interest bearing loans and borrowings	18	—	1,939,806
Total liabilities		<u>7,508,065</u>	<u>33,851,987</u>
Total equity and liabilities		<u>86,764,807</u>	<u>96,335,477</u>

The accompanying notes form an integral part of these consolidated financial statements.

**Consolidated statement of cash flows
for the years ended December 31, 2016 and 2017**

	Notes	December 31, 2016 £	December 31, 2017 £
Operating activities			
Loss before tax		(33,721,551)	(46,951,138)
Adjustments to reconcile loss before tax to net cash flows:			
Depreciation of property, plant and equipment, net of disposals	11	32,940	36,076
Share-based payment expense	24	6,494,018	3,651,898
Net foreign exchange (gain)/loss		(2,262,626)	1,384,225
Provision for social security contributions on employee share options		1,031,109	1,115,966
Interest earned	7	(374,906)	(826,855)
Loss on short-term deposits	7	—	338,279
Accrued interest on convertible loan		179,765	103,115
Transaction costs on bank loan	7	—	200,000
Interest on bank loan	7	—	327,123
Accreted interest on bank loan	7	—	66,935
Warrant fair value adjustment	7	—	54,473
Working capital adjustments:			
Increase in receivables		(1,219,202)	(839,751)
(Decrease)/Increase in payables and accruals		(768,402)	3,860,412
Tax credit received		946,681	5,331,271
Net cash flows used in operating activities		(29,662,174)	(32,147,971)
Investing activities			
Purchase of property, plant and equipment	11	(3,467)	(15,568)
Purchase of licence	12	—	(2,280,000)
Disposal of property, plant and equipment	11	1,175	—
Short-term investments	16	—	(2,500,000)
Interest earned		374,906	1,051,620
Net cash flows provided by investing activities		372,614	(3,743,948)
Financing activities			
Proceeds from issue of ordinary shares	17	67,888,820	15,000,000
Transaction costs on issue of ordinary shares	17	(2,995,864)	(729,632)
Proceeds from issue of convertible loan	18a	3,463,563	—
Proceeds from issue of bank loan	18b	—	20,000,000
Transaction costs on bank loan		—	(200,000)
Interest paid on bank loan		—	(327,123)
Net cash flows provided by financing activities		68,356,519	33,743,245
Net increase in cash and cash equivalents		39,066,959	(2,148,674)
Cash and cash equivalents at January 1		12,247,986	53,577,571
Effect of exchange rates changes on cash and cash equivalents		2,262,626	(1,384,225)
Cash and cash equivalents at December 31	15	<u>53,577,571</u>	<u>50,044,672</u>

The accompanying notes form an integral part of these consolidated financial statements.

**Consolidated statement of changes in equity
for the years ended December 31, 2016 and 2017**

	Issued capital £	Share premium £	Other capital reserves £	Other reserves £	Accumulated loss £	Total equity £
At January 1, 2016	<u>59,221</u>	<u>26,212,880</u>	<u>21,660,105</u>	<u>—</u>	<u>(12,188,961)</u>	<u>35,743,245</u>
Total comprehensive loss for the year	—	—	—	—	(28,390,280)	(28,390,280)
Issue of share capital (Note 17)	107,709	67,781,112	—	—	—	67,888,821
Share-based payments – share options (Note 24)	—	—	6,185,067	—	—	6,185,067
Share-based payments – LTIPS (Note 24)	—	—	133,601	—	—	133,601
Share-based payments – deferred bonus shares (Note 24)	—	—	175,350	—	—	175,350
Issue of share capital (Note 17)	26,092	15,977,271	(16,003,363)	—	—	—
Equity element of convertible loan (Note 18a)	—	—	516,802	—	—	516,802
Share capital reduction (Note 17)	—	(7,000,000)	—	7,000,000	—	—
Transaction costs on issuance of share capital (Note 17)	—	(2,995,864)	—	—	—	(2,995,864)
At December 31, 2016	<u>193,022</u>	<u>99,975,399</u>	<u>12,667,562</u>	<u>7,000,000</u>	<u>(40,579,241)</u>	<u>79,256,742</u>
Total comprehensive loss for the year	—	—	—	—	(38,799,054)	(38,799,054)
Share-based payments – share options (Note 24)	—	—	3,027,963	—	—	3,027,963
Share-based payments – LTIP (Note 24)	—	—	298,287	—	—	298,287
Share-based payments – DBSP (Note 24)	—	—	325,648	—	—	325,648
Share-based payments – Deferred equity consideration (Note 24)	—	—	1,331,288	—	—	1,331,288
Issue of share capital on April, 4 2017 (Note 17)	15,125	14,984,875	—	—	—	15,000,000
Issue of share capital on conversion of loan note (Note 17)	1,899	1,396,654	—	—	—	1,398,553
Issue of share capital for Novartis bonus shares (Note 17)	1,766	1,081,133	(1,082,899)	—	—	—
Equity element of convertible loan (Note 18a)	—	—	(208,680)	—	—	(208,680)
Conversion of convertible loan (Note 18a)	—	—	—	—	62,375	62,375
Issue of share capital on October, 31 2017 (Note 17)	1,473	1,518,527	—	—	—	1,520,000
Transaction costs on issuance of share capital (Note 17)	—	(729,632)	—	—	—	(729,632)
At December 31, 2017	<u>213,285</u>	<u>118,226,956</u>	<u>16,359,169</u>	<u>7,000,000</u>	<u>(79,315,920)</u>	<u>62,483,490</u>

The accompanying notes form an integral part of these consolidated financial statements.

Notes to the consolidated financial statements

1. Corporate information

Mereo BioPharma Group plc (the “Company”) is multi-asset biopharmaceutical company focused on the acquisition, development and commercialization of innovative therapeutics that aim to improve outcomes for patients with rare and specialty diseases.

We are a public limited company incorporated and domiciled in the United Kingdom, and registered in England, with our shares publicly traded on the Alternative Investment Market of the London Stock Exchange. Our registered office is located at Fourth Floor, 1 Cavendish Place, London W1G 0QF.

The consolidated financial statements of Mereo BioPharma Group plc and its subsidiaries (collectively, the “Group”) for the year ended December 31, 2017 were authorised for issue in accordance with a resolution of the Directors on February 26, 2017.

2. Significant accounting policies

2.1 Basis of preparation

The consolidated financial statements have been prepared in accordance with International Financial Reporting Standards (“IFRS”) as issued by the International Accounting Standards Board (“IASB”).

These financial statements are presented in pounds sterling (“Sterling”).

2.2 Revision of previously issued financial statements

We have reclassified the capital reduction undertaken in 2016 resulting in the reduction of the accumulated loss by £7.0 million and the crediting a new Other reserves by the same amount as set out in the Consolidated balance sheet and in the Consolidated statement of changes in equity.

2.3 Going concern

Though the Group continues to incur losses, the Directors believe it is appropriate to prepare the financial information on the going concern basis. This is because the Group's development of its products continues to progress according to plan and the funding secured to date will allow it to meet its liabilities as they fall due for at least 12 months from the date of authorisation for the issue of these consolidated financial statements.

2.4 Basis of consolidation

The consolidated financial information comprises the financial statements of Mereo BioPharma Group plc and its subsidiaries as at December 31, 2017. Subsidiaries are all entities over which the Group has control. The Group controls an entity when the Group is exposed to, or has rights to, variable returns from its involvement with the entity and has the ability to affect those returns through its power over the entity.

Subsidiaries are fully consolidated from the date on which control is transferred to the Group. They are deconsolidated from the date that control ceases. Intercompany transactions, balances and unrealised gains on transactions between Group companies are eliminated in preparing the consolidated financial statements. Accounting policies of subsidiaries are consistent with the policies adopted by the Group.

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The Group has an employee share trust to facilitate share transactions pursuant to certain employee share plans. Although the trust is a separate legal entity from the Group, it is consolidated into the Group's results in accordance with the IFRS 10 "Consolidated Financial Statements" rules on special purpose vehicles. The Group is deemed to control the trust principally because the trust cannot operate without the funding the Group provides.

All Group subsidiaries prepare yearly financial information to December 31 consistent with the Company.

2.5 Changes of accounting policies

a) Segment reporting

Effective in the third quarter of 2017 and following the completion of the exclusive license agreement with AstraZeneca for AZD- 9668, the Company has revised its policy and now reports as a single operating segment (See Note 4).

b) Other reserves

Other reserves arose on reduction of share premium. These reserves are available for distribution to shareholders in the future at a time when the Company has sufficient accumulated realized profits to make a distribution.

2.6 Summary of significant accounting policies

a) Taxation

Current income tax

Current income tax assets and liabilities are measured at the amount expected to be recovered from or paid to the taxation authorities, and include R&D tax credits receivable under the HM Revenue and Customs ("HMRC") small or medium enterprise ("SME") scheme, which provides additional taxation relief for qualifying expenditure on R&D activities, and allows for the surrender of tax losses in exchange for a cash payment from HMRC.

Current income tax relating to items recognized directly in equity is recognized in equity and not in the statement of comprehensive loss.

Income tax credit

The Company benefits from the U.K. research and development tax credit regime whereby a portion of the Company's losses can be surrendered for a cash rebate of up to 33.35% of eligible expenditures. Such credits are accounted for within the tax provision, in the year in which the expenditures were incurred.

Deferred tax

Deferred tax is provided using the liability method on temporary differences between the tax bases of assets and liabilities and their carrying amounts for financial reporting purposes at the reporting date.

Deferred income tax assets are recognized for all deductible temporary differences, carry-forward of unused tax credits and unused tax losses, to the extent that it is probable that taxable profit will be available against which the deductible temporary differences and the carry-forward of unused tax credits and unused tax losses can be utilised. The carrying amount of deferred income tax assets is reviewed at the end of each reporting period and reduced to the extent that it is no longer probable that

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sufficient taxable profit will be available to allow all or part of the deferred income tax asset to be utilised. Unrecognized deferred income tax assets are reassessed at the end of each reporting period and are recognized to the extent that it has become probable that future taxable profit will allow the deferred tax asset to be recovered.

Deferred tax assets and liabilities are measured on an undiscounted basis at the tax rates that are expected to apply to the year when the asset is realised, based on tax rates (and tax laws) enacted or substantively enacted at the end of the reporting period.

b) Foreign currencies

The functional currency of the Company and its subsidiaries is Sterling. Transactions in foreign currencies are initially recorded by the Group's entities at the rate ruling on the date the transaction first qualifies for recognition.

Differences arising on settlement or translation of monetary items are recognized in profit or loss.

Gains or losses on the retranslation of foreign currency balances at the year end are recognized in the consolidated statement of comprehensive loss under net foreign exchange gain.

c) Property, plant and equipment

Property, plant and equipment is stated at cost, net of accumulated depreciation and accumulated impairment losses, if any. Such cost includes the cost of replacing part of the plant and equipment if the recognition criteria are met. All other repair and maintenance costs are recognized in profit or loss as incurred.

Depreciation is calculated on a straight-line basis over the estimated useful lives of the assets, as follows:

- Leasehold improvements ten years
- Office equipment five years
- IT equipment three years

An item of property, plant and equipment and any significant part initially recognized is derecognized upon disposal or when no future economic benefits are expected from its use or disposal. Any gain or loss arising on derecognition of the asset (calculated as the difference between the net disposal proceeds and the carrying amount of the asset) is included in the statement of comprehensive loss when the asset is derecognized.

The residual values, useful lives and methods of depreciation of property, plant and equipment are reviewed at each financial year end and adjusted prospectively, if appropriate.

d) Leases

Leases in which a significant portion of the risks and rewards of ownership are retained by the lessor are classified as operating leases. Payments made under operating leases (net of any incentives received from the lessor) are charged to the statement of comprehensive loss on a straight-line basis over the period of the lease.

The Group leases its premises. The Group recognizes any lease incentives on a straight-line basis over the entire period of the lease, assuming that any break clauses available will not be exercised. By not exercising any break clauses, the Group receives a 50% rent discount from the landlord for a fixed period of time.

The determination of whether an arrangement is, or contains, a lease is based on the substance of the arrangement at the inception date. The arrangement is assessed for whether fulfilment of the arrangement is dependent on the use of a specific asset or assets or the arrangement conveys a right to use the asset or assets, even if that right is not explicitly specified in an arrangement.

e) Intangible assets

Intangible assets, relating to intellectual property rights acquired through licensing or assigning patents and knowhow, are initially recognized at cost which has been determined as the fair value of the consideration paid and payable. Consideration comprises cash paid together with the net present value of any provision for deferred cash consideration (see Note 2p) and the fair value of consideration settled in shares. The fair value of consideration is regularly reviewed based on the probability of achieving the contractual milestones. Where share transfer occurs, the cost is measured at fair value of the shares issued or to be issued in accordance with IFRS 2. Intangible assets are held at cost less accumulated amortization and provision for impairment, if any. Where a finite useful life of the acquired intangible asset cannot be determined or the intangible asset is not yet available for use, the asset is tested annually for impairment by allocating the assets to the cash-generating units to which they relate. Amortization would commence when product candidates underpinned by the intellectual property rights become available for commercial use. No amortization has been charged to date, as the product candidates underpinned by the intellectual property rights are not yet available for commercial use.

f) Fair value measurement

Fair value is the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. The fair value measurement is based on the presumption that the transaction to sell the asset or transfer the liability takes place either:

- In the principal market for the asset or liability
- Or
- In the absence of a principal market, in the most advantageous market for the asset or liability

The principal or the most advantageous market must be accessible by the Group.

The fair value of an asset or a liability is measured using the assumptions that market participants would use when pricing the asset or liability, assuming that market participants act in their economic best interest.

The Group uses valuation techniques that are appropriate in the circumstances and for which sufficient data are available to measure fair value, maximising the use of relevant observable inputs and minimising the use of unobservable inputs.

All assets and liabilities for which fair value is measured or disclosed in the financial statements are categorised within the fair value hierarchy, described as follows, based on the lowest level input that is significant to the fair value measurement as a whole:

- Level 1 — Quoted (unadjusted) market prices in active markets for identical assets or liabilities
- Level 2 — Valuation techniques for which the lowest level input that is significant to the fair value measurement is directly or indirectly observable
- Level 3 — Valuation techniques for which the lowest level input that is significant to the fair value measurement is unobservable

For assets and liabilities that are recognized in the financial statements on a recurring basis, the Group determines whether transfers have occurred between levels in the hierarchy by re-assessing categorisation (based on the lowest level input that is significant to the fair value measurement as a whole) at the end of each reporting period.

g) Impairment of non-financial assets

Further disclosures relating to impairment of non-financial assets are also provided in the following notes:

- Disclosures for significant assumptions Note 3
- Property, plant and equipment Note 11
- Intangible assets not yet available for use Notes 12 and 13

The Group assesses, at each reporting date, whether there is an indication that an asset may be impaired. If any indication exists, or when annual impairment testing for an asset is required, the Group estimates the asset's recoverable amount. An asset's recoverable amount is the higher of an asset's or cash-generating unit's ("CGU") fair value less costs of disposal and its value in use. The recoverable amount is determined for an individual asset, unless the asset does not generate cash inflows that are largely independent of those from other assets or groups of assets. When the carrying amount of an asset or CGU exceeds its recoverable amount, the asset is considered impaired and is written down to its recoverable amount.

In assessing value in use, the estimated future cash flows are discounted to their present value using a pre-tax discount rate that reflects current market assessments of the time value of money and the risks specific to the asset. In determining fair value less costs of disposal, recent market transactions are taken into account. If no such transactions can be identified, an appropriate valuation model is used. These calculations are corroborated by valuation multiples, quoted share prices for publicly traded companies or other available fair value indicators.

Impairment losses are recognized in the statement of comprehensive loss in expense categories consistent with the function of the impaired asset.

An assessment is made at each reporting date to determine whether there is an indication that previously recognized impairment losses no longer exist or have decreased. If such indication exists, the Group estimates the asset's or CGU's recoverable amount. A previously recognized impairment loss is reversed only if there has been a change in the assumptions used to determine the asset's recoverable amount since the last impairment loss was recognized. The reversal is limited so that the carrying amount of the asset does not exceed its recoverable amount, nor exceed the carrying amount that would have been determined, net of depreciation, had no impairment loss been recognized for the asset in prior years. Such reversal is recognized in the statement of comprehensive loss unless the asset is carried at a revalued amount, in which case the reversal is treated as a revaluation increase.

Intangible assets not yet available for use are tested for impairment annually as at December 31 at the CGU level, as appropriate, and when circumstances indicate that the carrying value may be impaired. An impairment test was performed at December 31, 2017.

h) Cash and short-term deposits

Cash and short-term deposits in the balance sheet comprise cash at banks and on hand and short-term deposits with a maturity of three months or less, which are subject to an insignificant risk of changes in value.

i) Short-term investments

Cash on deposit for terms greater than three months are recognized at fair value in the balance sheet.

j) Provisions

Provisions are recognized when the Group has a present obligation (legal or constructive) as a result of a past event, it is probable that an outflow of resources embodying economic benefits will be required to settle the obligation and a reliable estimate can be made of the amount of the obligation. When the Group expects some or all of a provision to be reimbursed, for example, under an insurance contract, the reimbursement is recognized as a separate asset, but only when the reimbursement is virtually certain. The expense relating to a provision is presented in the statement of comprehensive loss net of any reimbursement.

If the effect of the time value of money is material, provisions are discounted using a current pre-tax rate that reflects, when appropriate, the risks specific to the liability. When discounting is used, the increase in the provision due to the passage of time is recognized as a finance cost.

k) Share-based payments

Employees (including Executive Officers) of the Group receive remuneration in the form of share-based payments, whereby employees render services as consideration for equity instruments (equity-settled transactions).

Incentives in the form of shares are provided to employees under the Share Option Plan. Executive Officers are also provided with shares under a deferred bonus share plan ("DBSP Plan") and a long-term incentive plan ("LTIP Plan"). In accordance with IFRS 2 "Share-based Payment" ("IFRS 2"), charges for these incentives are expensed through the consolidated statement of comprehensive loss on a straight-line basis over their vesting period, based on the Group's estimate of shares that will eventually vest. The total amount to be expensed is determined by reference to the fair value of the options or awards at the date they were granted. For LTIP shares, the fair value excludes the impact of any non-market vesting conditions. The fair value of LTIP shares, which have market conditions attached, includes an adjustment based on the probability of the shares vesting at the end of the vesting period.

Under the 2015 plan, options were historically awarded to employees, non-executive directors and certain consultants. Share options awarded to non-employees under the 2015 plan are accounted for as for options awarded to employees as the value of non-employee services could be readily determined.

In accordance with IFRS 2, the cancellation of share options is accounted for as an acceleration of the vesting period and therefore any amount unrecognized that would otherwise have been charged in future accounting periods is recognized immediately. When options are forfeited, the accounting expense for any unvested awards is reversed.

Purchases, where consideration is satisfied by issuing equity shares, are accounted for as equity-settled share-based payment transactions in accordance with IFRS 2. Fair value is determined by the share price at the date of purchase.

l) Costs of issuing capital

The Group deducts directly attributable costs of issuing capital from the proceeds in accordance with IAS 39 "Financial Instruments: Recognition and Measurement". Incremental costs incurred and directly attributable to the offering of equity securities are deducted from the related proceeds of the offering. The net amount is recorded as share premium in the period when such shares are issued. Where such expenses are incurred prior to the offering they are recorded in prepayments until the offering completes. Other costs incurred in such offerings are expensed as incurred and included in general and administrative expenses.

m) Convertible loan instrument

Convertible loan notes are regarded as compound instruments consisting of a liability component and an equity component. At the date of issue the fair value of the liability component is estimated using a discount rate for an equivalent liability without the conversion feature. The difference between the proceeds of issue of the convertible loan note and the fair value assigned to the liability component, representing the embedded option to convert the liability into equity of the Group, is included in equity.

An exchange between an existing borrower and lender of debt instruments with 'substantially different' terms are accounted for as an extinguishment of the original financial liability and the recognition of a new financial liability as per IAS 39 and IFRS 9. Similarly, a substantial modification of the terms of an existing financial liability, or a part of it, (whether or not due to the financial difficulty of the debtor) should be accounted for as an extinguishment of the original financial liability and the recognition of a new financial liability.

In line with IAS 39 the terms of exchanged or modified debt are regarded as 'substantially different' if the net present value of the cash flows under the new terms (including any fees paid net of any fees received) discounted at the original effective interest rate is at least 10% different from the discounted present value of the remaining cash flows of the original debt instrument. Where such modifications are less than 10% different, the effective interest rate is adjusted to take account of the new terms.

n) Employee Benefit Trust

The Group operates an Employee Benefit Trust ("EBT"): Mereo BioPharma Group plc Employee Benefit Trust.

The EBT has been established to fulfil awards made under the Deferred Share Bonus Plan and the Long Term Incentive Plan. The EBT is a Jersey-based trust which is funded by a loan from the Company, which it will utilise to buy shares at nominal value from the Company in sufficient quantity to fulfil the envisaged awards. The EBT will acquire shares in the Company and these will be deducted from the shareholders' funds on the consolidated balance sheet at the cost of acquisition less proceeds on disposal.

In compliance with IAS 32 "Financial Instruments: Presentation" Group, shares held by the EBT are included in the consolidated balance sheet as a reduction in equity. Gains and losses on Group shares are recognized directly in equity.

The Group consolidated accounts treat the EBT as a wholly owned subsidiary company. Residual cash within the EBT is classified as a debtor (restricted cash) since it is not readily accessible by the Group.

o) Research and development costs

Expenditure on product development is capitalised as an intangible asset and amortised over the expected useful economic life of the product candidate concerned. Capitalisation commences from the point at which technical feasibility and commercial viability of the product candidate can be demonstrated and the Group is satisfied that it is probable that future economic benefits will result from the product candidate once completed. Capitalisation ceases when the product candidate receives regulatory approval for launch. No such costs have been capitalised to date.

Expenditure on research and development activities that do not meet the above criteria, including ongoing costs associated with acquired intellectual property rights and intellectual property rights

generated internally by the Group, is charged to the statement of comprehensive loss as incurred. Intellectual property and in-process research and development from asset acquisitions are recognized as intangible assets at cost.

p) Provisions for deferred cash consideration

Provisions for deferred cash consideration consist of future payments which are contractually committed but not yet certain. In respect of products which are not yet approved such deferred cash consideration excludes potential downstream milestones, royalties or other payments as these are deemed to be so uncertain as to be unquantifiable. Deferred cash consideration is recognized as a liability with the amounts calculated as the risk adjusted net present value of anticipated deferred payments.

The provision is reviewed at each balance sheet date and adjusted based on the likelihood of contractual milestone(s) being achieved and therefore the deferred payment being settled. Increases in the provision relating to changes in the probability are recognized as an intangible asset. Increases in the provision relating to the unwinding of the time value of money are recognized as a finance expense.

q) Bank loan and associated warrants

After initial recognition, interest-bearing loans and borrowings are subsequently measured at amortized cost using the effective interest rate (EIR) method. The EIR amortization is included as a finance charge in the statement of comprehensive loss. This category applies to interest-bearing borrowings, trade and other payables.

Associated warrants are measured at fair value with changes recorded through the statement of comprehensive loss (see note 20).

3. Significant accounting judgements, estimates and assumptions

The preparation of the consolidated accounts requires the management of the Group to make estimates and judgements that affect the reported amounts of assets, liabilities, revenues and expenses. The Group bases its estimates and judgements on historical experience and on various other assumptions that it considers to be reasonable. Actual results may differ from these estimates under different assumptions or conditions.

Share-based compensation

Incentives in the form of shares are provided to employees under a share option plan, long term incentive plan and deferred share bonus plan. The fair value of the employee services received in exchange for the grant of the options is recognized as an expense. The expense is based upon a number of assumptions disclosed in Note 24. The selection of different assumptions could affect the results of the Group.

Impairment of intangible assets and property, plant and equipment

An assessment was made in respect of indicators of impairment in the carrying value of the Group's intangible assets (see Note 13) and leasehold improvements, office equipment and IT equipment as at December 31, 2017. If such an indication exists, the recoverable amount of the asset, being the higher of the asset's fair value less costs to sell and value in use, is compared to the asset's carrying value. Any excess of the asset's carrying value over its recoverable amount is expensed to the income statement. The assessment of intangible assets involves a number of judgements regarding the likelihood of successful product approval, the costs of reaching approval and the subsequent commercial profitability of the product once approved.

Deferred license consideration

Deferred consideration in the form of cash is recognized as a provision at each balance sheet date, to the extent its amount is quantifiable at the inception of the arrangement. The amount provided is based on a number of judgements regarding the timing and progress of the related research. Deferred consideration in the form of shares is recognized as a share-based payment when it is probable that shares will be transferred.

Bank loan and associated warrants

As part of the bank loan, the Group has issued warrants to subscribe for shares. The fair value of the warrants issued is assessed at each balance sheet date based upon a number of assumptions, as disclosed in Note 20.

4. Segment information

The consolidation of product candidates into a single segment follows management's view of the business as a single portfolio of product candidates. Research and development ("R&D") expenses only are monitored at a product candidate level, however the Chief Operating Decision Maker ("CODM") makes decisions over resource allocation at an overall portfolio level. The Group's financing is managed and monitored on a consolidated basis. All non-current assets held by the Group are located in the United Kingdom.

The Company's CODM is the Executive Management team (comprised of the Chief Executive Officer, Chief Financial Officer, Chief Medical Officer, General Counsel and the Head of Corporate Development) which manages the operating results of the business.

5. Group information

Information about subsidiaries

The consolidated financial statements of the Group include:

Name	Principal activities	Country of incorporation	% equity interest December 31, 2016	% equity interest December 31, 2017
Mereo BioPharma 1 Limited	Pharmaceutical research and development	United Kingdom	100	100
Mereo BioPharma 2 Limited	Pharmaceutical research and development	United Kingdom	100	100
Mereo BioPharma 3 Limited	Pharmaceutical research and development	United Kingdom	100	100
Mereo BioPharma 4 Limited	Pharmaceutical research and development	United Kingdom	—	100
Mereo BioPharma Group plc Employee Benefit Trust	Employee share plan	Jersey	—	—

6. Compensation of key management personnel of the Group

Key management includes Directors (Executive and Non-Executive) and Executive Officers, the General Counsel, the Chief Medical Officer and the Head of Corporate Development. The compensation paid or payable to key management is set out below.

	Year ended December 31, 2016 £	Year ended December 31, 2017 £
Short-term benefits	2,111,712	2,756,979
Post-employment benefits	106,500	87,269
IFRS 2 Share-based payment charge	4,631,853	2,726,337
Total compensation paid to key management personnel	6,850,065	5,570,585

7. Finance income and Finance charge

	Year ended December 31, 2016 £	Year ended December 31, 2017 £
Finance income		
Bank interest earned	374,906	826,855
Finance charge		
Interest expense on convertible loan	(179,765)	(103,115)
Interest paid on bank loan	—	(327,123)
Accreted interest on bank loan	—	(66,935)
Transaction costs on bank loan	—	(200,000)
Loss on short-term deposits	—	(338,279)
Change in warrant fair value	—	(54,473)
Total Finance charge	(179,765)	(1,089,925)

8. Employee benefits expense

	December 31, 2016 £	December 31, 2017 £
Included in research & development expenses:		
Salaries	1,150,222	1,640,373
Social security costs	344,467	420,417
Pension contributions	50,864	77,425
Share-based payment expense	1,550,884	822,173
Included in general and administrative expenses:		
Salaries	2,132,920	2,253,393
Social security costs	1,040,409	1,159,548
Pension contributions	109,187	96,598
Share-based payment expense	4,943,133	2,829,725
Total employee benefits expense	11,322,086	9,299,652

9. Income tax

The Group is entitled to claim tax credits in the United Kingdom (the "UK") under the UK R&D SME scheme. The amount included in the financial statements represents the credit receivable by the Group for the year. The claims in respect of the year ended December 31, 2016 were received by the Group in May 2017. The year ended December 31, 2017 amounts have not yet been agreed with the relevant tax authorities.

	Year ended December 31 2016 £	Year ended December 31 2017 £
United Kingdom corporation tax R&D credit	5,331,271	8,152,084

The charge for the year can be reconciled to the loss per the income statement as follows:

	Year ended December 31 2016 £	Year ended December 31 2017 £
Loss before tax	(33,721,551)	(46,951,138)
Loss on ordinary activities before tax at the United Kingdom's statutory income tax rate of 19.25% (2016:20%)	6,744,310	9,038,094
Expenses not deductible for tax purposes (permanent differences)	(15,116)	(14,316)
Temporary timing differences	(1,300,044)	(711,677)
Research and development relief uplift	2,134,107	3,447,474
Losses (unrecognized)	(2,231,986)	(3,784,801)
Deferred income from MBG loan guarantee costs		177,310
Tax credit for the year	5,331,271	8,152,084

At December 31, 2017, the Group had tax losses to be carried forward of approximately £36,010,916 (2016: £16,343,508).

Deferred tax

Deferred tax relates to the following:

	December 31, 2016 £	December 31, 2017 £
Losses	2,778,396	6,121,400
Accelerated capital allowances	(9,883)	—
Other	2,210	—
Temporary differences trading	—	2,266,798
Net deferred tax asset	2,770,723	8,388,198

The deferred tax asset has not been recognized as there is uncertainty regarding when suitable future profits against which to offset the accumulated tax losses will arise. There is no expiration date for the accumulated tax losses.

A reduction in the rate of UK corporation tax to 19% from April 1, 2017 and to 17% from April 1, 2020 has been substantively enacted. The standard rate of corporation tax applied to reported loss is 19.25% (2016:20%) and any UK deferred tax assets and liabilities would be recognized at a rate of 17%.

10. Loss per share

Basic loss per share is calculated by dividing the loss attributable for the year to ordinary equity holders of the parent by the weighted average number of ordinary shares outstanding during the year. As net losses from continuing operations were recorded in the year, the dilutive potential shares are anti-dilutive for the earnings per share calculation.

	Year ended December 31, 2016		
	Loss £	Weighted shares number	Loss per share £
Basic and diluted	(28,390,280)	44,789,893	(0.63)

	Year ended December 31, 2017		
	Loss £	Weighted shares number	Loss per share £
Basic and diluted	(38,799,054)	69,012,348	(0.56)

The Group operates a number of share option plans (see Note 24) which could potentially dilute basic earnings per share in the future. In addition, there exist within equity 864,988 (2016: 1,453,520) shares to be issued which also have the potential to dilute basic earnings per share in future (see Note 17).

As part of a licence and option agreement with AstraZeneca (see Note 25), additional future payments of a maximum of 1,349,692 new ordinary shares would be payable on reaching certain clinical milestones.

Warrants totaling 696,490 were issued in 2017 that could potentially dilute basic earnings per share if converted.

There have been no other transactions involving ordinary shares or potential ordinary shares between the reporting date and the date of authorisation of these financial statements.

11. Property, plant and equipment

	Leasehold improvements £	Office equipment £	IT equipment £	Total £
Cost or valuation				
At January 1, 2016	155,494	20,024	40,360	215,878
Additions	—	—	3,467	3,467
Disposals	—	—	(1,175)	(1,175)
At December 31, 2016	155,494	20,024	42,652	218,170
Additions	—	10,107	5,461	15,568
Disposals	—	—	—	—
At December 31, 2017	155,494	30,131	48,113	233,738
Depreciation and impairment				
At January 1, 2016	(5,625)	(1,335)	(4,401)	(11,361)
Disposals	—	—	457	457
Depreciation for the year	(15,549)	(4,005)	(13,843)	(33,397)
At December 31, 2016	(21,174)	(5,340)	(17,787)	(44,301)
Disposals	—	—	—	—
Depreciation for the year	(15,549)	(5,386)	(15,141)	(36,076)
At December 31, 2017	(36,723)	(10,726)	(32,928)	(80,377)
Net book value				
At January 1, 2016	149,869	18,689	35,959	204,517
At December 31, 2016	134,320	14,684	24,865	173,869
At December 31, 2017	118,771	19,405	15,185	153,361

12. Intangible assets

	Acquired development programmes £
Cost at January 1, 2016 and December 31, 2016	25,812,941
Amortisation and impairment	
At January 1, 2016	—
Impairment (Note 13)	—
At December 31, 2016	—
Net book value	
At January 1, 2016	25,812,941
At December 31, 2016	25,812,941
Cost at January 1, 2017	25,812,941
Additions	7,192,288
At December 31, 2017	33,005,229
Amortisation and impairment	
At January 1, 2017	—
Impairment (Note 13)	—
At December 31, 2017	—
Net book value	
At January 1, 2017	25,812,941
At December 31, 2017	33,005,229

The Group's strategy is to acquire clinical-stage development programmes for the treatment of speciality and rare diseases from large pharmaceutical companies.

On October 28, 2017, the Group acquired the exclusive license for AZD-9668 and included the option to acquire certain assets from Astra Zeneca AB (AstraZeneca). AZD-9668 is being developed for the treatment of severe alpha-1 antitrypsin deficiency, at a cost of £7,192,288 as follows:

	December 31, 2017 £
Cash payment in October 2017	2,280,000
Equity issued (see Note 17)	1,520,000
Deferred equity consideration (see Note 24)	1,331,288
Present value of provision for deferred cash consideration (see Note 19)	2,061,000
	7,192,288

13. Impairment testing of intangible assets not yet available for use

Acquired or licensed development programmes not yet available for use are assessed annually for impairment.

Carrying amount of acquired and licensed development programmes:

	As at December 31, 2016			
	£			
	BPS-804 (setrusumab)	BGS-649 (leflutozole)	BCT-197 (acumapimod)	Total
Acquired development programmes	11,615,824	9,886,356	4,310,761	25,812,941

	As at December 31, 2017				
	£				
	BPS-804 (setrusumab)	AZD-9668 (alvelestat)	BGS-649 (leflutozole)	BCT-197 (acumapimod)	Total
Acquired and licensed development programmes	11,615,824	7,192,288	9,886,356	4,310,761	33,005,229

The Group considers the future development costs, the probability of successfully progressing each programme to product approval and likely commercial returns after product approval, among other factors, when reviewing for indicators of impairment. The results of this testing did not indicate any impairment of the acquired products' rights in the year to December 31, 2017. We believe that the likelihood of a materially different outcome using different assumptions is remote.

The acquired development programmes are assets which are not used in launched products. These assets have not yet begun to be amortised but have been tested for impairment by assessing their value in use. Value-in-use calculations for each programme are utilised to calculate the recoverable amount. The calculations use pre-tax cash flow projections covering the period through product development to commercial sales up to the later of loss of patent protection or market exclusivity, which extend beyond five years from the balance sheet date. Approved products are assumed to be out-licensed such that the Group receives signature fees, milestone receipts and royalties on sales; therefore, the Group does not incur any costs of commercialisation after out-licensing.

Key assumptions for the value-in-use calculations are described as follows:

- development costs to obtain regulatory approval—costs are estimated net of any contributions expected from collaborative arrangements with future partners. The Directors have developed cost estimates based on their previous experience and in conjunction with the expertise of their clinical development partners;
- launch dates of products—these reflect management's expected date of launch for products based on the timeline of development programmes required to obtain regulatory approval. The assumptions are based on the Directors' and clinical development partners' prior experience;
- probability of successful development—management estimates probabilities of success for each phase of development based on industry averages and knowledge of specific programmes;
- out-licensing signature fees, milestones and royalty rates on sales—management estimates these amounts based on prior experience and access to values from similar transactions in the industry, which are collated and accessible from specialist third-party sources;
- sales projections—these are based on management's internal projections using external market data and market research commissioned by the Group;
- profit margins and other operational expenses—these are based on the Group's internal projections of current product manufacturing costings, with input from manufacturing partners

where applicable, and estimates of operating costs based on management's prior industry experience;

- cash flow projections—the periods over which cash flows are forecast (based on the current patent protection periods relevant to the asset), are as follows:
 - BCT-197 —18 years;
 - BGS-649 —17 years; and
 - BPS-804 —14 years: and
 - AZD-9668 —16 years: and
- discount rates—the discount rate is estimated on a pre-tax basis reflecting the estimated cost of capital of the Group and is applied consistently across each of the operating segments. The cost of capital was calculated at 15.3% (2016: 11.2%).

At this stage of product development, the key sensitivity for all three development programmes is the probability of successful completion of clinical trials in order to obtain regulatory approval for sale. Therefore, full impairment of a development programme is expected should such related trials be unsuccessful.

14. Other receivables

	December 31, 2016 £	December 31, 2017 £
Rent deposit	293,328	293,328
Accrued interest	228,775	—
VAT recoverable	241,306	212,422
Cash held by Employee Benefit Trust	3,600	3,600
	767,009	509,350

15. Cash and short-term deposits

	December 31, 2016 £	December 31, 2017 £
Cash at banks and on hand	421,292	11,005,675
Short-term deposits	53,156,279	39,038,997
	53,577,571	50,044,672

Cash at banks earns interest at floating rates based on daily bank deposit rates. Short-term deposits are available immediately and earn fixed interest at the respective short-term deposit rates and are held in a diversified portfolio of counterparties.

16. Short-term investments

	December 31, 2016 £	December 31, 2017 £
Short-term investments	—	2,500,000

Short term investments consist of cash deposits held with greater than three month's term to maturity. None of these investments are held with terms greater than a year.

17. Issued capital and reserves

	Year ended December 31, 2016 £	Year ended December 31, 2017 £
Ordinary share capital		
Balance at beginning of year	59,221	193,022
Issuances in the year	133,801	20,263
Nominal share capital as at December 31	193,022	213,285
Ordinary shares issued and fully paid		
At January 1, 2016		19,740,296
Issued on June 9, 2016 for private financing round		39,464,540
Issued on June 9, 2016 for private placement		5,135,962
At December 31, 2016		64,340,798
Nominal value at December 31, 2016 (£)		0.003
Issued capital at December 31, 2016 (£)		193,022
At January 1, 2017		64,340,798
Issued on 3 April 2017		5,042,017
Issued on 26 April 2017 for conversion of loan note		1,221,361
Issued on 28 October 2017 for acquisition of licence		490,798
At December 31, 2017		71,094,974
Nominal value at December 31, 2017 (£)		0.003
Issued capital at December 31, 2017 (£)		213,285

Since January 1, 2016, the following alterations to the Company's share capital have been made:

- under the subscription agreement dated July 28, 2015, as amended by an agreement dated June 1, 2016, the Company issued and allotted 39,464,540 ordinary shares of £0.003 in nominal value in the capital of the Company on June 9, 2016 at a price of £1.84 per share. 39,699 of these ordinary shares were issued to WG Partners LLP, for no cash consideration, as payment for financial advisory services;
- on March 21, 2016 the Directors of the Company signed a solvency statement with the agreement of all shareholders and undertook a capital reduction, reducing the share premium account by £7,000,000 and crediting a new Other reserve by the same amount;
- under a private placement dated June 9, 2016, the Company issued and allotted 5,135,962 ordinary shares of £0.003 in nominal value in the capital of the Company on June 9, 2016 at a price of £2.21 per share; and
- on June 9, 2016, the Company's ordinary shares were admitted to trading on the AIM market of the London Stock Exchange.
- under a placement dated April 3, 2017, the Company issued and allotted 5,042,017 ordinary shares of £0.003 in nominal value in the capital of the Company on April 3, 2017 at a price of £2.975 per share to institutional investors. Gross cash received was £15,000,000.
- on April 26, 2017 Novartis converted £1,398,552 of loan notes dated 3 June 2016 into 632,829 ordinary shares of £0.003 in nominal value in the capital of the Company at the fixed conversion price of £2.21 per share. Under the terms of the Notes, Novartis also received 588,532 bonus shares

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- on October 31, 2017, Mereo BioPharma Group plc issued and allotted 490,798 ordinary shares of £0.003 in nominal value in the capital of the Company to AstraZeneca AB as part payment for the acquisition by Mereo BioPharma 4 Ltd of an exclusive licence and option to acquire certain assets

Share premium	£
At January 1, 2016	26,212,880
Share capital reduction on March 21, 2016	(7,000,000)
Issuance of share capital for private financing round on June 9, 2016	72,423,314
Issuance of share capital for private placement on June 9, 2016	11,335,069
Transaction costs for issued share capital	(2,995,864)
At December 31, 2016	99,975,399
Issued on 3 April 2017 for private financing round	14,984,875
Issued on 26 April 2017 for conversion of loan note	2,477,787
Issued on 28 October 2017 for acquisition of licence	1,518,527
Transaction costs for issued share capital	(729,632)
At December 31, 2017	118,226,956

Other capital reserves

	Shares to be issued £	Share based payments £	Equity component of convertible loan instrument £	Total £
At January 1, 2016	18,677,840	2,982,265	—	21,660,105
Share-based payments expense during 2016	—	6,494,018	—	6,494,018
Shares issued	(16,003,363)	—	—	(16,003,363)
Equity component of convertible loan instrument	—	—	516,802	516,802
At December 31, 2016	2,674,477	9,476,283	516,802	12,667,562
Share-based payments expense during 2017	—	4,983,186	—	4,983,186
Shares issued	(1,082,899)	—	—	(1,082,899)
Equity component of convertible loan instrument	—	—	(208,680)	(208,680)
At December 31, 2017	1,591,578	14,459,469	308,122	16,359,169

Share-based payments

The Group has a number of share option plans under which options to subscribe for the Group's shares have been granted to certain Executives, Non-Executive Directors and employees (see Note 24 for further details).

The share-based payment reserve is used to recognise (a) the value of equity-settled share-based payments provided to employees, including key management personnel, as part of their remuneration and (b) deferred equity consideration. Refer to Note 24 for further details of these plans. Of the £6,494,018 share-based payment expense in 2016, £298,836 is an accelerated charge relating to 500,000 share options which were cancelled on June 9, 2016.

Shares issued/to be issued

Shares to be issued at January 1, 2016 of £18,677,840 represented a maximum potential 10,151,000 bonus shares due to Novartis under the terms of an investment in the prior year. Of the 44,600,502 ordinary shares issued on June 9, 2016, 8,697,480 shares were issued to Novartis as fully paid up bonus shares (for £nil consideration), the number of which was calculated to maintain its shareholding at 19.5%. The fair value of these shares was £1.84 per share. At December 31, 2016, £2,674,477 representing a maximum of 1,453,520 shares at £1.84 were remaining to be issued to Novartis pro rata to their percentage shareholding as and when the Company issues further ordinary shares.

Of the 1,221,361 ordinary shares issued on April 26, 2017, 588,532 shares were issued to Novartis as fully paid up bonus shares (for £nil consideration), the number of which was calculated to maintain its shareholding at 19.5%. The fair value of these shares was £1.84 per share. At December 31, 2017, £1,591,578 representing a maximum of 864,988 shares at £1.84 were remaining to be issued to Novartis pro rata to their percentage shareholding as and when the Company issues further ordinary shares.

Equity component of convertible loan instrument

The convertible loan notes issued to Novartis are a compound instrument consisting of a liability and an equity component (see Note 18a). The value of the equity component (cost of the conversion option) as at 31 December 2017 is £308,122 (2016: £516,802).

Accumulated deficit

	Year ended December 31, 2016 £	Year ended December 31, 2017 £
Other reserves	7,000,000	7,000,000
Accumulated losses	(40,579,241)	(79,315,920)
Accumulated deficit	(33,579,241)	(72,315,920)

On March 21, 2016 the Directors of the Company signed a solvency statement with the agreement of all shareholders and undertook a capital reduction, reducing the share premium account by £7,000,000 and crediting a new Other Reserve by the same amount.

18. Interest bearing loans and borrowings

	Year ended December 31, 2016 £	Year ended December 31, 2017 £
Novartis Notes - see Note 18a	3,126,526	1,977,393
Bank loan -see Note 18b	—	18,774,924
At December 31	3,126,526	20,752,317
Current	—	1,939,806
Non-current	3,126,526	18,812,511

18a. Novartis Notes

On June 3, 2016, the Company issued 3,463,563 £1 unsecured convertible loan notes ("Novartis Notes") to Novartis Pharma AG, a shareholder of the Company (see Note 26) in consideration for an

investment in cash by Novartis at the time of the private placement on June 9, 2016. The Novartis Notes attract an interest rate of 4% per annum and accruing daily and constitute direct, unsecured obligations of the Company ranking ahead of any other unsecured obligations of the Company.

On April 26, 2017 Novartis converted £1,398,553 of loan notes into 632,829 ordinary shares at the fixed conversion price of £2.21 per share. This has been recorded as a £1,187,974 reduction in interest bearing loans and borrowings, a reduction in other capital reserves of £208,680, and a reduction in accumulated loss of £62,375. Under the terms of the Notes, Novartis also received 588,532 bonus shares. Novartis holds £2,065,011 principal value of Notes at December 31, 2017 representing 934,394 ordinary shares if converted, together with 864,988 potential bonus shares, together these represent 2.5% of the current share capital of the Company as at December 31, 2017.

In August 2017, in connection with the new loan agreements (see Note 18b), Novartis agreed to amend the terms of its Novartis Notes. Under the revised terms of the Novartis Notes, the loan is subordinated to the Silicon Valley Bank and Kreos Capital loan such that Novartis shall be entitled, at any time up to the repayment of the foregoing loan, being March 2, 2021, to serve a conversion notice on the Company to convert all or some only of the outstanding Novartis Notes into fully paid ordinary shares at a conversion price of £2.21 per share. To the extent the Novartis Notes are not converted at that date, the outstanding principal amount of the Novartis Notes, together with any accrued and unconverted interest, is redeemable. Upon conversion of any Novartis Notes, in addition to the relevant number of conversion shares, Novartis is entitled to receive an additional number of ordinary shares in the Company equal to the number of conversion shares into which such Novartis Notes are to convert, multiplied by 0.93, up to a maximum aggregate number of 864,988 such bonus shares.

The value of the debt component of the Notes at the date of issue was calculated as £2,946,761. The cash flows attached to the Note up to the Maturity Date were calculated and discounted at an appropriate venture debt rate of 10%. The carrying amount at December 31, 2017 is £1,977,393 (2016: £3,126,526).

The value of the equity component of the Notes at December 31, 2017 was calculated as £308,123 (2016: £516,802).

18b. Bank loan

On August 7, 2017, we entered into a loan agreement with Silicon Valley Bank and Kreos Capital V (UK) Limited, which provides for total borrowings of £20.0 million and the issue of warrants over shares in the Company (see Note 20). We borrowed £10.0 million on each of August 21, 2017 (Tranche 1) and December 29, 2017 (Tranche 2) for general working capital purposes. We are obligated to make interest-only payments on the loan amount until September 30, 2018, and thereafter we are obligated to pay interest and principal in 30 equal monthly installments until March 31, 2021, the maturity date. The loan bears interest at an annual fixed rate equal to 9.0%. In addition a final payment of 7.5% of the principal loan amount is due upon the earlier of the maturity date, prepayment in whole of the loan amount, mandatory repayment, acceleration of the loan, and the loan becoming immediately due and payable due to an event of default. The loan is secured by substantially all of our assets, including intellectual property rights owned or controlled by us. The terms of the debt facility include an interest only period to September 30, 2018, a thirty-month capital and interest repayment period thereafter, a 9% headline interest rate and customary security over all assets of the Group.

The fair value of warrants issued as part of Tranche 1 on August 21, 2017 was £657,676. The fair value of the loan liability of Tranche 1 on August 21, 2017 was £9,342,324. Application of the effective interest method is required to accrete the initial loan liability value up to the face value of the loan at the end of the loan term. This non-cash interest charge will be made in each statutory reporting period. The annual value of this interest charge is £182,133, which is an effective interest rate of 1.95%.

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The fair value of warrants issued as part of Tranche 2 on December 29, 2017 was £634,335. The fair value of the loan liability of Tranche 2 on December 29, 2017 was £9,365,665. Application of the effective interest method is required to accrete the initial loan liability value up to the face value of the loan at the end of the loan term. This non-cash interest charge will be made in each statutory reporting period. The annual value of this interest charge is £194,892, which is an effective interest rate of 2.08%.

The total carrying value of the loan at 31 December 2017 was £18,774,924. £1,939,806 is a current liability and £16,835,118 is a non-current liability. A total of £66,935 of non-cash interest has been charged to the statement of comprehensive loss in the period.

19. Provisions

Summary

	Year ended December 31, 2016 £	Year ended December 31, 2017 £
Social security contributions on share options	1,172,420	2,288,386
Provision for deferred cash consideration	—	2,061,000
At December 31	1,172,420	4,349,386
Current	—	274,000
Non-current	1,172,420	4,075,386

	Year ended December 31, 2016 £	Year ended December 31, 2017 £
Social security contributions on share options		
At beginning of year	141,311	1,172,420
Accretion of discount	7,293	—
Arising during the year	1,084,181	1,115,966
Released	(60,365)	—
At December 31	1,172,420	2,288,386
Current	—	—
Non-current	1,172,420	2,288,386

The provision for social security contributions on share options is calculated based on the number of options outstanding at the reporting date that are expected to be exercised. The provision is based on the estimated gain arising on exercise of the share options, using the best estimate of the market price at the balance sheet date. Since the Directors assume the options will be held for their full contractual life of ten years (see Note 24) the liability has been classified as non-current. The provision has been discounted.

	Year ended December 31, 2016 £	Year ended December 31, 2017 £
Provision for deferred cash consideration		
At beginning of year	—	—
Arising during the year	—	2,061,000
At December 31	—	2,061,000
Current	—	274,000
Non-current	—	1,787,000

The deferred cash consideration is the estimate of the quantifiable but not certain future cash payment obligations due to AstraZeneca for the acquisition of certain assets (see Note 12). This liability is calculated as the risk adjusted net present value of future cash payments to be made by the Group. The payments are dependent on reaching certain milestones based on the commencement and outcome of clinical trials. The likelihood of achieving such milestones is reviewed at the balance sheet date and the provision is increased or decreased as appropriate.

20. Warrant liability

	Year ended December 31, 2016 £	Year ended December 31, 2017 £
At beginning of year	—	—
Arising during the year	—	1,346,484
At December 31	—	1,346,484

As part of the bank loan facility (see Note 18b), 363,156 warrants to subscribe for shares were issued to the lenders on August 21, 2017. These warrants will be capable of exercise until August 7, 2027 at an exercise price of £3.029. A further 333,334 warrants were issued to the lenders on December 29, 2017. These warrants will be capable of exercise until August 7, 2027 at an exercise price of £3.30. The total of 696,490 warrants is equivalent to 0.98% of ordinary share capital at December 31, 2017.

The terms of the warrant instrument allow for a cashless exercise. In line with IAS32, the future number of shares to be issued to the warrant holder under a cashless exercise can only be determined at that future date. At each balance sheet date the fair value of the warrants will be assessed using the Black-Scholes model taking into account appropriate amendments to inputs in respect of volatility and remaining expected life of the warrants.

The following table lists the weighted average inputs to the models used for the fair value of warrants granted during the period ended December 31, 2017:

	Year ended 31 December 2017
Expected volatility (%)	50-51
Risk-free interest rate (%)	1.10–1.25
Expected life of share options (years)	9.6-10
Market price of ordinary shares (£)	3.00–3.25
Model used	Black Scholes

The fair value of the warrants at grant was £1,292,011. At December 31, 2017 it was £1,346,484.

Since there is no historical data in relation to the expected life of the warrants the contractual life of the options was used in calculating the expense for the year.

Volatility was estimated by reference to the share price volatility of a group of comparable companies over a retrospective year equal to the expected life of the warrants.

21. Trade and other payables

	December 31, 2016 £	December 31, 2017 £
Trade payables	994,901	2,860,303
Social security and other taxes	113,205	144,348
Other payables	13,001	19,375
	<u>1,121,107</u>	<u>3,024,026</u>

Terms and conditions of the above financial liabilities:

- trade payables are non-interest bearing and are normally settled on 30-day terms; and
- other payables are non-interest bearing and have an average term of one month.

22. Changes in liabilities arising from financing activities

	Total Interest bearing loans and borrowings	Total Other liabilities	Total
January 1, 2017	3,126,526	—	3,126,526
Cash			
Net increase in bank loan	18,507,989	—	18,507,989
Increase in warrant liability	—	1,292,011	1,292,011
Interest payments	(327,123)	—	(327,123)
Non-cash			
Conversion of Novartis notes	(1,252,248)	—	(1,252,248)
Bank loan transaction costs	200,000	—	200,000
Change in fair value warrant	—	54,473	54,473
Provision for deferred cash consideration	—	2,061,000	2,061,000
Interest accrual	327,123	—	327,123
Accreted interest	170,050	—	170,050
December 31, 2017	<u>20,752,317</u>	<u>3,407,484</u>	<u>24,159,801</u>

23. Financial and capital risk measurement and Fair value measurement

23.1. Capital risk management

For the purpose of the Group's capital management, capital includes issued capital, share premium, the equity component of a convertible loan note and all other equity reserves attributable to the equity holders of the parent.

The Group's objectives when managing capital are to safeguard the ability to continue as a going concern and ensure that sufficient capital is in place to fund the Group's research and development activities. The Group's principal method of adjusting the capital available is through issuing new shares or arranging suitable debt financing, including any related warrants. The Group's share capital and share premium are disclosed in Note 17. The Group's loans are disclosed in note 18. The Group monitors the availability of capital with regard to its committed and planned forecast future expenditure on an ongoing basis.

23.2. Financial risk management objectives and policies

Monitoring of financial risk is part of the Board's ongoing risk management, the effectiveness of which is reviewed annually. Our agreed policies are implemented by the Chief Financial Officer, who submits periodic reports to the Board. We seek to maintain a balance between equity capital and convertible and secured debt to provide sufficient cash resources to execute our business plan. In addition, we maintain a balance between cash held on deposit and short term investments in sterling and other currencies to reduce its exposure to foreign exchange fluctuations in respect of our planned expenditure. During the year, in order to maintain a strong cash runway we completed an equity placing and arranged and drew down a new bank debt facility, which includes an initial interest-only period until September 2018.

Except for the bank loans and the existing convertible loan notes issued in 2016, the Group's principal financial instruments comprise trade payables which arise directly from its operations and are not designed as a means of raising finance for the Group's operations. The Group has various financial assets, such as receivables and cash and short-term deposits. The Group does not consider that its financial instruments gave rise to any material financial risks during the year to December 31, 2017.

Interest rate risk

The Group's policy in relation to interest rate risk is to monitor short and medium-term interest rates and to place cash on deposit for periods that optimise the amount of interest earned while maintaining access to sufficient funds to meet day-to-day cash requirements.

The interest payable on both the convertible loan note and on the bank loan is fixed. Consequently, there is no material exposure to interest rate risk in respect of interest payable.

Foreign currency risk

The Group currently has no revenue. The majority of operating costs are denominated in Sterling, Euros and U.S. dollars ("USD"). Foreign exchange risk arises from commercial transactions and recognized assets and liabilities in foreign currencies. In relation to foreign currency risk, the Group's policy is to hold the majority of its funds in Sterling and to hold sufficient USD to fund planned commitments for the next 12 months on a rolling basis with short term spot purchases to manage commitments in other currencies.

Credit risks

The Group's policy is to place funds with financial institutions which have a minimum long-term credit rating with S&P of A. The Group also allocates a quota to individual institutions in respect of cash deposits and also seeks to diversify its investments where this is consistent with achieving competitive rates of return. It is the Group's policy to place not more than £10 million with any one investment counterparty and no more than £5m with any one cash deposit counter party.

Cash flow and liquidity risk

Credit risk from balances with banks and financial institutions is managed by the Group's finance department in accordance with the Group's policy. Investments of funds are made only with approved counterparties and within credit limits assigned to each counterparty. Counterparty credit limits are reviewed by the Group's Board of Directors on an annual basis, and may be updated throughout the year subject to approval of the Group's Audit and Risk Committee. The limits are set to minimise the concentration of risks and therefore mitigate financial loss through a counterparty's potential failure to make payments.

The Group's maximum exposure to credit risk for the components of the balance sheet at December 31, 2017 is the carrying amounts.

The Group monitors its funding requirements through preparation of short-term, mid-term and long-term forecasts. All short-term deposits are immediately convertible to liquid funds without penalty and are recorded in the balance sheet at their open market value. Please refer to Note 2.3 "Going Concern" regarding the Directors' assessment of liquidity for further information.

23.3. Fair value hierarchy

Fair value measurement hierarchy for liabilities as at December 31, 2017:

		Fair Value Measurement using			
	Date of valuation	Total	Quoted prices in active markets (Level 1)	Significant observable inputs (Level 2)	Significant unobservable inputs (Level 3)
Liabilities measured at fair value:					
Provision for deferred cash consideration (Note 19)	December 31, 2017	£ 2,061,000			£ 2,061,000
Warrant liability (Note 20)	December 31, 2017	£ 1,346,484			£ 1,346,484
Liabilities for which fair values are disclosed					
Convertible loan (Note 18a)	December 31, 2017	£ 1,977,393			£ 1,977,393
Bank loan (Note 18b)	December 31, 2017	£18,774,924			£18,774,924

There were no transfers between Level 1 and Level 2 during 2017

Fair value measurement hierarchy for liabilities as at December 31, 2016:

		Fair Value Measurement using			
			Quoted prices in active markets (Level 1)	Significant observable inputs (Level 2)	Significant unobservable inputs (Level 3)
	<u>Date of valuation</u>	<u>Total</u>			
Liabilities for which fair values are disclosed					
Convertible loan (Note 18a)	December 31, 2016	£3,126,526			£3,126,526

There were no transfers between Level 1 and Level 2 during 2016

Set out below is a comparison, by class, of the carrying amounts and fair values of the Group's financial instruments:

	December 31, 2016		December 31, 2017	
	Carrying amount £	Fair value £	Carrying amount £	Fair value £
Liabilities				
Provision for deferred cash consideration	—	—	2,061,000	2,061,000
Warrant liability	—	—	1,346,484	1,346,484

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The management of the Group assessed that the fair values of cash and short-term deposits, other receivables, trade payables, and other current liabilities approximate their carrying amounts largely due to the short-term maturities of these instruments.

The following methods and assumptions were used to estimate the fair values:

- The fair value of the provision for deferred cash consideration is estimated by discounting future cash flows using rates currently available for debt on similar terms and credit risk. In addition to being sensitive to a reasonably possible change in the forecast cash flows or the discount rate, the fair value of the deferred cash consideration is also sensitive to a reasonably possible change in the probability of reaching certain milestones. The valuation requires management to use unobservable inputs in the model, of which the significant unobservable inputs are disclosed in the tables below. Management regularly assesses a range of reasonably possible alternatives for those significant unobservable inputs and determines their impact on the total fair value.
- The warrant liability is estimated using the Black-Scholes model taking into account appropriate amendments to inputs in respect of volatility and remaining expected life of the warrants, cost of capital, probability of success and interest rates.

The significant unobservable inputs used in the fair value measurements categorized within Level 3 of the fair value hierarchy, together with a quantitative sensitivity analysis as at December 31, 2017 and 2016 are as shown below:

	Valuation technique	Significant unobservable inputs	Range (weighted average)	Sensitivity of the input to fair value
Provision for deferred cash consideration	DCF	WACC	2017: 15.3%	1% increase / (decrease) would result in a decrease / (increase) in fair value by £30,000.
		Probability of success	2017: 28 – 85%	10% increase / (decrease) would result in an increase / (decrease) in fair value by £600,000.
Warrant liability	Black Scholes	Risk free interest rate	2017: 1.25%	1% increase / (decrease) would result in an increase / (decrease) of £46,000.
		Volatility	2017: 50%	10% increase / (decrease) would result in an increase / (decrease) of £200,000.
		Remaining life	2017: 3519 days	Increase / (decrease) of 365 days would result in an increase / (decrease) of £54,000.

The table below summarizes the maturity profile of the Group's financial liabilities based on contractual undiscounted payments at December 31, 2017:

	Up to 1 year	1-3 Years	3-5 Years	Over 5 Years	Total
Novartis Notes	£ 82,600	£ 165,427	£2,078,815	—	£ 2,326,842
Bank loan	£3,574,208	£17,793,665	£2,982,805	—	£24,350,678
Operating lease (see Note 25)	£ 743,858	£ 535,203	—	—	£ 1,279,061
	<u>£4,400,666</u>	<u>£18,494,295</u>	<u>£5,061,620</u>	<u>—</u>	<u>£27,956,581</u>

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The table below summarizes our contractual obligations at December 31, 2016:

	Payments Due by Period				Total
	Up to 1 year	1-3 Years	3-5 Years	Over 5 Years	
Novartis Notes	£ 138,543	£3,660,559	—	—	£3,799,102
Bank loan	—	—	—	—	—
Operating lease (see Note 25)	£ 325,920	£ 651,840	£202,736	—	£1,180,496
	<u>£ 464,463</u>	<u>£4,312,399</u>	<u>£202,736</u>	<u>—</u>	<u>£4,979,598</u>

We may incur potential payments upon our achievement of clinical, regulatory and commercial milestones, as applicable, or royalty payments that we may be required to make under license agreements we have entered into with various entities pursuant to which we have in-licensed certain intellectual property, including our license agreements with Novartis and AstraZeneca. Due to the uncertainty of the achievement and timing of the events requiring payment under these agreements, the amounts to be paid by us are not fixed or determinable at this time.

24. Share-based payments

The charge for employee-related share-based payments under IFRS 2 arises across the following plans:

	December 31, 2016 £	December 31, 2017 £
2015 Plan	6,185,067	2,441,671
Share Option Plan	—	586,291
LTIP	133,601	298,287
DBSP	175,350	325,649
Total	<u>6,494,018</u>	<u>3,651,898</u>

The 2015 Plan

Under the Mereo BioPharma Group Limited Share Option Plan (the “2015 Plan”), the Group, at its discretion, granted share options to employees, including executive management, and Non-Executive Directors. Share options vest over four years for executive management and employees and over three years for Non-Executive Directors. There are no performance conditions attached to the options issued under the Option Plan. The fair value of share options granted was estimated at the date of grant using a Black Scholes pricing model, taking into account the terms and conditions upon which the share options were granted. The fair value calculation does not include any allowance for dividends as the Company has no available profits for distribution.

The exercise price of the share options will be equal to the market price of the underlying shares on the date of grant, less a discount agreed with the Group's institutional investors. The contractual term of the share options is ten years.

Of the £6,185,067 expense recognized under the option plan for employee services received during 2016, £298,836 is an accelerated charge relating to 500,000 options which were cancelled on June 9, 2016.

No share options were issued during the year under the 2015 Share Plan.

Movements during the year

The following table illustrates the number and weighted average exercise prices (WAEF) of, and movements in, share options during the year:

	2016 Number	2016 WAEF £	2017 Number	2017 WAEF £
Outstanding at beginning of year	8,964,394	1.29	9,198,655	1.32
Granted during the year	1,316,117	1.49	—	—
Cancelled during the year	(500,000)	1.29	—	—
Forfeited during the year	(581,856)	1.29	(74,045)	1.29
Outstanding at December 31	<u>9,198,655</u>	<u>1.32</u>	<u>9,124,610</u>	<u>1.32</u>
Exercisable at December 31	<u>3,115,337</u>	<u>1.29</u>	<u>5,655,676</u>	<u>1.31</u>

The weighted average remaining contractual life for the share options outstanding as at December 31, 2017 was 7.6 years (2016: 8.3 years).

There were no options granted in 2017. The weighted average fair value of options granted during 2016 was £1.29.

Options outstanding at the end of the year had an exercise price of between £1.29 and £2.21.

The following tables list the weighted average inputs to the models used for the fair value of share options granted during the years ended December 31, 2016 and 2017:

	Year ended December 31, 2016	Year ended December 31, 2017
Expected volatility (%)	56	—
Risk-free interest rate (%)	1.48–2.07	—
Expected life of share options (years)	10	—
Market price of ordinary shares (£)	1.84–2.21	—
Model used	Black Scholes	—

Since there is no historical data in relation to the expected life of the share options the contractual life of the options was used in calculating the expense for the year.

Volatility was estimated by reference to the share price volatility of a group of comparable companies over a retrospective year equal to the expected life of the share options.

The Mereo BioPharma Group plc Share Option Plan

The Mereo BioPharma Group plc Share Option Plan ("Share Option Plan") provides for the grant of options to acquire our ordinary shares to employees, executive directors and executive officers. Options may be granted to all eligible employees on commencement of employment and may be granted on a periodic basis after that. Under the Share Option Plan, our board of directors may determine if the vesting of an option will be subject to the satisfaction of a performance condition. With regard to an option which is subject to satisfaction of a performance condition, the option will normally vest on the later of: (i) the date on which our board of directors determines that the performance condition has been satisfied; and (ii) the third anniversary of the date of grant. With regard to an option which is not subject to the satisfaction of a performance condition, the option will normally vest on the third anniversary of the date of grant, or such other date determined by our board of directors and

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notified to the participant. Once an option has vested, it may be exercised during the period ending on the tenth anniversary of the date of grant, after which time it will lapse. The exercise price of an option may not be less than the greater of: (i) the market value of a share on the date of grant; or (ii) if the shares are to be subscribed, the nominal value of a share. Options are not currently subject to performance conditions other than continued service with us and typically vest on the third anniversary of the date of grant, after which they remain exercisable generally until the tenth anniversary of the grant date. Our board of directors may determine that an option be settled in cash or by net exercise of the option.

Movements during the period

The following table illustrates the number and weighted average exercise prices (WAEP) of, and movements in, options for the Share Option Plan during the period:

	2016 Number	2016 WAEP £	2017 Number	2017 WAEP £
Outstanding at beginning of year	—	—	—	—
Granted during the year	—	—	1,593,188	3.05
Cancelled during the year	—	—	—	—
Forfeited during the year	—	—	(15,000)	3.03
Outstanding at December 31	—	—	1,578,188	3.05
Exercisable at December 31	—	—	—	—

The weighted average remaining contractual life for the share options outstanding as at December 31, 2017 was 9.4 years.

The weighted average fair value of options granted during the year was £1.85.

Options outstanding at the end of the year had an exercise price of between £3.03 and £3.23.

The following tables list the weighted average inputs to the models used for the fair value of share options granted during the year ended December 31, 2017:

	Year ended December 31, 2016	Year ended December 31, 2017
Expected volatility (%)	—	49-51
Risk-free interest rate (%)	—	1.06-1.33
Expected life of share options (years)	—	10
Market price of ordinary shares (£)	—	3.03-3.23
Model used	—	Black Scholes

Since there is no historical data in relation to the expected life of the share options the contractual life of the options was used in calculating the expense for the year.

Volatility was estimated by reference to the share price volatility of a group of comparable companies over a retrospective year equal to the expected life of the share options.

Long Term Incentive Plan

Under the Company's Long Term Incentive Plan (LTIP), initiated in 2016, the Group, at its discretion, may grant nil-cost options to acquire shares to employees. Under the LTIP rules, vesting of

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75% of the options issued to employees is subject to a share price performance condition (the "Share Price Element") and vesting of 25% of the options is subject to achievement of strategic operational targets (the "Strategic Element"). Share options vest over a maximum of five years, dependent upon achievement of these targets.

The fair value of the LTIP Share Price Element is estimated at the date of grant using a Monte Carlo pricing model, taking into account the terms and conditions upon which the share options were granted.

The fair value of the LTIP Strategic Element is estimated at the date of grant using a Black Scholes pricing model, taking into account the terms and conditions upon which the share options were granted, and the expense recorded is based upon the expected level of achievement of strategic targets.

The fair value calculations do not include any allowance for dividends as the Company has no available profits for distribution.

The contractual term of the LTIP options is five years.

The expense recognized for employee services received during the year to December 31, 2017 was £298,287 (2016: £133,601).

Movements during the year

The following table illustrates the number of, and movements in, LTIP options during the year:

	2016 Number	2017 Number
Granted during the year	1,199,658	185,950
Cancelled during the year	—	—
Forfeited during the year	(234,162)	—
Outstanding at December 31	965,496	1,151,446
Exercisable at December 31	—	—

The weighted average remaining contractual life for the LTIP options outstanding as at December 31, 2017 was 2.9 years (2016: 3.7 years).

The weighted average fair value of LTIP options granted during the year was £1.99 (2016: £1.21).

The following tables list the weighted average inputs to the models used for the fair value of LTIP options granted during the years ended December 31:

LTIP Share Price Element

	Year ended December 31, 2016	Year ended December 31, 2017
Expected volatility (%)	48.9	51.7
Risk-free interest rate (%)	0.48–0.74	0.17–0.39
Expected life of share options (years)	3–5	3–5
Market price of ordinary shares (£)	2.21	3.03
Model used	Monte Carlo	Monte Carlo

LTIP Strategic Element

	Year ended December 31, 2016	Year ended December 31, 2017
Expected volatility (%)	48.9	51.7
Risk-free interest rate (%)	0.74	0.39
Expected life of share options (years)	5	5
Market price of ordinary shares (£)	2.21	3.03
Model used	Black Scholes	Black Scholes

Since there is no historical data in relation to the expected life of the LTIP options the contractual life of the options has been used in calculating the expense for the year.

Volatility is estimated by reference to the share price volatility of a group of comparable companies over a retrospective year equal to the expected life of the LTIP options.

Deferred Bonus Share Plan

Under the Company's Deferred Bonus Share Plan (DBSP), 30% of the annual bonus for the executive management team is payable in deferred shares, which are governed by the DBSP rules. At the date of grant of the awards, the monetary bonus amount will be divided by the closing share price to give the number of shares issued to the employee under the DBSP. The number of shares is fixed and not subject to adjustment between the issue date and vesting date. Under the DBSP, awards vest after three years from the grant date of the award. There are no further performance conditions attached to the award, nor any service conditions (including no requirement for continued employment once the awards have been made). The plan does allow for adjustment of awards in the event of a material misstatement of Group's accounts or fraud or misconduct on the part of an individual. The plan also allows for adjustment of awards in the event there was an error in calculating the vesting of the awards.

Since the awards are issued at £nil cost they will be satisfied by the issue of shares from the EBT.

The following table illustrates the number of, and movements in, DBSP options during the year:

	Year ended December 31, 2016	Year ended December 31, 2017
Outstanding at January 1	—	62,180
Awarded during the year	62,180	100,820
Granted during the year	—	—
Outstanding at December 31	62,180	163,000
Exercisable at December 31	—	—

The weighted average remaining contractual life for the DBSP options outstanding as at December 31, 2017 was 3.6 years (2016: 4 years).

The weighted average fair value of deferred share bonus plan options granted during the year was £3.23 (2016: £2.80).

Deferred Equity Consideration

In October 2017, our wholly owned subsidiary Mereo BioPharma 4 Limited entered into an exclusive license and option agreement, or the License Agreement, to obtain from AstraZeneca an

exclusive worldwide, sub-licensable license under AstraZeneca's intellectual property rights relating to AZD-9668, with an option to acquire such intellectual property rights following commencement of a pivotal trial and payment of related milestone payments, or the Option, together with the acquisition of certain related assets.

Under the agreement with Astrazeneca, we may issue up to 1,349,693 ordinary shares which are dependent on achieving certain milestones.

In respect of milestones that are probable, we have accounted for, but not yet issued, 429,448 ordinary shares which have been measured at fair value, being £3.10, giving a total of £1,331,288.

25. Commitments and contingencies

Operating lease commitments—Group as lessee

Future minimum rentals payable under non-cancellable operating leases as at December 31, 2017 are as follows:

	December 31, 2016 £	December 31, 2017 £
Within one year	325,920	743,858
After one year but not more than three years	651,840	535,203
After three years but not more than five years	202,736	—
More than five years	—	—
	<u>1,180,496</u>	<u>1,279,061</u>

The Group has entered into a lease for its premises at Fourth Floor, 1 Cavendish Place, London W1G 0QF. The term of the lease agreement is from August 17, 2015 through to August 16, 2025. The total lease expense for the year ended December 31, 2017 was £293,328 (2016:£293,328).

The premises comprise approximately 4,000 square feet. The principal rent for the premises is £162,960 per annum through December 16, 2016 and £325,920 per annum thereafter, subject to increase on August 17, 2020 based on the open market value of the premises (the "Principal Rent"). In addition to the Principal Rent, the Group is responsible for value added tax on the Principal Rent and certain insurance costs and service charges incurred by the landlord.

The Group may break the lease agreement on August 16, 2020 by providing six months' prior written notice to the landlord. If the Group does not exercise its break option, the landlord will decrease by 50% the Principal Rent for the period from August 16, 2020 through to April 15, 2021.

The Group has entered into a lease for six High Resolution peripheral quantitative computed tomography (HRpQCT) scanners for use in its ongoing clinical studies.

Each scanner has a lease term of 12 months from the date on which delivery of that scanner occurred. The Company has the right to extend the lease period for a further six months at any point during the lease term. This option may be exercised in respect of any of the individual scanners and does not have to be exercised in respect of all the scanners.

Finance leases—Group as lessee

The Group did not have any leasing arrangements classifying as finance leases at December 31, 2017.

Financial commitments

Each of Mereo BioPharma 1 Ltd, Mereo BioPharma 2 Ltd and Mereo BioPharma 3 Ltd issued to Novartis loan notes (the Novartis notes) (which were assigned by Novartis to the Company in exchange for ordinary shares pursuant to the Subscription Agreement) and each of Mereo BioPharma 1 Ltd, Mereo BioPharma 2 Ltd and Mereo BioPharma 3 Ltd agreed to make future payments to Novartis comprising amounts equal to ascending specified percentages of tiered annual worldwide net sales (beginning at high single digits and reaching into double digits at higher sales) by such subsidiary of products that include the assets acquired. The levels of ascending percentages of tiered annual worldwide net sales are the same for each of Mereo BioPharma 1, Mereo BioPharma 2 and Mereo BioPharma 3 under the respective Purchase Agreements.

Each of Mereo BioPharma 1 Ltd, Mereo BioPharma 2 Ltd and Mereo BioPharma 3 Ltd further agreed that in the event it transfers, licenses, assigns or leases all or substantially all of its assets, it will pay Novartis a percentage of the proceeds of such transaction. The Company will retain the majority of the proceeds from such a transaction. Such percentage is the same for each of Mereo BioPharma 1 Ltd, Mereo BioPharma 2 Ltd and Mereo BioPharma 3 Ltd under the respective Purchase Agreements. The payment of a percentage of proceeds is not payable with respect to any transaction involving equity interests of Mereo BioPharma Group plc, a merger or consolidation of Mereo BioPharma Group plc, or a sale of any assets of Mereo BioPharma Group plc.

In October 2017, our wholly owned subsidiary Mereo BioPharma 4 Limited entered into an exclusive license and option agreement, or the License Agreement, to obtain from AstraZeneca an exclusive worldwide, sub-licensable license under AstraZeneca's intellectual property rights relating to AZD-9668, with an option to acquire such intellectual property rights following commencement of a pivotal trial and payment of related milestone payments, or the Option, together with the acquisition of certain related assets. Upon entering into the License Agreement, we made a payment of \$3.0 million and issued 490,798 ordinary shares to AstraZeneca, for an aggregate upfront payment equal to \$5.0 million. In connection with certain development and regulatory milestones, we have agreed to make payments of up to \$115.5 million in the aggregate and issue additional ordinary shares to AstraZeneca for licensed products containing AZD-9668. In addition, we have agreed to make payments to AstraZeneca based on specified commercial milestones of the product. In the event that we sub-license AZD-9668, we have also agreed to pay a specified percentage of sublicensing revenue to AstraZeneca. Otherwise, we have agreed to make royalty payments to AstraZeneca equal to ascending specified percentages of tiered annual worldwide net sales by us or our affiliates of licensed products (subject to certain reductions), ranging from the high single digits to low double digits. Royalties will be payable on a licensed product-by-licensed product and country-by-country basis until the later of ten years after the first commercial sale of such licensed product in such country and expiration of the last patent covering such licensed product in such country that would be sufficient to prevent generic entry. Under the License Agreement, we may freely grant sub-licenses to affiliates upon notice to AstraZeneca and we must obtain AstraZeneca's consent, not be unreasonably withheld, to grant sub-licenses to a third party. We have agreed to use commercially reasonable efforts to develop and commercialize at least one licensed product.

The License Agreement will expire on the expiry of the last-to-expire royalty term with respect to all licensed products. Upon the expiration of the royalty term for a licensed product in a particular country, the licenses to us for such product in such country will become fully-paid and irrevocable. Prior

to exercise of the Option, if at all, we may terminate the License Agreement upon prior written notice. Either party may terminate the agreement upon prior written notice for the other party's material breach that remains uncured for a specified period of time or insolvency. AstraZeneca has agreed to a three-year non-competition restriction in relation to the direct or indirect commercialization or development of NE inhibitors for the treatment of AATD. In addition, AstraZeneca agreed not to assert any AstraZeneca intellectual property rights that were included in the scope of the License Agreement against us.

26. Related party disclosures

The following transactions have been entered into with related parties for the year ended December 31, 2016 and 2017.

Novartis Pharma AG ("Novartis") holds shares in the Company at December 31, 2016. On June 3, 2016, the Group issued 3,463,563 £1 unsecured convertible loan notes (the Novartis Notes) to Novartis and received £3,463,563 from Novartis in consideration (Note 19).

The Group purchased goods and services from Novartis in the year as set out below:

	December 31, 2016 £	December 31, 2017 £
Manufacture and supply of clinical trial material	968,219	4,610,106

The amount outstanding to be paid to Novartis at December 31, 2017 was £nil (2016: £35,249).

The purchases from related parties are made on terms equivalent to those that prevail in arm's length transactions.

27. Standards issued but not yet effective

The standards and interpretations that were issued, but not yet effective, up to the date of issuance of the Group's financial statements are disclosed below. The Group intends to adopt these standards, if applicable, when they become effective.

IFRS 9 Financial Instruments

IFRS 9 applies to reporting periods on or after January 1, 2018. The Group is currently assessing the impact of IFRS 9 and plans to adopt the new standard on the required effective date.

IFRS 15 Revenue from Contracts with Customers

IFRS 15 "Revenue from Contracts with Customers" ("IFRS 15") was issued in May 2014 and establishes a new five-step model that will apply to revenue arising from contracts with customers. Under IFRS 15 revenue is recognized at an amount that reflects the consideration to which an entity expects to be entitled in exchange for transferring goods or services to a customer. The principles in IFRS 15 provide a more structured approach to measuring and recognising revenue.

The new revenue standard is applicable to all entities and will supersede all current revenue recognition requirements under IFRS. Either a full or modified retrospective application is required for annual periods beginning on or after January 1, 2018 with early adoption permitted. As the Group is not currently, nor will it for the foreseeable future, generating revenues, IFRS 15 will be adopted when the Group has an arrangement within the scope of the standard.

IFRS 16 Leases

IFRS 16 “Leases” (“IFRS 16”) specifies how an IFRS reporter will recognise, measure, present and disclose leases. The standard provides a single lessee accounting model, requiring lessees to recognise assets and liabilities for all leases unless the lease term is twelve months or less or the underlying asset has a low value. Lessors continue to classify leases as operating or finance, with IFRS 16’s approach to lessor accounting substantially unchanged from its predecessor, IAS 17 “Leases”.

IFRS 16 was issued in January 2016 and applies to annual reporting periods beginning on or after January 1, 2019.

The Group is currently assessing the impact of IFRS 16 and plans to adopt the new standard on the required effective date.

Other standards

The following standards and interpretations, applicable for annual periods beginning on or after January 1, 2017, are not expected to have any material impact on the results of the Group or the presentation of the financial statements:

- IFRS 10 “Consolidated Financial Statements”—Amendments regarding the sale or contribution of assets between an investor and its associate or joint venture and amendments regarding the application of the consolidation exception
- IFRS 11 “Joint Arrangements”—Amendments regarding the accounting for acquisitions of an interest in a joint operation
- IFRS 12 “Disclosure of Interests in Other Entities”—Amendments regarding the application of the consolidation exception
- IFRS 14 “Regulatory Deferral Accounts”
- IAS 1 “Presentation of Financial Statements”—Amendments resulting from the disclosure initiative
- IAS 7 “Statement of Cash Flows”—Amendments resulting from the disclosure initiative
- IAS 12 “Income Taxes”—Amendments to recognition of deferred tax assets for unrealised losses
- IAS 16 “Property, Plant and Equipment” (“IAS 16”)—Amendments regarding the clarification of acceptable methods of depreciation and amortisation and amendments bringing bearer plants into the scope of IAS 16
- IAS 27 “Separate Financial Statements (as amended in 2011)”—Amendments reinstating the equity method as an accounting option for investments in subsidiaries, joint ventures and associates in an entity’s separate financial statements
- IAS 28 “Investments in Associates and Joint Ventures”—Amendments regarding the application of the consolidation exception
- IAS 38 “Intangible Assets”—Amendments regarding the clarification of acceptable methods of depreciation and amortisation
- IAS 41 “Agriculture”—Amendments bringing bearer plants into the scope of IAS 16
- Amendments resulting from September 2014 Annual Improvements to IFRSs:

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- IFRS 2 “Classification and Measurement of Share-based Payment” Transactions
- IFRS 5 “Non-current Assets Held for Sale and Discontinued Operations”
- IFRS 7 “Financial Instruments: Disclosures”
- IFRIC Interpretation 22 “Foreign Currency Transactions and Advance Consideration”
- IAS 19 “Employee Benefits”
- IAS 34 “Interim Financial Reporting”

**15,892,917 Ordinary Shares
(including Ordinary Shares in the form
of American Depositary Shares)**



PROSPECTUS

Cowen

BMO Capital Markets

RBC Capital Markets

JMP Securities

Cantor Fitzgerald Europe

, 2018

Until , 2018 (25 days after the date of this prospectus), all dealers that buy, sell or trade ADSs or ordinary shares, whether or not participating in the global offering, may be required to deliver a prospectus. This delivery requirement is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

PART II—INFORMATION NOT REQUIRED IN THE PROSPECTUS

Item 6. Indemnification of directors and officers

Members of the registrant's board of directors have the benefit of the following indemnification provisions in the registrant's Articles of Association:

Current and former members of the registrant's board of directors may be indemnified for:

- (a) any liability incurred by that director in connection with any negligence, default, breach of duty, or breach of trust in relation to the registrant or an associated company;
- (b) any liability incurred by that director in connection with the activities of the registrant or an associated company in its capacity as a trustee of an occupational pension scheme; and
- (c) any other liability incurred by that director as an officer of the registrant or an associated company.

In addition, members of the registrant's board of directors who have received payment from the registrant under these indemnification provisions must repay the amount they received in accordance with the Statutes or in any other circumstances that the registrant may prescribe or where the registrant has reserved the right to require repayment.

The underwriting agreement the registrant will enter into in connection with the offering of ADSs being registered hereby provides that the underwriters will indemnify, under certain conditions, the registrant's board of directors and its officers against certain liabilities arising in connection with the U.S. offering.

Item 7. Recent sales of unregistered securities

Issuance of Share Capital

- On March 10, 2015, the registrant issued an ordinary share of nominal value £1 to its founder for aggregate consideration of £1.
- On April 21, 2015, the registrant issued 4,999 ordinary shares of nominal value £1 each to its founders for aggregate consideration of £4,999.
- On July 29, 2015, the registrant effected subdivision of its 5,000 ordinary shares at a 1:1,000 ratio, resulting in there being 5,000,000 ordinary shares of nominal value £0.001 each.
- On July 29, 2015, the registrant issued 14,740,296 ordinary shares of nominal value £0.001 each to new investors for aggregate consideration of £20.0 million in cash and the assignment to the registrant of loan notes in an aggregate amount of £25.8 million.
- On November 27, 2015, the registrant issued 39,480,592 ordinary shares of nominal value £0.001 each to existing investors in connection with a recapitalization of the registrant. Following such issuance, the ordinary shares of the registrant were consolidated at a 3:1 ratio, resulting in there being 19,740,296 ordinary shares of nominal value £0.003 per ordinary share.
- On June 9, 2016, the registrant issued 44,600,502 ordinary shares of nominal value £0.003 each to new and existing investors for aggregate consideration of £84.0 million.
- On April 3, 2017, the registrant issued 5,042,017 ordinary shares of nominal value £0.003 each to new and existing investors for aggregate consideration of £15.0 million.
- On April 26, 2017, the registrant issued 1,221,361 ordinary shares of nominal value £0.003 each upon the conversion of £1.4 million of unsecured convertible loan notes.
- On October 31, 2017, the registrant issued 490,798 ordinary shares of nominal value £0.003 each to a new investor in connection with a licensing agreement.

Issuance of Notes

On June 3, 2016, the registrant issued 3,463,563 unsecured convertible loan notes for aggregate consideration of £3,463,563.

Options

From its inception in March 2015 through December 31, 2015, the registrant granted stock options to purchase an aggregate of 8,964,394 ordinary shares with exercise prices of £1.29 per ordinary share to certain employees, senior management, and directors in connection with services provided to the registrant by such parties.

From January 1, 2016 through December 31, 2016, the registrant granted stock options to purchase an aggregate of 2,515,775 ordinary shares with exercise prices ranging from nil to £2.21 per ordinary share to certain employees, senior management, and directors in connection with services provided to the registrant by such parties.

From January 1, 2017 through December 31, 2017, the registrant granted stock options to purchase an aggregate of 1,841,318 ordinary shares with exercise prices ranging from nil to £3.23 per ordinary share to certain employees, senior management, and directors in connection with services provided to the registrant by such parties.

Warrants

On August 21, 2017, the registrant issued warrants to purchase 363,156 ordinary shares at an exercise price of £3.029 each.

On December 29, 2017, the registrant issued warrants to purchase 333,334 ordinary shares at an exercise price of £3.300 each.

All of the foregoing issuances of share capital, notes, options, and warrants were made outside of the United States pursuant to Regulation S or to U.S. entities pursuant to Section 4(a)(2) of the Securities Act of 1933, as amended, or the Securities Act.

Item 8. Exhibits and financial statements

(a) **Exhibits.** The exhibits to this registration statement are listed in the Exhibit Index to this registration statement and incorporated herein by reference.

(b) **Financial Statement Schedules.** Schedules have been omitted because the information required to be set forth therein is not applicable or is shown in our combined financial statements or the notes thereto.

Item 9. Undertakings

- (a) The undersigned registrant hereby undertakes to provide to the underwriters at the closing specified in the underwriting agreement, certificates in such denominations and registered in such names as required by the underwriter to permit prompt delivery to each purchaser.
- (b) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the U.S. Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in

connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

(c) The undersigned registrant hereby undertakes that:

- (1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.
- (2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

EXHIBIT INDEX

<u>Exhibit Number</u>	<u>Exhibit Description</u>
1.1	Form of Underwriting Agreement
3.1	Articles of Association, as currently in effect
4.1*	Form of Deposit Agreement
4.2*	Form of American Depositary Receipt (included in Exhibit 4.1)
4.3*	Form of Warrant Instrument
5.1*	Opinion of Latham & Watkins LLP
10.1*	Underlease by and between the registrant and O&H (Cavendish Place) Limited, dated August 17, 2015
10.2*	Contract of Employment, dated July 29, 2015, between the registrant and Denise Scots-Knight
10.3*	Contract of Employment, dated July 29, 2015, and Deed of Amendment, dated November 24, 2017, between the registrant and Alastair MacKinnon
10.4*	Contract of Employment, dated July 29, 2015, between the registrant and Charles Sermon
10.5*	Contract of Employment, dated November 7, 2016, between the registrant and Richard Jones
10.6*	Consultancy Agreement, dated February 1, 2018, by and among the registrant, John Richard & Associates, LLC, and John Richard
10.6.1*	Contract of Employment, dated February 26, 2018, between the registrant and John Richard
10.7*	Letter of Appointment, dated July 29, 2015, between the registrant and Dr. Peter Fellner
10.8*	Letter of Appointment, dated July 29, 2015, between the registrant and Frank Armstrong
10.9*	Letter of Appointment, dated July 29, 2015, between the registrant and Peter Bains
10.10*	Letter of Appointment, dated October 28, 2015, between the registrant and Paul Blackburn
10.11*	Letter of Appointment, dated July 29, 2015, between the registrant and Anders Ekblom
10.12*	Letter of Appointment, dated July 29, 2015, between the registrant and Kunal Kashyap
10.13*	Rules of the Mereo BioPharma Group plc Share Option Scheme, as adopted March 4, 2016 and amended April 4, 2017 and March 20, 2018 and form of option documentation
10.14*	Scheme Rules of Mereo BioPharma Group Limited Share Option Scheme, as adopted July 8, 2015
10.15*	Rules of the Mereo BioPharma Group plc Long Term Incentive Plan, as adopted March 4, 2016 and amended March 20, 2018
10.16*	Rules of the Mereo BioPharma Group plc Deferred Bonus Share Plan, as adopted March 4, 2016 and amended March 20, 2018
10.17*	Rules of the Mereo BioPharma Group plc Share Option Scheme for Non-Executive Directors, as adopted March 20, 2018 and form of option documentation
10.18†*	BCT197 Asset Purchase Agreement, dated July 28, 2015, by and between Mereo BioPharma 1 Limited and Novartis Pharma AG
10.19†*	BGS649 Asset Purchase Agreement, dated July 28, 2015, by and between Mereo BioPharma 2 Limited and Novartis Pharma AG

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<u>Exhibit Number</u>	<u>Exhibit Description</u>
10.20†*	<u>BPS804 Asset Purchase Agreement, dated July 28, 2015, by and between Mereo BioPharma 3 Limited and Novartis Pharma AG</u>
10.21†*	<u>Sublicense Agreement, dated July 29, 2015, by and between Mereo BioPharma 3 Limited and Novartis Pharma AG</u>
10.22†*	<u>Exclusive License and Option Agreement, dated October 28, 2017, by and between Mereo BioPharma 4 Limited and AstraZeneca AB</u>
10.23*	<u>Loan Agreement, dated August 7, 2017, by and among the registrant, as borrower, the guarantors party thereto, Silicon Valley Bank, as a lender, and Kreos Capital V (UK) Limited, as a lender, agent and security agent</u>
10.24*	<u>Form of Deed of Indemnity for board members</u>
10.25*	<u>Convertible Loan Note Instrument relating to Mereo BioPharma Group plc, dated June 3, 2016, by the registrant, including Deeds of Amendment thereto, between the registrant and Novartis Pharma AG</u>
21.1*	<u>List of Subsidiaries</u>
23.1	<u>Consent of Ernst & Young LLP, independent registered public accounting firm</u>
23.2*	<u>Consent of Latham & Watkins LLP (included in Exhibit 5.1)</u>
24.1*	<u>Powers of Attorney</u>

* Previously filed.

† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment and this exhibit has been filed separately with the SEC.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form F-1 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in London, the United Kingdom on April 9, 2018.

MEREO BIOPHARMA GROUP PLC

By: /s/ Denise Scots-Knight

Name: Denise Scots-Knight, Ph.D.

Title: Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1933, as amended, this registration statement has been signed by the following persons on April 9, 2018 in the capacities indicated:

<u>Name</u>	<u>Title</u>
<u>/s/ Denise Scots-Knight</u> Denise Scots-Knight, Ph.D.	Chief Executive Officer and Member of the Board (Principal Executive Officer)
<u>*</u> Richard Jones	Chief Financial Officer and Member of the Board (Principal Financial Officer and Principal Accounting Officer)
<u>*</u> Peter Fellner, Ph.D.	Chairman of the Board
<u>*</u> Frank Armstrong, MBChB	Member of the Board
<u>*</u> Peter Bains	Member of the Board
<u>*</u> Paul Blackburn	Member of the Board
<u>*</u> Anders Ekblom, M.D., Ph.D.	Member of the Board
<u>*</u> Kunal Kashyap	Member of the Board

*By: /s/ Denise Scots-Knight
Denise Scots-Knight, Ph.D.,
Attorney-in-fact

SIGNATURE OF AUTHORIZED U.S. REPRESENTATIVE OF REGISTRANT

Pursuant to the requirements of the Securities Act of 1933, as amended, the undersigned, the duly authorized representative in the United States of Mereo BioPharma Group plc has signed this registration statement on April 9, 2018.

By: /s/ Colleen A. Devries

Name: Colleen A. Devries

Title: SVP on behalf of Cogency Global Inc.

MEREO BIOPHARMA GROUP PLC
[●] Ordinary Shares
and
[●] American Depositary Shares
Representing [●] Ordinary Shares
(Nominal Value £0.003 Each)

UNDERWRITING AGREEMENT

[●], 2018

COWEN AND COMPANY, LLC
 BMO CAPITAL MARKETS CORP.
 RBC CAPITAL MARKETS, LLC,

As Representatives of the several Underwriters named in Schedule A hereto

c/o Cowen and Company, LLC
 599 Lexington Avenue
 New York, New York 10022

c/o BMO Capital Markets Corp.
 3 Times Square, 25th Floor
 New York, New York 10036

c/o RBC Capital Markets LLC
 3 World Financial Center
 200 Vesey Street
 New York, New York 10281

Dear Sirs and Madams:

1. *INTRODUCTORY.* Mereo BioPharma Group plc, a public limited company incorporated under the laws of England and Wales with registered number 09481161 (the “**Company**”), proposes to issue and sell, pursuant to the terms of this Underwriting Agreement (the “**Agreement**”), to the several underwriters named in Schedule A hereto (the “**Underwriters**,” or, each, an “**Underwriter**”), an aggregate of [●] ordinary shares, nominal value £0.003 each (the “**Ordinary Shares**”), of the Company (the “**Firm Shares**”) and [●] American Depositary Shares (“**ADSs**”), each representing [●] Ordinary Shares (the “**Firm ADSs**”). The Firm Shares and the Firm ADSs are collectively hereinafter referred to as the “**Firm Securities**.” The Company also proposes to issue and sell to the Underwriters, upon the terms and conditions set forth in Section 3 hereof, up to an additional [●] ADSs (the “**Optional ADSs**”). The Firm Securities and, if and to the extent such option is exercised, the Optional ADSs are referred to herein as the “**Offered Securities**.” Unless context otherwise requires, each reference to the Firm Securities, the Optional ADSs and the Offered Securities herein also includes the Ordinary Shares represented by the ADSs. Cowen and Company, LLC (“**Cowen**”), BMO Capital Markets Corp. (“**BMO**”) and RBC Capital Markets LLC are acting as representatives of the several Underwriters and in such capacity are hereinafter referred to as the “**Representatives**.”

The ADSs will be evidenced by American Depositary Receipts (the “**ADRs**”) to be issued pursuant to a deposit agreement, dated on or about the Closing Date (the “**Deposit Agreement**”), among the Company, Citibank N.A., as depositary (the “**Depositary**”), and the holders from time to time of the ADRs evidencing the ADSs issued thereunder. The Company shall, following subscription by the Underwriters of the Firm ADSs and, if applicable, the Optional ADSs, deposit, on behalf of the Underwriters, the Ordinary Shares represented by such ADSs with Citibank N.A., London Branch, as custodian (the “**Custodian**”) for the Depositary, which shall deliver such ADSs to the Representatives for the account of the several Underwriters for subsequent delivery to the other several Underwriters or the investors, as the case may be.

2. **REPRESENTATIONS AND WARRANTIES OF THE COMPANY.** The Company represents and warrants to the several Underwriters, as of the date hereof and as of each Closing Date (as defined below), and agrees with the several Underwriters, that:

(a) A registration statement of the Company on Form F-1 (File No. 333—223883) (including all pre-effective amendments thereto, and all post-effective amendments thereto filed before execution of this Agreement, the “**Initial Registration Statement**”) in respect of the Offered Securities has been filed with the Securities and Exchange Commission (the “**Commission**”). The Initial Registration Statement in the form heretofore delivered to the Representatives, and, excluding exhibits thereto, to the Representatives for each of the other Underwriters, has been declared effective by the Commission in such form and complies in all material respects with the requirements of the Securities Act of 1933, as amended (the “**Securities Act**”), and the rules and regulations of the Commission thereunder (the “**Rules and Regulations**”). Other than (i) the Initial Registration Statement, (ii) a registration statement, if any, increasing the size of the offering filed pursuant to Rule 462(b) under the Securities Act and the Rules and Regulations (a “**Rule 462(b) Registration Statement**”), (iii) a registration statement on Form F-6 (File No. 333-223890) covering the registration of the ADSs to be issued and sold by the Company to the Underwriters hereunder under the Securities Act and the Rules and Regulations (the “**ADS Registration Statement**”), (iv) any Preliminary Prospectus (as defined below), (v) the Prospectus (as defined below) contemplated by this Agreement to be filed pursuant to Rule 424(b) of the Rules and Regulations in accordance with Section 4(a) hereof and (vi) any Issuer Free Writing Prospectus (as defined below), no other document with respect to the offer and sale of the Offered Securities has heretofore been filed with the Commission. No stop order suspending the effectiveness of the Initial Registration Statement, any post-effective amendment thereto, the Rule 462(b) Registration Statement, if any, or the ADS Registration Statement has been issued, and no proceeding for that purpose or pursuant to Section 8A of the Securities Act has been initiated or threatened by the Commission (any preliminary prospectus included in the Initial Registration Statement or filed with the Commission pursuant to Rule 424(a) of the Rules and Regulations is hereinafter called a “**Preliminary Prospectus**”). The Initial Registration Statement and the Rule 462(b) Registration Statement, if any, in each case including all exhibits thereto and including (y) the information contained in the Prospectus filed with the Commission pursuant to Rule 424(b) of the Rules and Regulations and deemed by virtue of Rule 430A under the Securities Act to be part of the Initial Registration Statement at the time it became effective and (z) the documents incorporated by reference in the Rule 462(b) Registration Statement at the time the Rule 462(b) Registration Statement became effective, are hereinafter collectively called the “**Registration Statement**.” The final prospectus, in the form filed pursuant to and within the time limits described in Rule 424(b) under the Rules and Regulations, is hereinafter called the “**Prospectus**.”

(b) As of the Applicable Time (as defined below) and as of the Closing Date or the Option Closing Date (as defined below), as the case may be, neither (i) the General Use Free Writing Prospectus(es) (as defined below) issued at or prior to the Applicable Time, the Pricing Prospectus (as defined below) and the information included in Schedule C hereto, all considered together (collectively, the “**General Disclosure Package**”), (ii) any individual Limited Use Free Writing Prospectus (as defined

below), (iii) the bona fide electronic road show (as defined in Rule 433(h)(5) of the Rules and Regulations), nor (iv) any individual Written Testing-the-Waters Communication, when considered together with the General Disclosure Package, included or will include any untrue statement of a material fact or omitted or will omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading; *provided, however*, that the Company makes no representations or warranties as to information contained in or omitted from the Pricing Prospectus in reliance upon, and in conformity with, written information furnished to the Company through the Representatives by or on behalf of any Underwriter specifically for inclusion therein, which information the parties hereto agree is limited to the Underwriters' Information (as defined in Section 17 hereof). As used in this paragraph (b) and elsewhere in this Agreement:

"Applicable Time" means [•] [A/P].M., New York time, on the date of this Agreement or such other time as agreed to by the Company and the Representatives.

"General Use Free Writing Prospectus" means any Issuer Free Writing Prospectus that is identified in Schedule B to this Agreement.

"Issuer Free Writing Prospectus" means any "issuer free writing prospectus," as defined in Rule 433 of the Rules and Regulations relating to the Offered Securities in the form filed or required to be filed with the Commission or, if not required to be filed, in the form retained in the Company's records pursuant to Rule 433(g) of the Rules and Regulations.

"Limited Use Free Writing Prospectuses" means any Issuer Free Writing Prospectus that is not a General Use Free Writing Prospectus.

"Pricing Prospectus" means the Preliminary Prospectus relating to the Offered Securities that is included in the Registration Statement immediately prior to the Applicable Time.

"Written Testing-the-Waters Communication" means any Testing-the-Waters Communication (as defined below) that is a written communication within the meaning of Rule 405 of the Rules and Regulations.

(c) No order preventing or suspending the use of any Preliminary Prospectus, any Issuer Free Writing Prospectus or the Prospectus relating to the proposed offering of the Offered Securities has been issued by the Commission, and no proceeding for that purpose or pursuant to Section 8A of the Securities Act has been instituted or threatened by the Commission, and each Preliminary Prospectus, at the time of filing thereof, conformed in all material respects to the requirements of the Securities Act and the Rules and Regulations, and did not contain an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading; *provided, however*, that the Company makes no representations or warranties as to information contained in or omitted from any Preliminary Prospectus, in reliance upon, and in conformity with, written information furnished to the Company through the Representatives by or on behalf of any Underwriter specifically for inclusion therein, which information the parties hereto agree is limited to the Underwriters' Information.

(d) At the respective times the Registration Statement and any amendments thereto and the ADS Registration Statement and any amendments thereto became or become effective and at each Closing Date, the Registration Statement and any amendments thereto and the ADS Registration Statement and any amendments thereto conformed and will conform in all material respects to the requirements of the Securities Act and the Rules and Regulations, and did not and will not contain any untrue statement of a material fact or omit to state any material fact required to be stated therein or

necessary to make the statements therein not misleading; and the Prospectus and any amendments or supplements thereto, at the time the Prospectus or any amendment or supplement thereto was issued and at each Closing Date, conformed and will conform in all material respects to the requirements of the Securities Act and the Rules and Regulations, and did not and will not contain an untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein, in light of the circumstances under which they were made, not misleading; *provided, however*, that the foregoing representations and warranties in this paragraph (d) shall not apply to information contained in or omitted from the Registration Statement, the ADS Registration Statement or the Prospectus or any amendment or supplement thereto, in reliance upon, and in conformity with, written information furnished to the Company through the Representatives by or on behalf of any Underwriter specifically for inclusion therein, which information the parties hereto agree is limited to the Underwriters' Information. The Prospectus contains or will contain all required information under Rule 430A.

(e) Each Issuer Free Writing Prospectus, as of its issue date and at all subsequent times through the completion of the public offer and sale of the Offered Securities or until any earlier date that the Company notified or notifies the Representatives as described in Section 4(h) hereof, did not, does not and will not include any information that conflicted, conflicts or will conflict with the information contained in the Registration Statement, the ADS Registration Statement, the Pricing Prospectus or the Prospectus, or included or would include an untrue statement of a material fact or, omitted or would omit to state a material fact required to be stated therein or necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading; *provided, however*, that the foregoing representations and warranties in this paragraph (e) shall not apply to information contained in or omitted from the Registration Statement, the ADS Registration Statement or the Prospectus, or any amendment or supplement thereto, in reliance upon, and in conformity with, written information furnished to the Company through the Representatives by or on behalf of any Underwriter specifically for inclusion therein, which information the parties hereto agree is limited to the Underwriters' Information.

(f) The Company is a "foreign private issuer" within the meaning of Rule 405 under the Securities Act.

(g) The Company has not, directly or indirectly, distributed and will not distribute any offering material in connection with the offering and sale of the Offered Securities other than any Preliminary Prospectus, the Prospectus and other materials, if any, permitted under the Securities Act and consistent with Section 4(e) below. The Company will file with the Commission all Issuer Free Writing Prospectuses (other than a "road show" as described in Rule 433(d)(8) of the Rules and Regulations) in the time and manner required under Rules 163(b)(2) and 433(d) of the Rules and Regulations. From and after twelve (12) months prior to the date of this Agreement, the Company has not taken any action which would constitute an offer of the Offered Securities to the public in any Member State of the European Economic Area which has implemented Directive 2003/71/EC as amended (including by Directive 2010/73/EU and any relevant implementing measures in the relevant Member State (the "**EU Prospectus Directive**")) for which a prospectus would need to be approved and published, in accordance with the EU Prospectus Directive, as implemented in such relevant jurisdiction.

(h) From the time of the initial confidential submission of the Registration Statement to the Commission (or, if earlier, the first date on which the Company engaged directly or through any person authorized to act on its behalf in any Testing-the-Waters Communications) through the date hereof, the Company has been and is an "emerging growth company," as defined in Section 2(a) of the Securities Act (an "**Emerging Growth Company**"). "**Testing-the-Waters Communication**" means any oral or written communication with potential investors undertaken in reliance on Section 5(d) of the Securities Act.

(i) At the time of filing the Initial Registration Statement, the ADS Registration Statement, any Rule 462(b) Registration Statement and any post-effective amendments thereto, and at the date hereof, the Company was not, and the Company currently is not, an “ineligible issuer,” as defined in Rule 405 of the Rules and Regulations.

(j) The Company (a) has not engaged in any Testing-the-Waters Communication other than Testing-the-Waters Communications with the consent of the Representatives with entities that are qualified institutional buyers within the meaning of Rule 144A under the Securities Act or institutions that are accredited investors within the meaning of Rule 501 under the Securities Act and (b) has not authorized anyone other than the Representatives to engage in Testing-the-Waters Communications. The Company reconfirms that the Representatives have been authorized to act on its behalf in undertaking Testing-the-Waters Communications. The Company has not distributed or approved for distribution any Written Testing-the-Waters Communications in each case in connection with the offering of the Offered Securities.

(k) The Company has been duly incorporated and is validly existing as a public limited company under the laws of England and Wales. Each subsidiary of the Company has been duly incorporated and is validly existing as a private limited company under the laws of England and Wales. The Company and each of its subsidiaries are duly qualified to do business and is in good standing, to the extent such concept applies, in each jurisdiction in which their respective ownership or lease of property or the conduct of their respective businesses requires such qualification and have all power and authority (corporate or other) necessary to own or hold their respective properties and to conduct the businesses in which they are engaged, except where the failure to so qualify or be in good standing, if applicable, or have such power or authority (corporate or other) would not (i) have, individually or in the aggregate, a material adverse effect on the business, properties, assets, management, financial position, shareholders’ equity, results of operations or prospects of the Company and its subsidiaries, taken as a whole, or (ii) impair in any material respect the ability of the Company to perform its obligations under this Agreement or to consummate any transactions contemplated by this Agreement, the General Disclosure Package or the Prospectus (any such effect as described in clauses (i) or (ii), a “**Material Adverse Effect**”). The Company does not own or control, directly or indirectly, any interest in any corporation, partnership, limited liability company, association or other entity, other than as listed in Schedule E hereto.

(l) This Agreement has been duly authorized, executed and delivered by the Company.

(m) The Deposit Agreement has been duly authorized, executed and delivered by the Company and, assuming due authorization, execution and delivery by the Depositary, constitutes a valid and legally binding obligation of the Company, enforceable in accordance with its terms, except as the enforceability thereof may be limited by bankruptcy, insolvency, reorganization or similar laws relating to or affecting creditors’ rights generally or by general equitable principles. Upon due issuance by the Depositary of the ADRs evidencing the Offered Securities in the form of ADSs against the deposit of the Ordinary Shares in respect thereof in accordance with the provisions of the Deposit Agreement, such ADRs will be duly and validly issued and the persons in whose names the ADRs are registered will be entitled to the rights specified therein and in the Deposit Agreement. The issuance and sale of the Offered Securities in the form of ADSs by the Company and the deposit of the Ordinary Shares with the Depositary and the issuance of the ADRs evidencing such Offered Securities as contemplated by this Agreement and the Deposit Agreement will not trigger any anti-dilution rights of any holder of any Ordinary Shares or ADSs, securities convertible into or exchangeable or exercisable for Ordinary Shares or ADSs or options, warrants or other rights to purchase Ordinary Shares or ADSs or any other securities of the Company with respect to such Ordinary Shares, ADSs, securities, options, warrants or rights, save for any rights of pre-emption under the United Kingdom Companies Act 2006 (“**CA 2006**”) that have

been duly waived or disappplied. The Deposit Agreement and the ADRs conform in all material respects to each description thereof in the Registration Statement, General Disclosure Package and Prospectus. Each holder of ADRs issued pursuant to the Deposit Agreement shall be entitled, subject to the Deposit Agreement, to seek enforcement of its rights through the Depositary or its nominee registered as a representative of the holders of the ADRs in a direct suit, action or proceeding against the Company.

(n) The Offered Securities in the form of Ordinary Shares to be issued and sold by the Company to the Underwriters hereunder have been duly and validly authorized (including pursuant to section 551 of the CA 2006) and, when allotted, issued and delivered against payment therefor as provided herein, will be duly and validly allotted and issued, fully paid, not subject to any call for the payment of further capital and free of any liens, encumbrances, rights of first refusal, preemptive or other similar rights, save for any rights of pre-emption under the CA 2006 that have been duly waived or disappplied and will conform to the descriptions thereof in the Registration Statement, the General Disclosure Package and the Prospectus. The Ordinary Shares represented by ADSs may be freely deposited by the Company with the Custodian for the Depositary against issuance of ADRs evidencing such Offered Securities in the form of ADSs, as contemplated by the Deposit Agreement. The Offered Securities in the form of ADSs have been duly authorized for issuance and sale pursuant to this Agreement (including, in respect of Ordinary Shares represented by the ADSs, pursuant to section 551 of the CA 2006) and, when issued and delivered against payment therefor as provided herein, will be duly and validly issued, fully paid and nonassessable, and free of any liens, encumbrances, rights of first refusal, preemptive or other similar rights, and will conform to the descriptions thereof in the Registration Statement, the General Disclosure Package and the Prospectus. The issuance of the Offered Securities is not subject to any liens, encumbrances, rights of first refusal, preemptive or similar rights (including those provided by section 561 (1) of the CA 2006 in respect of the Ordinary Shares represented by ADSs). Upon the issuance, sale and delivery to the Underwriters of the Offered Securities, and payment therefor, the Underwriters will acquire good, marketable and valid title to such Offered Securities, free and clear of all pledges, liens, security interests, charges, claims or encumbrances.

(o) The Company has an issued and outstanding share capital as set forth under the heading “Capitalization” in the Pricing Prospectus, and all of the issued shares of the Company have been duly and validly authorized and issued, are fully paid, and are not subject to any call for the payment of further capital and are free of any preemptive or other similar rights, and have been issued in compliance with the Company’s articles of association and applicable company and securities laws, and conform to the description thereof contained in the General Disclosure Package and the Prospectus under the heading “Description of Share Capital and Articles of Association.” All of the Company’s options and other rights to purchase or exchange any securities for shares of the Company’s capital stock have been duly authorized and validly granted or issued and were granted or issued in compliance with applicable company and securities laws. None of the outstanding Ordinary Shares were issued in violation of any preemptive rights, rights of first refusal or other similar rights to subscribe for or purchase securities of the Company. As of the date set forth in the General Disclosure Package, there were no authorized or outstanding shares, options, warrants, preemptive rights, rights of first refusal or other rights to purchase, or equity or debt securities convertible into or exchangeable or exercisable for, any shares of the Company or any of its subsidiaries, other than those described above or described in the General Disclosure Package. Since such date, the Company has not issued any securities other than Ordinary Shares issued upon the exercise of share options or other awards outstanding under the Company’s share option plans, options or other securities granted or issued pursuant to the Company’s existing equity compensation plans or other plans, the issuance of Ordinary Shares pursuant to employee stock purchase plans, or the issuance of Ordinary Shares pursuant to the terms of those certain convertible notes issued by the Company to Novartis Pharma AG on June 2, 2016 (the “Novartis Notes”) or upon the exercise of warrants described in the General Disclosure Package. The description of the Company’s share option, share bonus and other share plans or arrangements, and the options or other rights granted thereunder, as

described in the General Disclosure Package and the Prospectus, accurately and fairly present the information required to be shown with respect to such plans, arrangements, options and rights. All of the outstanding issued share capital of each subsidiary of the Company has been duly and validly authorized and issued, is fully paid, nonassessable and free of any preemptive or other similar rights, and has been issued in compliance with applicable company and securities laws and is owned directly by the Company free and clear of any claim, lien, encumbrance, security interest, restriction on voting or transfer or other claim of any third party.

(p) The issuance and sale of the Offered Securities as contemplated hereby will not cause any holder of any share capital, securities convertible into or exchangeable or exercisable for share capital or options, warrants or other rights to purchase share capital or any other securities of the Company to have any right to acquire any preferred shares of the Company.

(q) The execution, delivery and performance of this Agreement by the Company, the issue and sale of the Offered Securities by the Company, the deposit of the Ordinary Shares represented by ADSs with the Custodian for the Depositary, and the consummation of the transactions contemplated hereby will not (with or without notice or lapse of time or both) (i) conflict with or result in a breach or violation of any of the terms or provisions of, constitute a default or a Debt Repayment Triggering Event (as defined below) under, or result in the creation or imposition of any lien, encumbrance, security interest, claim or charge upon any property or assets of the Company or any of its subsidiaries pursuant to, any indenture, mortgage, deed of trust, loan agreement or other agreement or instrument to which the Company is a party or by which the Company or any of its subsidiaries is bound or to which any of the property or assets of the Company or any of its subsidiaries is subject, (ii) result in any violation of the provisions of the articles of association of the Company or any of its subsidiaries or (iii) result in the violation of any U.S. or non-U.S. law, statute, rule, regulation, judgment, order or decree of any court or governmental or regulatory agency or authority, having jurisdiction over the Company or any of its subsidiaries or any of their respective properties or assets except, in the case of clauses (i) to (iii) above, to the extent that any such conflict, breach, violation or default that would not, individually or in the aggregate, have a Material Adverse Effect. A “**Debt Repayment Triggering Event**” means any event or condition that gives, or with the giving of notice or lapse of time would give the holder of any note, debenture or other evidence of indebtedness (or any person acting on such holder’s behalf) the right to require the repurchase, redemption or repayment of all or a portion of such indebtedness by the Company or any of its subsidiaries.

(r) Except for the registration of the Offered Securities under the Securities Act and Exchange Act (as defined below) and applicable U.S. state securities laws and such consents, approvals, authorizations, orders and registrations or qualifications as may be required by the Financial Industry Regulatory Authority, Inc. (“**FINRA**”), The Nasdaq Global Market (the “**Exchange**”), the UK Financial Conduct Authority and the London Stock Exchange plc (the “**London Stock Exchange**”), or pursuant to the AIM Rules for Companies published by the London Stock Exchange from time to time (the “**AIM Rules for Companies**”), or pursuant to the CA 2006, the United Kingdom Financial Services and Markets Act 2000, as amended, and/or EU Regulation (EU 596/2014) on market abuse (the “**Market Abuse Regulation**”), in connection with the purchase and distribution of the Offered Securities by the Underwriters, the listing of the Offered Securities on the Exchange and the admission of the Ordinary Shares to be sold by the Company hereunder to trading on the AIM market operated by the London Stock Exchange (“**AIM**”), as applicable, no consent, approval, authorization or order of, or filing, qualification or registration (each, an “**Authorization**”) with, any U.S. or non-U.S. court, governmental or regulatory agency or authority, which has not been made, obtained or taken and is not in full force and effect, is required for the execution, delivery and performance of this Agreement or the Deposit Agreement by the Company, the issuance and sale of the Offered Securities, the deposit of the Ordinary Shares represented by ADSs with the Custodian for the Depositary or the consummation of the transactions contemplated

hereby; and no event has occurred that allows or results in, or after notice or lapse of time or both would allow or result in, revocation, suspension, termination or invalidation of any such Authorization or any other impairment of the rights of the holder or maker of any such Authorization. All corporate approvals (including those of shareholders) necessary for the Company to consummate the transactions contemplated by this Agreement have been obtained and are in effect.

(s) Ernst & Young LLP, who have certified certain financial statements of the Company and its subsidiaries included in the Registration Statement, the General Disclosure Package and the Prospectus, is an independent registered public accounting firm with respect to the Company within the meaning of Article 2-01 of Regulation S-X and the Public Company Accounting Oversight Board (United States) (the “**PCAOB**”) and applicable laws of England and Wales.

(t) The financial statements, together with the related notes, included in the General Disclosure Package, the Prospectus and in the Registration Statement present fairly, in all material respects, the financial position and the results of operations and changes in financial position of the Company and its subsidiaries at the respective dates or for the respective periods therein specified. Such statements and related notes have been prepared in accordance with International Financial Reporting Standards (“**IFRS**”) as issued by the European Union and the International Accounting Standards Board (“**IASB**”) applied on a consistent basis throughout the periods involved except as may be set forth in the related notes included in the General Disclosure Package. The financial statements, together with the related notes, included in the General Disclosure Package and the Prospectus comply in all material respects with Regulation S-X. No other financial statements or supporting schedules or exhibits are required by Regulation S-X to be described or included in the Registration Statement, the General Disclosure Package or the Prospectus. The pro forma and pro forma as adjusted financial information included in the Registration Statement, the General Disclosure Package and the Prospectus have been properly compiled and prepared in accordance with the applicable requirements of Rule 11-02 of Regulation S-X and present fairly, in all material respects, the information shown therein, and the assumptions used in the preparation thereof are reasonable and the adjustments used therein are appropriate to give effect to the transactions and circumstances referred to therein. The summary and selected financial data included in the General Disclosure Package, the Prospectus and the Registration Statement present fairly, in all material respects, the information shown therein as at the respective dates and for the respective periods specified and are derived from the consolidated financial statements set forth in the Registration Statement, the Pricing Prospectus and the Prospectus and other financial information.

(u) Neither the Company nor any of its subsidiaries has sustained, since the date of the latest audited financial statements included in the General Disclosure Package, (i) any material loss or interference with its business from fire, explosion, flood or other calamity, whether or not covered by insurance, or from any labor dispute or action, order or decree of any court or governmental or regulatory authority, otherwise than as set forth or contemplated in the General Disclosure Package, or (ii) any change in the capital stock (other than the issuance of Ordinary Shares or other securities of the Company upon exercise, exchange, vesting, or conversion of awards granted pursuant to, and the grant of awards under, existing equity incentive plans described in the Registration Statement, the General Disclosure Package and the Prospectus or the issuance of Ordinary Shares pursuant to the terms of the Novartis Notes or warrants, each as described in the Registration Statement, the General Disclosure Package and the Prospectus) or long-term debt of the Company or any of its subsidiaries, or any dividend or distribution of any kind declared, set aside for payment, paid or made by the Company on any class of capital stock, or any material adverse changes, or, to the Company’s knowledge, any development involving a prospective material adverse change, in or affecting the business, properties, assets, management, financial position, shareholders’ equity, results of operations or prospects of the Company and its subsidiaries, taken as a whole, otherwise than as set forth or contemplated in the General Disclosure Package.

(v) Neither the Company nor any of its subsidiaries is a party to any corporate integrity agreements, monitoring agreements, consent decrees, settlement orders, or similar agreements with or imposed by any governmental or regulatory authority. The Company and each of its subsidiaries is in compliance with all applicable U.S. or non-U.S. laws, rules, regulations, orders and decrees governing its business and the regulation of pharmaceuticals or biohazardous substances or materials, including without limitation the U.S. federal Food, Drug and Cosmetic Act, U.S. data privacy and securities laws and U.S. health care fraud and abuse laws, except where noncompliance would not, individually or in the aggregate, have a Material Adverse Effect.

(w) Neither the Company nor any of its subsidiaries is in (i) violation of its articles of association, (ii) violation of the AIM Rules for Companies and/or, assuming compliance by the Underwriters with the requirements and restrictions described under the captions “Underwriting—Selling Restrictions—European Economic Area” and “—United Kingdom” in the Registration Statement, the General Disclosure Package and the Prospectus, the UK Financial Conduct Authority’s Prospectus Rules, (iii) default in any respect, and no event has occurred which, with notice or lapse of time or both, would constitute such a default, in the due performance or observance of any term, covenant or condition contained in any indenture, mortgage, deed of trust, loan agreement, lease or other agreement or instrument to which it is a party or by which it is bound or to which any of its property or assets is subject (including, without limitation, those administered by the U.S. Food and Drug Administration of the U.S. Department of Health and Human Services (the “**FDA**”), the European Medicines Agency (the “**EMA**”) or comparable U.S. or non-U.S. governmental authorities of competent jurisdiction) or (iv) violation in any respect of any other law, ordinance, governmental rule, regulation or court order, decree or judgment to which it or its property or assets may be subject except, in the case of clauses (ii) through (iv) above, for any such violation or default that would not reasonably be expected to have, individually or in the aggregate, a Material Adverse Effect.

(x) The Company and each of its subsidiaries possess all licenses, certificates, authorizations and permits issued by, and has made all declarations and filings with, the appropriate U.S. or non-U.S. governmental or regulatory authorities of competent jurisdiction (including, without limitation, the FDA, the EMA or comparable U.S. or non-U.S. governmental authorities of competent jurisdiction) that are necessary for the ownership or lease of their respective properties or the conduct of their respective businesses as described in the Registration Statement, General Disclosure Package and the Prospectus (collectively, the “**Governmental Permits**”), except where any failures to possess or make the same would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect. The Company and its subsidiaries are in compliance with all such Governmental Permits, and all such Governmental Permits are valid and in full force and effect, except where such non-compliance, invalidity or failure to be in full force and effect would not reasonably be expected, individually or in the aggregate, to have a Material Adverse Effect. Neither the Company nor any subsidiary has received written notification of any revocation, modification, suspension, termination or invalidation (or proceedings related thereto) of any such Governmental Permit and the Company has no knowledge that any such Governmental Permit requiring renewal will not be renewed. The Company and each of its subsidiaries have filed, obtained, maintained or submitted all material reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments as required by any applicable laws or Governmental Permits, and all such reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments were complete and accurate on the date filed in all material respects (or were corrected or supplemented by a subsequent submission), except where the failure to so file, obtain, maintain or submit, or such incompleteness or inaccuracy, would not reasonably be expected to have a Material Adverse Effect.

(y) The studies, tests and preclinical studies or clinical trials conducted by or on behalf of the Company and its subsidiaries that are described in the General Disclosure Package and the Prospectus (the “**Company Studies and Trials**”) were and, if still pending, are being, conducted in all material respects in accordance with applicable laws and regulations; the descriptions of the results of the Company Studies and Trials contained in the Registration Statement, General Disclosure Package and the Prospectus are accurate in all material respects; the Company has no knowledge of any other studies or trials not described in the General Disclosure Package and the Prospectus, the results of which materially call into question the results described or referred to in the General Disclosure Package and the Prospectus; and the Company has not received any written notices or correspondence from the FDA, the EMA or comparable U.S. or non-U.S. governmental authorities of competent jurisdiction requiring the termination, suspension or material modification of any Company Studies and Trials where such termination, suspension or material modification would reasonably be expected to have a Material Adverse Effect. Neither the Company, nor its subsidiaries nor to the Company’s knowledge, any of their respective directors, officers, employees or agents is debarred, suspended or excluded, or has been convicted of any crime that would result in a debarment, suspension or exclusion from any U.S. federal or state government health care program or human clinical research.

(z) The Company is not and, after giving effect to the offering of the Offered Securities and the application of the proceeds thereof as described in the General Disclosure Package and the Prospectus, will not be required to register as an “investment company” or an entity “controlled” by an “investment company” within the meaning of the U.S. Investment Company Act of 1940, as amended, and the rules and regulations of the Commission thereunder.

(aa) There are no business relationships or related person transactions involving the Company or any of its subsidiaries or any other person required to be described in the General Disclosure Package and the Prospectus that have not been described as required.

(bb) Neither the Company nor, to the Company’s knowledge, any of its officers, directors or affiliates has taken or will take, directly or indirectly, any action designed or intended to stabilize or manipulate the price of any security of the Company, or which caused or resulted in, or which might in the future reasonably be expected to cause or result in, stabilization or manipulation of the price of any security of the Company, save where such action was carried out in conformity with Article 5 of the Market Abuse Regulation and the delegated regulation(s) thereunder (or, prior to the Market Abuse Regulation coming into effect on July 3, 2016, the price stabilizing rules of the UK Financial Conduct Authority).

(cc) The Company and each of its subsidiaries owns or possesses the valid right to use all (i) patents, patent applications, trademarks, trademark registrations, service marks, service mark registrations, Internet domain name registrations, copyrights, copyright registrations, licenses and trade secret rights (collectively, “**Intellectual Property Rights**”) and (ii) inventions, software, works of authorships, trademarks, service marks, trade names, databases, formulae, know how, Internet domain names and other intellectual property (including trade secrets and other unpatented and/or unpatentable proprietary confidential information, systems, or procedures) (collectively, “**Intellectual Property Assets**”) that, to the Company’s knowledge, are necessary to conduct their respective businesses as currently conducted, and as proposed to be conducted and described in the Registration Statement, General Disclosure Package and the Prospectus. Neither the Company nor any of its subsidiaries has received any opinion from its legal counsel concluding that any activities of its business infringes, misappropriates, or otherwise violates, valid and enforceable Intellectual Property Rights of any other person. Neither the Company nor any of its subsidiaries has received written notice of any challenge, which is to their knowledge still pending, by any other person to the rights of the Company and its subsidiaries with respect to any Intellectual Property Rights or Intellectual Property Assets owned or

exclusively licensed by the Company or its subsidiaries. To the Company's knowledge, the Company's and its respective subsidiaries' businesses as now conducted and as proposed to be conducted as described in the Registration Statement, General Disclosure Package and the Prospectus do not and will not give rise to any infringement of, any misappropriation of, or other violation of, any valid and enforceable Intellectual Property Rights of any other person. Except as disclosed in the Registration Statement, General Disclosure Package, and Prospectus, to the Company's knowledge, there are no third parties who have rights to any Intellectual Property Rights described in the Registration Statement, General Disclosure Package and the Prospectus as being owned by or exclusively licensed to the Company (collectively, "**Company Intellectual Property Rights**"), including no liens, security interests, or other encumbrances, except for customary reversionary rights of third-party licensors with respect to Intellectual Property Rights that are disclosed as licensed to the Company or one or more of its subsidiaries. To the Company's knowledge, there is no infringement by third parties of any Company Intellectual Property Rights. To the Company's knowledge, there are no material defects in any of the patents or patent applications included in the Company Intellectual Property Rights disclosed in the Registration Statement, General Disclosure Package and the Prospectus as being owned by or exclusively licensed to the Company. To the Company's knowledge, all licenses for the use of the Company Intellectual Property Rights described in the Registration Statement, the General Disclosure Package and the Prospectus as exclusively licensed to the Company or its subsidiaries (collectively, "**Company In-Licenses**") are valid, binding upon and enforceable by or against the Company or its subsidiaries and by or against the other parties thereto in accordance with their terms. The Company and each of its subsidiaries has complied in all material respects with all Company In-Licenses, and is not in breach of any Company In-License. Neither the Company nor any of its subsidiaries has received written notice of any asserted or threatened claim of breach of any Company In-License, and the Company has no knowledge of any breach by any other person of any Company In-License. Except as described in the General Disclosure Package, there is no pending, and the Company has not received written notice of any threatened, action, suit, proceeding, or claim against the Company or any of its subsidiaries (i) alleging the infringement by the Company or any of its subsidiaries of any patent, trademark, service mark, trade name, copyright, trade secret, license or other intellectual property right or franchise right of any person; or (ii) challenging the validity, enforceability, or scope of any Company Intellectual Property Rights owned by, and to the Company's knowledge, exclusively licensed to the Company, including no interferences, oppositions, reexaminations, or government proceedings, and the Company is unaware of any facts which would form a reasonable basis for any such action, suit, proceeding, or claim. The Company and its subsidiaries have taken all reasonable steps to protect, maintain and safeguard the Company Intellectual Property Rights, including the execution of appropriate nondisclosure, confidentiality agreements and invention assignments with their employees, and to the Company's knowledge, no employee of the Company is in or has been in violation of any term of any employment contract, patent disclosure agreement, invention assignment agreement, non-competition agreement, non-solicitation agreement, nondisclosure agreement, or any restrictive covenant to or with a former employer where the basis of such violation relates to such employee's employment with the Company. To the Company's knowledge, the duty of candor and good faith as required by the United States Patent and Trademark Office during the prosecution of the United States patents and patent applications included in the Company Intellectual Property Rights owned by the Company have been complied with; and in all foreign offices having similar requirements, all such requirements have been complied with. The consummation of the transactions contemplated by this Agreement will not result in the loss or impairment of or payment of any additional amounts with respect to, nor require the consent of any other person in respect of, the Company's or any of its subsidiaries' right to own, use, or hold for use any of the Company Intellectual Property Rights described in the Registration Statement, the General Disclosure Package and the Prospectus as owned by or licensed to the Company for use in the conduct of the business of the Company or its subsidiaries as currently conducted. The Company has at all times complied with all applicable U.S. or non-U.S. laws relating to privacy, data protection, and the collection and use of personal information collected, used, or held for use by the Company in the conduct of the

Company's business, except where the failure to so comply would not reasonably be expected to have a Material Adverse Effect. Except where such claim would not reasonably be expected to have a Material Adverse Effect, no claims have been asserted or threatened in writing against the Company alleging a violation of any person's privacy or personal information or data rights and the consummation of the transactions contemplated hereby will not breach or otherwise cause any violation of any law related to privacy, data protection, or the collection and use of personal information collected, used, or held for use by the Company in the conduct of the Company's business. The Company and each of its subsidiaries has taken all necessary actions to obtain ownership of all works of authorship and inventions made by its employees, consultants and contractors during the time they were employed by or under contract with the Company or any of its subsidiaries and which relate to the Company's business. All key employees have signed confidentiality and invention assignment agreements with the Company.

(dd) The Company and its subsidiaries own no real property. The Company and its subsidiaries have valid and marketable rights to lease or otherwise use, all items of real or personal property which are material to the business of the Company and its subsidiaries taken as a whole, in each case free and clear of all liens, encumbrances, security interests, claims and defects that, individually or in the aggregate, could reasonably be expected to materially affect the value of such property or interfere with the use made and proposed to be made of such property by the Company; and all of the leases and subleases material to the business of the Company, and under which the Company holds properties described in the General Disclosure Package and the Prospectus, are in full force and effect and the Company has not received any notice of any material claim of any sort that has been asserted by anyone adverse to the rights of the Company under any of the leases or subleases mentioned above, or affecting or questioning the rights of the Company to the continued possession of the leased or subleased premises under any such lease or sublease.

(ee) There is (A) no unfair labor practice complaint pending against the Company, nor, to the Company's knowledge, threatened against it, before any U.S. or non-U.S. governmental authorities of competent jurisdiction (including the U.S. National Labor Relations Board and any U.S. state or local labor relations board or any foreign labor relations board), and no significant grievance or significant arbitration proceeding arising out of or under any collective bargaining agreement is so pending against the Company, or, to the Company's knowledge, threatened against it and (B) no labor disturbance by or dispute with, employees of the Company exists or, to the Company's knowledge, is contemplated or threatened, and the Company is not aware of any existing or imminent labor disturbance by the employees of any of the Company's principal suppliers, manufacturers, customers or contractors, that would reasonably be expected, individually or in the aggregate, to have a Material Adverse Effect. The Company is not aware that any key employee or significant group of employees of the Company or any subsidiary plans to terminate employment with the Company.

(ff) The Company is in compliance with all U.S. and non-U.S. rules, laws and regulations issued by governmental authorities of competent jurisdiction relating to the use, treatment, storage and disposal of hazardous or toxic substances or waste and protection of health and safety or the environment which are applicable to its business (the "**Environmental Laws**"). Except as would not be reasonably expected, individually or in the aggregate, to have a Material Adverse Effect, (i) there has been no storage, generation, transportation, handling, treatment, disposal, discharge, emission, or other release of any kind of toxic or other wastes or other hazardous substances by, due to, or caused by the Company (or, to the Company's knowledge, any other entity for whose acts or omissions the Company is or may otherwise be liable) upon any of the property now or previously owned or leased by the Company, or upon any other property, in violation of any law, statute, ordinance, rule, regulation, order, judgment, decree or permit or which would, under any law, statute, ordinance, rule (including rule of common law), regulation, order, judgment, decree or permit, give rise to any liability; and (ii) there has been no disposal, discharge, emission or other release of any kind on to such property or into the environment surrounding

such property of any toxic or other wastes or other hazardous substances. In the ordinary course of business, the Company conducts periodic reviews of the effect of Environmental Laws on the business and assets of the Company and its subsidiaries, in the course of which the Company identifies and evaluates associated costs and liabilities (including, without limitation, any capital or operating expenditures required for clean-up, closure of properties or compliance with Environmental Laws or Governmental Permits issued thereunder, any related constraints on operating activities and any potential liabilities to third parties). The Company has not identified any such associated costs and liabilities that would reasonably be expected to have, individually or in the aggregate, a Material Adverse Effect.

(gg) The Company and its subsidiaries (i) have filed all necessary U.S. and non-U.S. (federal, state, local and foreign) tax returns (or properly requested extensions with respect to such returns), and such returns were when filed, and remain, complete and correct (ii) have paid all federal, state, local and foreign taxes required to be paid and any related assessments, fines, penalties or governmental charges due and payable for which it is liable, except as may be being contested in good faith by appropriate proceedings, and (iii) do not have any tax deficiency or claims outstanding or assessed or, to its knowledge, proposed against it, except, in each of (i), (ii) and (iii) above, as would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect. The accruals and reserves on the books and records of the Company and its subsidiaries in respect of tax liabilities for any taxable period not yet finally determined are adequate to meet any assessments and related liabilities for any such period.

(hh) Except as described in the Registration Statement or the Prospectus, no stamp duty, stamp duty reserve, registration, transfer or other similar taxes or duties ("**Transfer Taxes**") are payable in the United Kingdom by or on behalf of the Underwriters in connection with (i) the creation and issuance and delivery of the Ordinary Shares by the Company in the manner contemplated by this Agreement and the Deposit Agreement; (ii) the delivery of the Ordinary Shares by the Company to or for the account of the Underwriters in the manner contemplated by this Agreement (and for the avoidance of doubt, the "manner contemplated by this Agreement" is that such delivery of Ordinary Shares shall form part of the issuance of such Ordinary Shares to or for the account of the Underwriters); (iii) the delivery of the Ordinary Shares by the Company to the Depositary in the manner contemplated by the Deposit Agreement; (iv) the issuance of the Firm ADSs to or for the account of the Underwriters, in each case in the manner contemplated by this Agreement and the Deposit Agreement; (v) the initial sale and delivery by the Underwriters of the Offered Securities (or the ADRs evidencing the Firm ADSs and the Optional ADSs) to purchasers thereof in the manner contemplated by this Agreement; or (vi) the execution and delivery of this Agreement or the Deposit Agreement.

(ii) The Company carries or is covered by insurance in such amounts and covering such risks as is adequate for the conduct of its business and the value of their respective properties and as is generally deemed customary for companies engaged in similar businesses in similar industries. The Company has no reason to believe that it will not be able to renew its existing insurance coverage as and when such coverage expires or to obtain similar coverage from similar insurers as may be necessary to continue its business at a cost that would not have a Material Adverse Effect. All policies of insurance owned by the Company are, to the Company's knowledge, in full force and effect and the Company is in compliance in all material respects with the terms of such policies. The Company has not received written notice from any insurer, agent of such insurer or the broker of the Company that any material capital improvements or any other material expenditures (other than premium payments) are required or necessary to be made in order to continue such insurance. Except for customary deductibles, the Company does not insure risk of loss through any captive insurance, risk retention group, reciprocal group or by means of any fund or pool of assets specifically set aside for contingent liabilities other than as described in the General Disclosure Package.

(jj) Except as described in the General Disclosure Package and the Prospectus, the Company and each of its subsidiaries has established and maintains a system of “*internal control over financial reporting*” (as such term is defined in Rule 13a-15(f) of the General Rules and Regulations under the Securities Exchange Act of 1934, as amended (such act, the “**Exchange Act**,” and such rules and regulations, the “**Exchange Act Rules**”)) that enables the Company to comply with the AIM Rules for Companies and the Exchange Act and has been designed by its principal executive and principal financial officers, or under their supervision, to provide reasonable assurances that: (i) transactions are executed in accordance with management’s general or specific authorizations; (ii) transactions are recorded as necessary to permit preparation of financial statements in conformity with IFRS as issued by IASB and to maintain accountability for assets; (iii) access to assets is permitted only in accordance with management’s general or specific authorization; and (iv) the recorded accountability for assets is compared with existing assets at reasonable intervals and appropriate action is taken with respect to any differences. The internal control over financial reporting of the Company and its subsidiaries are effective. Except as described in the General Disclosure Package, since the end of the Company’s most recently audited fiscal year, there has been (A) no material weakness in the Company’s internal control over financial reporting (whether or not remediated) and (B) no change in the Company’s internal control over financial reporting that has materially affected, or is reasonably likely to materially affect, the Company’s internal control over financial reporting. The Company’s internal control over financial reporting is overseen or will be overseen, when required in accordance with the Exchange Act Rules, by the audit and risk committee (the “**Audit Committee**”) of the board of directors of the Company (the “**Board**”). Except as described in the General Disclosure Package and the Prospectus, the Company has not publicly disclosed or reported to the Audit Committee or to the Board, and within the next ninety (90) days the Company does not reasonably expect to publicly disclose or report to the Audit Committee or the Board, a significant deficiency, material weakness, change in internal control over financial reporting or fraud involving management or other employees who have a significant role in the internal control over financial reporting (each, an “**Internal Control Event**”) or any material violation of, or failure to comply in all material respects with, U.S. federal securities laws.

(kk) The Company has not received any notice, oral or written, from the Board stating that it is reviewing or investigating, and neither the Company’s independent auditors nor the Audit Committee have recommended that the Board review or investigate, (i) adding to, deleting, changing the application of or changing the Company’s disclosure with respect to, any of the Company’s material accounting policies, (ii) any matter which could result in a restatement of the Company’s financial statements for any annual or interim period during the current or prior three (3) fiscal years, or (iii) any Internal Control Event.

(ll) Except as described in the General Disclosure Package and the Prospectus, the Company has established and maintains disclosure controls and procedures (as such is defined in Rule 13a-15(e) of the Exchange Act Rules) that enable the Company to comply with the requirements of the AIM Rules for Companies and the Exchange Act; such disclosure controls and procedures have been designed to ensure that material information relating to the Company and its consolidated subsidiaries which is required to be disclosed by the Company in reports that they file or submit is recorded, processed, summarized and reported within the time periods specified by the London Stock Exchange and the Commission, including controls and procedures designed to ensure that such information is accumulated and communicated to the Company’s management to allow timely decisions regarding disclosures. The Company has conducted, or will conduct when required, evaluations of the effectiveness of its disclosure controls as required by Rule 13a-15 of the Exchange Act.

(mm) The minute books of the Company and its subsidiaries have been made available to the Underwriters and counsel to the Underwriters, and such books (i) contain a complete summary of all meetings and actions of the Board (including each Board committee) and shareholders of the Company and its subsidiaries (or analogous governing bodies and interest holders, as applicable) since the time of its incorporation through the date of the latest meeting and action, and (ii) accurately in all material respects reflect all transactions referred to in such minutes.

(nn) There is no license, lease, contract, or other agreement or document required by the Securities Act or by the Rules and Regulations to be described in the General Disclosure Package or to be filed as an exhibit to the Registration Statement which is not so described therein or filed therewith as required; and all descriptions of any such licenses, leases, contracts, or other agreements or documents contained in the General Disclosure Package are accurate and complete descriptions of such documents in all material respects. Other than as described in the General Disclosure Package, no such license, lease, contract or other agreement has been suspended or terminated for convenience or default by the Company or any of the other parties thereto, and the Company and its subsidiaries have not received notice of and the Company does not have knowledge of any such pending or threatened suspension or termination.

(oo) No relationship, direct or indirect, exists between or among the Company or any of its subsidiaries, on the one hand, and the directors, officers, shareholders (or analogous interest holders), customers or suppliers of the Company or any of its affiliates, on the other hand, which is required by the Securities Act or by the Rules and Regulations to be described in the General Disclosure Package and the Prospectus and which is not so described.

(pp) No person or entity has the right to require registration of shares of Ordinary Shares, ADSs or other securities of the Company or any of its subsidiaries because of the filing or effectiveness of the Registration Statement, the ADS Registration Statement or otherwise, except for persons and entities who have expressly waived such right in writing or who have been given timely and proper written notice and have failed to exercise such right within the time or times required under the terms and conditions of such right. Except as described in the General Disclosure Package, there are no persons with registration rights or similar rights to have any securities registered by the Company or any of its subsidiaries under the Securities Act.

(qq) The Company does not own any “margin securities” as that term is defined in Regulation U of the Board of Governors of the Federal Reserve System (the “**Federal Reserve Board**”), and none of the proceeds of the sale of the Offered Securities will be used, directly or indirectly, for the purpose of purchasing or carrying any margin security, for the purpose of reducing or retiring any indebtedness which was originally incurred to purchase or carry any margin security or for any other purpose which might cause any of the Offered Securities to be considered a “purpose credit” within the meanings of Regulation T, U or X of the Federal Reserve Board.

(rr) Other than this Agreement, neither the Company nor any of its subsidiaries is a party to any contract, agreement or understanding with any person that would give rise to a valid claim against the Company or any of its subsidiaries, or the Underwriters for a brokerage commission, finder’s fee or like payment in connection with the offering and sale of the Offered Securities or any transaction contemplated by this Agreement, the Registration Statement, the General Disclosure Package or the Prospectus.

(ss) Since the date as of which information is given in the General Disclosure Package through the date hereof, and except for the obligations created by this Agreement and as set forth in the General Disclosure Package, the Company has not (i) issued or granted any securities other than options to purchase Ordinary Shares pursuant to the Company’s share option plan, (ii) incurred any material liability or obligation, direct or contingent, other than liabilities and obligations which were incurred in the ordinary course of business, (iii) entered into any material transaction other than in the ordinary course of business or (iv) declared or paid any dividend on its shares.

(tt) If applicable, all of the information provided to the Underwriters or to counsel for the Underwriters by the Company, and to the Company's knowledge, by its officers and directors and the holders of any securities (debt or equity) or options to acquire any securities of the Company in connection with letters, filings or other supplemental information provided to FINRA pursuant to FINRA Rule 5110 or 5121 is true, correct and complete in all material respects as of the date hereof.

(uu) Except as described in the General Disclosure Package, no subsidiary of the Company is currently prohibited, directly or indirectly, under any agreement or other instrument to which it is a party or is subject, from paying any dividends to the Company, from making any other distribution on such subsidiary's shares, from repaying to the Company any loans or advances to such subsidiary from the Company or from transferring any of such subsidiary's properties or assets to the Company or any other subsidiary of the Company.

(vv) No forward-looking statement (within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act) contained in either the General Disclosure Package, or the Prospectus has been made or reaffirmed without a reasonable basis or has been disclosed other than in good faith.

(ww) The Offered Securities in the form of ADSs have been approved for listing subject to notice of issuance on the Exchange. A registration statement has been filed on Form 8-A pursuant to Section 12 of the Exchange Act, which registration statement complies in all material respects with the Exchange Act.

(xx) The Company is in compliance with all listing and admission requirements and continuing obligations pursuant to the AIM Rules for Companies, the Market Abuse Regulation and the UK Disclosure Guidance and Transparency Rules made by the UK Financial Conduct Authority as amended from time to time (as applicable to the Company).

(yy) The Company has taken all actions reasonably necessary to ensure that, upon and at all times after the effectiveness of the Registration Statement, it will be in compliance in all material respects with all applicable provisions of the Sarbanes-Oxley Act of 2002 and the rules and regulations promulgated in connection therewith (the "**Sarbanes-Oxley Act**") that are then in effect.

(zz) Neither the Company nor any of its subsidiaries nor, to the Company's knowledge, any director, officer, employee, agent, affiliate, or other person acting on behalf of the Company or any of its subsidiaries, has (i) used any corporate funds for unlawful contributions, gifts, entertainment or other unlawful expenses relating to political activity, (ii) made any direct or indirect unlawful payment to U.S. or non-U.S. government officials or employees, political parties or campaigns, political party officials, or candidates for political office from corporate funds, (iii) violated or is in violation of any applicable provision of the U.S. Foreign Corrupt Practices Act of 1977, as amended, or any applicable anti-corruption laws, rules, or regulations of England and Wales or any other jurisdiction in which the Company conducts business; or (iv) made any other unlawful bribe, rebate, payoff, influence payment, kickback, or other unlawful payment to any U.S. or non-U.S. government official or employee, political party or campaign, political party official, or candidate for political office.

(aaa) There are no transactions, arrangements or other relationships between and/or among the Company, any of its affiliates (as such term is defined in Rule 405 of the Rules and Regulations) and any unconsolidated entity, including, but not limited to, any structured finance, special purpose or limited purpose entity that could reasonably be expected to materially affect the Company's liquidity or the availability of or requirements for its capital resources required to be described in the General Disclosure Package and the Prospectus which have not been described as required.

(bbb) There are no outstanding loans, advances (except normal advances for business expenses in the ordinary course of business) or guarantees of indebtedness by the Company to or for the benefit of any of the officers or directors of the Company or any of their respective family members, except as disclosed in the Registration Statement, the General Disclosure Package and the Prospectus. All transactions by the Company with office holders or control persons of the Company have been duly approved by the Board, or duly appointed committees or officers thereof, if and to the extent required under the laws of England and Wales.

(ccc) The statistical and market-related data included in the Registration Statement, the General Disclosure Package and the Prospectus are based on or derived from sources that the Company believes to be reliable and accurate, and such data agree with the sources from which they are derived. All consents of third parties required for the inclusion and use of such data in the Registration Statement, the General Disclosure Package and the Prospectus have been obtained.

(ddd) The operations of the Company and its subsidiaries are and have been conducted at all times in compliance with applicable financial recordkeeping and reporting requirements, including those of the U.S. Bank Secrecy Act, as amended by Title III of the Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism Act of 2001 (USA PATRIOT Act), and the applicable money laundering statutes of jurisdictions where the Company and its subsidiaries conduct business, the rules and regulations thereunder and any related or similar rules, regulations or guidelines, issued, administered or enforced by any governmental agency (collectively, the “**Money Laundering Laws**”), and no action, suit or proceeding by or before any court or governmental or regulatory authority or any arbitrator involving the Company or any of its subsidiaries with respect to the Money Laundering Laws is pending, or to the Company’s knowledge, threatened.

(eee) Neither the Company nor any of its subsidiaries nor, to the Company’s knowledge, any director, officer, agent, employee, affiliate, or other person acting on behalf of the Company or any of its subsidiaries is (i) a person, or is owned or controlled by a person that is, designated on the Specially Designated Nationals and Blocked Persons List or Foreign Sanctions Evaders List, which are both maintained by the Office of Foreign Assets Control of the U.S. Department of Treasury (“**OFAC**”), or any applicable prohibited party list maintained by the United Nations Security Council, the European Union, Her Majesty’s Treasury or other relevant sanctions authority, nor (ii) currently subject to any sanctions administered by OFAC, the United Nations Security Council, the European Union, Her Majesty’s Treasury or any other relevant sanctions authority (collectively, “**Relevant Sanctions Authorities**”). The Company is not located, organized or resident in a country or territory that is the subject of an embargo by the U.S. government (the “**Embargoed Countries**”), including Cuba, Iran, North Korea, Sudan, Syria, and the Crimea. Unless authorized by the Relevant Sanctions Authorities, the Company will not directly or indirectly use the proceeds of the offering, or lend, contribute or otherwise make available such proceeds to any subsidiary, joint venture partner or other person or entity, for the purpose of financing the activities of or business with any Embargoed Country or any person currently subject to any sanctions administered by the Relevant Sanctions Authorities, or in any manner that will result in a violation by any person (including any person participating in the transactions, whether as an underwriter, advisor, investor or otherwise) of sanctions administered by the Relevant Sanctions Authorities.

(fff) Neither the Company nor, to the Company’s knowledge, any of its affiliates (within the meaning of FINRA Rule 5121(f)(1)) directly or indirectly controls, is controlled by, or is under common control with, or is an associated person (within the meaning of Article I, Section 1(rr) of the By-laws of FINRA) of, any of the Underwriters.

(ggg) The directors of the Company have considered the compliance by the Company with the provisions of the UK Corporate Governance Code (2016) as published by the UK Financial Reporting Council (the “**UK Corporate Governance Code**”), and the Company strives, where practicable for a company of its size and nature, to comply with the standards of good practice prescribed by the UK Corporate Governance Code.

(hhh) The choice of the laws of the State of New York as the governing law of this Agreement is a valid choice of law under the laws of England and Wales and will be recognized by courts in England and Wales except as may be limited by general principles of equity and except where to do so would be inconsistent with or overridden by the Regulation (EC) No 593/2008 on the Law Applicable to Contractual Obligations (Rome I). The Company has the corporate power to submit, and pursuant to Section 16 of this Agreement, has legally, validly, effectively and irrevocably submitted, to the personal jurisdiction of each New York State and United States federal court sitting in The City of New York, New York (each, a “**New York Court**”) and has validly and irrevocably waived any objection to the laying of venue of any suit, action or proceeding brought in any such court; and the Company has the power to designate, appoint and empower an authorized agent for service of process in any action arising out of or relating to this Agreement, the Registration Statement, the General Disclosure Package, the Prospectus or the offering of the Offered Securities in any New York Court and service of process effected on such authorized agent will be effective to notify the Company of any action under this Agreement.

(iii) Neither the Company nor any of its subsidiaries nor any of their respective properties, assets or revenues enjoy any rights of immunity from legal proceedings or the execution of judgement or other attachment in England and Wales, pursuant to the State Immunity Act 1978, or the United States, pursuant to the Foreign Sovereign Immunities Act 1976, with respect to this Agreement, the Deposit Agreement or the Offered Securities.

(jjj) This Agreement and the Deposit Agreement are each in proper form to be enforceable in England and Wales in accordance with its terms; to ensure the legality, validity, enforceability or admissibility into evidence in England and Wales of this Agreement or the Deposit Agreement it is not necessary that this Agreement or the Deposit Agreement, respectively, be filed or recorded with any court or other authority in England and Wales (other than court filings in the ordinary course of proceedings).

(kkk) Any final judgment for a fixed or readily calculable sum of money rendered by a New York Court having jurisdiction under its own domestic laws and recognized by the English courts as having jurisdiction (according to English conflicts of laws principles and rules of English private international law at the time when proceedings were initiated) to give such final judgment in respect of any suit, action or proceeding against the Company based upon this Agreement or the Deposit Agreement and any instruments or agreements entered into for the consummation of the transactions contemplated herein and therein would be declared enforceable against the Company, without re-examination or review of the merits of the cause of action in respect of which the original judgment was given or re-litigation of the matters adjudicated upon, by the courts of England and Wales; provided, however, that the Company may have defenses open to it and enforcement may not be permitted if, among other things, (a) the judgment was obtained by fraud, or in proceedings contrary to natural or substantial justice, or contravenes public policy in England or the Human Rights Act 1998 (or any subordinate legislation made thereunder, to the extent applicable); (b) the judgment is for a sum payable in respect of taxes, or other charges of a like nature or is in respect of a fine or other penalty or otherwise based on a foreign law that an English court considers to relate to a penal, revenue or other public law; (c) the judgment amounts to

judgment on a matter previously determined by an English court or conflicts with a judgment on the same matter given by a court other than a New York Court or was obtained in breach of a jurisdiction or arbitration clause except with the agreement of the defendant or the defendant's subsequent submission to the jurisdiction of the court; (d) the judgment is given in proceedings brought in breach of an agreement for the settlement of disputes; (e) the judgment has been arrived at by doubling, trebling or otherwise multiplying a sum assessed as compensation for the loss or damage sustained, or is a judgment that is otherwise specified in section 5 of the Protection of Trading Interests Act 1980, or is a judgment based on measures designated by the Secretary of State under section 1 of that Act; and (f) enforcement proceedings are not commenced within six years of the date of such judgment. The Company is not aware of any reason why the enforcement in England and Wales of such a New York Court judgment would be, as of the date hereof, contrary to public policy of England and Wales or the Human Rights Act 1998 (or any subordinate legislation made thereunder, to the extent applicable).

(lll) Except as provided by laws or statutes generally applicable to transactions of the type described in this Agreement, neither the Company nor any of its respective properties, assets or revenues has any right of immunity under United Kingdom, New York or United States law, from any legal action, suit or proceeding, from the giving of any relief in any such legal action, suit or proceeding, from set-off or counterclaim, from the jurisdiction of any law of the United Kingdom, New York or United States federal court, from service of process, attachment upon or prior judgment, or attachment in aid of execution of judgment, or from execution of a judgment, or other legal process or proceeding for the giving of any relief or for the enforcement of a judgment, in any such court, with respect to its obligations, liabilities or any other matter under or arising out of or in connection with this Agreement or the Deposit Agreement. To the extent that the Company or any of its respective properties, assets or revenues may have or may hereafter become entitled to any such right of immunity in any such court in which proceedings may at any time be commenced, the Company waives or will waive such right to the extent permitted by law and has consented to such relief and enforcement as provided in Section 16 of this Agreement.

(mmm) There are no debt securities or preferred stock issued, or guaranteed, by the Company that are rated by a "nationally recognized statistical rating organization," as that term is defined by the Commission for purposes of Section 3(a)(62) of the Exchange Act.

Any certificate signed by or on behalf of the Company and delivered to the Representatives or to counsel to the Underwriters pursuant to the terms of this Agreement shall be deemed to be a representation and warranty by the Company to each Underwriter as to the matters covered thereby.

3. *PURCHASE, SALE AND DELIVERY OF OFFERED SECURITIES.* On the basis of the representations, warranties and agreements herein contained, but subject to the terms and conditions herein set forth, the Company agrees to issue and sell to the Underwriters, and the Underwriters agree, severally and not jointly, to purchase from the Company the respective numbers of Firm Securities set forth opposite the names of the Underwriters in Schedule A hereto.

The purchase price to be paid by the Underwriters to the Company for the Ordinary Shares will be £[•] per Ordinary Share (the "**Ordinary Share Purchase Price**") and the purchase price to be paid by the Underwriters to the Company for the ADSs will be \$[•] per ADS (the "**ADS Purchase Price**"). The Ordinary Share Purchase Price and the ADS Purchase Price are collectively hereinafter referred to as the "**Purchase Price**."

The Company will deliver, or caused to be delivered, the Firm Securities to the Representatives for the respective accounts of the several Underwriters, through the facilities of The Depository Trust Company ("**DTC**") and CREST, as applicable, issued in such names and in such denominations as the

Representatives may direct by notice in writing to the Company given at or prior to 9:00 A.M., New York time, on the Closing Date against payment of the aggregate Purchase Price therefor by wire transfer in federal (same day) funds to an account at a bank specified by the Company and reasonably acceptable to the Representatives payable to the order of the Company for the Firm Securities sold by them all at the offices of Cooley LLP, 1114 Avenue of the Americas, New York, New York, 10036-7798. Time shall be of the essence, and delivery at the time and place specified pursuant to this Agreement is a further condition of the obligations of each Underwriter hereunder. The time and date of the delivery and payment shall be at [•]:00 [A/P].M., New York time, on [•], 2018, in accordance with Rule 15c6-1 of the Exchange Act. The time and date of such payment and delivery are herein referred to as the “**Closing Date**”. The Closing Date and the location of delivery of, and the form of payment for, the Firm Securities may be varied by agreement among the Company and the Representatives.

For the purpose of covering any over-allotments in connection with the distribution and sale of the Firm Securities as contemplated by the Prospectus, the Underwriters may purchase all or less than all of the Optional ADSs. The purchase price per ADS to be paid for the Optional ADSs shall be the ADS Purchase Price. The Company agrees to sell to the Underwriters the number of Optional ADSs specified in the written notice delivered by the Representatives to the Company described below and the Underwriters agree, severally and not jointly, to purchase such Optional ADSs. Such Optional ADSs shall be purchased from the Company for the account of each Underwriter in the same proportion as the number of Firm Securities set forth opposite such Underwriter’s name in Schedule A bears to the total number of Firm Securities (subject to adjustment by the Representatives to eliminate fractions). The option granted hereby may be exercised as to all or any part of the Optional ADSs at any time, and from time to time, not more than thirty (30) days subsequent to the date of this Agreement. No Optional ADSs shall be sold and delivered unless the Firm Securities previously has been, or simultaneously is being, sold and delivered. The right to purchase the Optional ADSs or any portion thereof may be surrendered and terminated at any time upon notice by the Representatives to the Company.

The option granted hereby may be exercised by written notice being given to the Company by Representatives setting forth the number of Optional ADSs to be purchased by the Underwriters and the date and time for delivery of and payment for the Optional ADSs. Each date and time for delivery of and payment for the Optional ADSs (which may be the Closing Date, but not earlier) is herein called the “**Option Closing Date**” and shall in no event be earlier than two (2) business days nor later than five (5) business days after written notice is given. The Option Closing Date and the Closing Date are herein called the “**Closing Dates**.”

The Company will deliver, or cause to be delivered, the Optional ADSs to the Representatives for the respective accounts of the several Underwriters through the facilities of DTC issued in such names and in such denominations as the Representatives may direct by notice in writing to the Company given at or prior to 9:00 A.M., New York time, on the Option Closing Date against payment of the aggregate Purchase Price therefor by wire transfer in federal (same day) funds to an account at a bank specified by the Company and reasonably acceptable to the Representatives payable to the order of the Company, at the offices of Cooley LLP, 1114 Avenue of the Americas, New York, New York, 10036-7798. Time shall be of the essence, and delivery at the time and place specified pursuant to this Agreement is a further condition of the obligations of each Underwriter hereunder. The Option Closing Date and the location of delivery of, and the form of payment for, the Optional ADSs may be varied by agreement between the Company and the Representatives.

The several Underwriters propose to offer the Offered Securities for sale upon the terms and conditions set forth in the Prospectus.

4. *FURTHER AGREEMENTS OF THE COMPANY.* The Company agrees with the several Underwriters:

(a) To prepare the Rule 462(b) Registration Statement, if necessary, in a form approved by the Representatives and file such Rule 462(b) Registration Statement with the Commission by 10:00 P.M., New York time, on the date hereof, and the Company shall at the time of filing either pay to the Commission the filing fee for the Rule 462(b) Registration Statement or give irrevocable instructions for the payment of such fee pursuant to Rule 111(b) under the Rules and Regulations; to prepare the Prospectus in a form approved by the Representatives containing information previously omitted at the time of effectiveness of the Registration Statement in reliance on Rule 430A of the Rules and Regulations and to file such Prospectus pursuant to Rule 424(b) of the Rules and Regulations not later than the second (2nd) business day following the execution and delivery of this Agreement or, if applicable, such earlier time as may be required by Rule 430A of the Rules and Regulations; to notify the Representatives immediately of the Company's intention to file or prepare any supplement or amendment to the Registration Statement, the ADS Registration Statement or to the Prospectus and to make no amendment or supplement to the Registration Statement, the ADS Registration Statement, the General Disclosure Package or to the Prospectus to which the Representatives shall reasonably object by notice to the Company after a reasonable period to review; to advise the Representatives, promptly after it receives notice thereof, of the time when any amendment to the Registration Statement or the ADS Registration Statement has been filed or becomes effective or any supplement to the General Disclosure Package, or the Prospectus or any amended Prospectus or any Issuer Free Writing Prospectus or any Written Testing-the-Waters Communication has been filed and to furnish the Underwriters with copies thereof; to file promptly all material required to be filed by the Company with the Commission pursuant to Rules 433(d) or 163(b)(2) of the Rules and Regulations, as the case may be; to advise the Representatives, promptly after it receives notice thereof, of the issuance by the Commission of any stop order or of any order preventing or suspending the use of any Preliminary Prospectus, any Issuer Free Writing Prospectus, the Prospectus or any Written Testing-the-Waters Communication, of the suspension of the qualification of the Offered Securities for offering or sale in any jurisdiction, of the initiation or threatening of any proceeding for any such purpose, or of any request by the Commission for the amending or supplementing of the Registration Statement, the General Disclosure Package or the Prospectus or for additional information; and, in the event of the issuance of any stop order or of any order preventing or suspending the use of any Preliminary Prospectus, any Issuer Free Writing Prospectus or the Prospectus or suspending any such qualification, and promptly to use its best efforts to obtain the withdrawal of such order.

(b) The Company will promptly notify the Representatives if the Company ceases to be an Emerging Growth Company at any time prior to the later of (i) the completion of the distribution of the Firm Securities within the meaning of the Securities Act and (ii) completion of the Lock-Up Period (as defined below).

(c) If at any time following the distribution of any Written Testing-the-Waters Communication there occurred or occurs an event or development as a result of which such Written Testing-the-Waters Communication included or would include an untrue statement of a material fact or omitted or would omit to state a material fact required to be stated therein or necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading, the Company will promptly notify the Representatives and will promptly amend or supplement, at its own expense, such Written Testing-the-Waters Communication to eliminate or correct such untrue statement or omission.

(d) The Company represents and agrees that, unless it obtains the prior written consent of the Representatives, and each Underwriter represents and agrees that, unless it obtains the prior written consent of the Company and the Representatives, it has not made and will not, make any offer relating to the Offered Securities that would constitute a “free writing prospectus” as defined in Rule 405 of the Rules and Regulations (each, a “**Permitted Free Writing Prospectus**”); *provided, however*, that the prior written consent of the Company and the Representatives hereto shall be deemed to have been given in respect of the Issuer Free Writing Prospectuses included in Schedule B hereto. The Company represents that it has treated and agrees that it will treat each Permitted Free Writing Prospectus as an Issuer Free Writing Prospectus, comply with the requirements of Rules 164 and 433 of the Rules and Regulations applicable to any Issuer Free Writing Prospectus, including the requirements relating to timely filing with the Commission, legending and record keeping, and will not take any action that would result in an Underwriter or the Company being required to file with the Commission pursuant to Rule 433(d) of the Rules and Regulations a free writing prospectus prepared by or on behalf of such Underwriter that such Underwriter otherwise would not have been required to file thereunder. The Company will satisfy the condition in Rule 433 of the Rules and Regulations to avoid a requirement to file with the Commission any electronic road show.

(e) The Company agrees, prior to each Closing Date, to deposit Ordinary Shares underlying the ADSs with the Custodian on behalf of the Depositary in accordance with the provisions of the Deposit Agreement and otherwise to comply with the Deposit Agreement so that ADRs evidencing the applicable Offered Securities will be issued by the Depositary against receipt of such Ordinary Shares and delivered to the Underwriters at such Closing Date.

(f) If at any time when a prospectus relating to the Offered Securities is (or, but for the exception afforded by Rule 172 promulgated under the Securities Act, would be) required by the Securities Act to be delivered in connection with sales of the Offered Securities, any event occurs or condition exists as a result of which the Prospectus as then amended or supplemented would include any untrue statement of a material fact, or omit to state any material fact necessary to make the statements therein, in light of the circumstances under which they were made when the Prospectus is delivered (or in lieu thereof, the notice referred to in Rule 173(a) of the Rules and Regulations), not misleading, or if it is necessary at any time to amend or supplement the Registration Statement, the ADS Registration Statement or the Prospectus to comply with the Securities Act, then the Company will promptly notify the Representatives thereof and upon their request will prepare an appropriate amendment or supplement in form and substance satisfactory to the Representatives which will correct such statement or omission or effect such compliance and will use its reasonable best efforts to have any amendment to any Registration Statement or the ADS Registration Statement declared effective as soon as possible. The Company will furnish without charge to each Underwriter and to any dealer in securities as many copies as the Representatives may from time to time reasonably request of such amendment or supplement.

(g) If the General Disclosure Package is being used to solicit offers to buy the Offered Securities at a time when the Prospectus is not yet available to prospective purchasers and any event shall occur as a result of which, in the judgment of the Company or in the reasonable opinion of the Underwriters, it becomes necessary to amend or supplement the General Disclosure Package in order to make the statements therein, in the light of the circumstances then prevailing, not misleading, or to make the statements therein not conflict with the information contained in the Registration Statement then on file and not superseded or modified, or if it is necessary at any time to amend or supplement the General Disclosure Package to comply with any law, the Company promptly will prepare, file with the Commission (if required) and furnish to the Underwriters and any dealers an appropriate amendment or supplement to the General Disclosure Package.

(h) If at any time following issuance of an Issuer Free Writing Prospectus there occurred or occurs an event or development as a result of which such Issuer Free Writing Prospectus conflicted or will conflict with the information contained in the Registration Statement, Pricing

Prospectus or Prospectus and not superseded or modified or included or would include an untrue statement of a material fact or omitted or would omit to state a material fact required to be stated therein or necessary in order to make the statements therein, in the light of the circumstances prevailing at the subsequent time, not misleading, the Company has promptly notified or will promptly notify the Representatives so that any use of the Issuer Free Writing Prospectus may cease until it is amended or supplemented and has promptly amended or will promptly amend or supplement, at its own expense, such Issuer Free Writing Prospectus to eliminate or correct such conflict, untrue statement or omission. The foregoing sentence does not apply to statements in or omissions from any Issuer Free Writing Prospectus in reliance upon, and in conformity with, written information furnished to the Company through the Representatives by or on behalf of any Underwriter specifically for inclusion therein, which information the parties hereto agree is limited to the Underwriters' Information.

(i) To the extent not available on the Commission's Electronic Data Gathering, Analysis and Retrieval system or any successor system ("EDGAR"), upon the request of the Representatives, to furnish promptly to the Representatives and to counsel for the Underwriters a signed copy of each of the Registration Statement or the ADS Registration Statement as originally filed with the Commission, and of each amendment thereto filed with the Commission, including all consents and exhibits filed therewith.

(j) To deliver promptly to the Representatives in New York such number of the following documents as the Representatives shall reasonably request: (i) conformed copies of the Registration Statement and the ADS Registration Statement as originally filed with the Commission (in each case excluding exhibits); (ii) each Preliminary Prospectus; (iii) any Issuer Free Writing Prospectus; (the delivery of the documents referred to in clauses (i), (ii) and (iii) of this paragraph (i) to be made not later than 10:00 A.M., New York time, on the business day following the execution and delivery of this Agreement); (iv) the Prospectus; (v) conformed copies of any amendment to the Registration Statement or the ADS Registration Statement (in each case excluding exhibits); and (vi) any amendment or supplement to the General Disclosure Package or the Prospectus (the delivery of the documents referred to in clauses (iv), (v) and (vi) of this paragraph (j) to be made not later than 10:00 A.M., New York time, on the business day following the date of such amendment or supplement).

(k) To make generally available to its shareholders as soon as practicable, but in any event not later than sixteen (16) months after the effective date of the Registration Statement (as defined in Rule 158(c) of the Rules and Regulations), an earnings statement of the Company and its subsidiaries (which need not be audited) complying with Section 11(a) of the Securities Act (including, at the option of the Company, Rule 158); and to furnish to its shareholders as soon as practicable after the end of each fiscal year an annual report (including a balance sheet and statements of income, shareholders' equity and cash flows of the Company certified by independent public accountants) and as soon as possible after the second fiscal quarter of each fiscal year (beginning with the first second fiscal quarter after the effective date of such Registration Statement), consolidated summary financial information of the Company for the first half of the fiscal year in reasonable detail.

(l) To take promptly from time to time such actions as the Representatives may reasonably request to qualify the Offered Securities for offering and sale under the securities or Blue Sky laws of such U.S. or non-U.S. jurisdictions as the Representatives may designate and to continue such qualifications in effect, and to comply with such laws, for so long as required to permit the offer and sale of the Offered Securities in such jurisdictions; *provided, however*, that the Company shall not be obligated to (i) qualify as a foreign corporation in any jurisdiction in which it is not so qualified, (ii) file a general consent to service of process in any jurisdiction or (iii) subject itself to taxation in any such jurisdiction if it is not otherwise so subject.

(m) Upon request, during the period of five (5) years from the date hereof, to deliver to each of the Underwriters, (i) as soon as they are available, copies of all reports or other communications (financial or other) furnished to shareholders of the Company, and (ii) as soon as they are available, copies of any reports and financial statements furnished or filed with the Commission or any national securities exchange on which the Offered Securities are listed. However, so long as the Company is subject to the reporting requirements of either Section 13 or Section 15(d) of the Exchange Act and is timely filing reports with the Commission on its EDGAR system, it is not required to furnish such reports or statements to the Underwriters.

(n) During the period commencing on and including the date hereof and ending on and including the one hundred eightieth (180th) day following the date of this Agreement (as the same may be extended as described below, the “**Lock-Up Period**”), the Company will not, without the prior written consent of Cowen and BMO (which consent may be withheld at the sole discretion of Cowen or BMO), directly or indirectly offer, sell (including, without limitation, any short sale), assign, transfer, pledge, contract to sell, establish an open “put equivalent position” within the meaning of Rule 16a-1(h) under the Exchange Act, or otherwise dispose of, or announce the offering of, or file any registration statement under the Securities Act in respect of, any ADSs, Ordinary Shares, options, rights or warrants to acquire ADSs, securities exchangeable or exercisable for or convertible into ADSs or Ordinary Shares (other than as contemplated by this Agreement with respect to the Offered Securities) or publicly announce any intention to do any of the foregoing; *provided, however*, that the Company may: (i) issue and sell the Offered Securities pursuant to this Agreement; (ii) issue Ordinary Shares, ADSs, options to purchase Ordinary Shares or ADSs, or other awards pursuant to any director or employee incentive plan, stock ownership plan or dividend reinvestment plan of the Company in effect on the date hereof and described in the General Disclosure Package and issue Ordinary Shares or ADSs upon the exercise, exchange, vesting, or conversion of options or other awards issued in accordance with this clause (ii); (iii) issue Ordinary Shares pursuant to the conversion of securities or the exercise of warrants, which securities or warrants are outstanding on the date hereof and described in the General Disclosure Package, including, without limitation, the Novartis Notes; (iv) adopt a new equity incentive plan, file a registration statement on Form S-8 under the Securities Act to register the offer and sale of securities on such new equity incentive plan or on equity incentive plans described in the General Disclosure Package, and issue securities pursuant to such equity incentive plans (including, without limitation, the issuance of Ordinary Shares upon the exercise of options or other securities issued pursuant to such equity incentive plans); *provided* that (1) such equity incentive plans satisfy the transaction requirements of General Instruction A.1 of Form S-8 under the Securities Act and (2) this clause (iv) shall not be available unless each recipient of Ordinary Shares, or securities exchangeable or exercisable for or convertible into Ordinary Shares, pursuant to such equity incentive plans shall be contractually prohibited from selling, offering, disposing of or otherwise transferring any such shares or securities during the remainder of the Lock-Up Period; and (v) issue ADSs or Ordinary Shares in connection with any joint venture, commercial or collaborative relationship or the acquisition or license by the Company of the securities, business, property or other assets of another person or entity or pursuant to any employee benefit plan as assumed by the Company in connection with any such acquisition; *provided* that ADSs and Ordinary Shares issued under this clause (v) shall not in the aggregate exceed ten percent (10%) of the Company’s outstanding share capital immediately following the consummation of the offering of the Offered Securities contemplated by this Agreement. In addition, the Company will cause each person and entity listed in Schedule D to furnish to Cowen and BMO, prior to the Closing Date, an agreement in the form of Exhibit I hereto.

(o) If Cowen and BMO, in their sole discretion, agree to release or waive the restrictions set forth in a lock-up letter described in Section 4(n) hereof for an officer or director of the Company, Cowen and BMO will provide the Company with notice of the impending release or waiver at least three (3) business days before the effective date of the release or waiver, the Company agrees to announce the impending release or waiver by a press release substantially in the form of Exhibit II hereto through a major news service at least two (2) business days before the effective date of the release or waiver.

(p) To supply the Representatives with copies of all written correspondence and to advise the Representatives of all oral correspondence to and from, and all documents issued to and by, the Commission in connection with the registration of the Offered Securities under the Securities Act or any of the Registration Statement, the ADS Registration Statement, any Preliminary Prospectus or the Prospectus, or any amendment or supplement thereto.

(q) Prior to the latest of the Closing Dates, not to issue any press release or other communication directly or indirectly or hold any press conference with respect to the Company, its condition, financial or otherwise, or earnings, business affairs or business prospects (except for routine marketing communications in the ordinary course of business and consistent with the past practices of the Company and of which the Representatives are notified), without the prior written consent of the Representatives, unless in the judgment of the Company and its counsel, and after notification to the Representatives, such press release or communication is required by law or regulation, including any applicable stock exchange rules.

(r) Until the Representatives shall have notified the Company of the completion of the resale of the Offered Securities, that the Company will not, and will use its reasonable best efforts to cause its affiliated purchasers (as defined in Regulation M under the Exchange Act Rules) not to, either alone or with one or more other persons, bid for or purchase, for any account in which it or any of its affiliated purchasers has a beneficial interest, any Offered Securities, or attempt to induce any person to purchase any Offered Securities; and not to, and to use its reasonable best efforts to cause its affiliated purchasers not to, make bids or purchases for the purpose of creating actual, or apparent, active trading in or of raising the price of the Offered Securities.

(s) Not to take any action prior to the latest of the Closing Dates which would require the Prospectus to be amended or supplemented pursuant to Section 4(f).

(t) To at all times comply in all material respects with all applicable provisions of the Sarbanes-Oxley Act in effect from time to time and to file with the Commission such information on Form 20-F as may be required by Rule 463 of the Rules and Regulations.

(u) To maintain, at its expense, a registrar and transfer agent and a depository for the Offered Securities, as applicable.

(v) To apply the net proceeds from the issuance and sale of the Offered Securities as set forth in the Registration Statement, the General Disclosure Package and the Prospectus under the heading "Use of Proceeds," and except as disclosed in the General Disclosure Package, the Company does not intend to use any of the proceeds from the sale of the Offered Securities hereunder to repay any outstanding debt owed to any affiliate of any Underwriter. The Company shall manage its affairs and investments in such a manner as not to be or become an "investment company" within the meaning of the Investment Company Act and the rules and regulations thereunder.

(w) To use its reasonable best efforts to list, subject to notice of issuance, the Offered Securities on the Exchange.

(x) To use its reasonable best efforts to do and perform all things required to be done or performed under this Agreement by the Company prior to each Closing Date and to satisfy all conditions precedent to the delivery of the Firm Securities and the Optional ADSs.

(y) Upon request of any Underwriter, to furnish, or cause to be furnished, to such Underwriter an electronic version of the Company's trademarks, service marks and corporate logo for use on the website, if any, operated by such Underwriter for the purpose of facilitating the on-line offering of the Offered Securities (the "**License**"); *provided, however*, that the License shall be used solely for the purpose described above, is granted without any fee and may not be assigned or transferred.

5. PAYMENT OF EXPENSES.

(a) The Company agrees to pay, or reimburse if paid by any Underwriter, whether or not the transactions contemplated hereby are consummated or this Agreement is terminated: (a) the costs incident to the authorization, issuance, sale, preparation and delivery of the Offered Securities and any taxes payable in that connection; (b) the costs incident to the registration of the Offered Securities under the Securities Act and the Exchange Act; (c) the costs incident to the preparation, printing and distribution of the Registration Statement, the ADS Registration Statement, any Preliminary Prospectus, any Issuer Free Writing Prospectus, the General Disclosure Package, the Prospectus, any amendments, supplements and exhibits thereto and the costs of printing, reproducing and distributing this Agreement, the Deposit Agreement and any closing documents by mail, telex or other means of communications; (d) the fees and expenses (including related fees and expenses of counsel for the Underwriters) incurred in connection with securing any required review by FINRA of the terms of the sale of the Offered Securities and any filings made with FINRA relating to the offering of the Offered Securities up to a maximum of \$35,000 in the aggregate, plus VAT and disbursements; (e) any applicable listing or other fees for the Ordinary Shares and ADSs; (f) the fees and expenses (including related fees and expenses of counsel to the Underwriters) of qualifying the Offered Securities under the securities laws of the several jurisdictions as provided in Section 4(l) and of preparing, printing and distributing wrappers, Blue Sky memoranda and legal investment surveys up to a maximum of \$10,000; (g) the cost of preparing and printing stock certificates; (h) all fees and expenses of the registrar and transfer agent, agent for service of process and/or depository of the Offered Securities; (i) the costs and expenses (including, without limitation, any damages or other amounts payable in connection with the legal or contractual liability) associated with the reforming of any contracts for sale of the Offered Securities made by the Underwriters caused by a breach of the representation contained in Section 2(b); (j) the costs and expenses of the Company relating to investor presentations on any "road show" undertaken in connection with the marketing of the offering of the Offered Securities, including, without limitation, expenses associated with the preparation or dissemination of any electronic road show, expenses associated with the production of road show slides and graphics, fees and expenses of any consultants engaged in connection with the road show presentations with the prior approval of the Company, travel and lodging expenses of the officers of the Company and such consultants, and 50% of the cost of any aircraft chartered in connection with the road show (the remaining 50% of the cost of such aircraft to be paid by the Underwriters); (k) all other costs and expenses of the Company incident to the offering of the Offered Securities or the performance of the obligations of the Company under this Agreement and the Deposit Agreement (including, without limitation, the fees and expenses of the Company's counsel and the Company's independent accountants); *provided, however*, that, except to the extent otherwise provided in this Section 5 and in Sections 9 and 10, the Underwriters shall pay their own costs and expenses, including the fees and expenses of their counsel not contemplated herein, any transfer taxes on the resale of any Offered Securities by them and the expenses of advertising any offering of the Offered Securities made by the Underwriters.

(b) The Company will indemnify and hold harmless the Underwriters against any Transfer Taxes, including any interest and penalties, which are required to be paid or are incurred in connection with (i) the issuance and delivery of the Offered Securities by the Company or the Depositary (as applicable) in the manner contemplated by this Agreement, the Deposit Agreement and the Prospectus, (ii) the initial sale and delivery by the Underwriters of the Offered Securities to purchasers thereof in the manner contemplated by this Agreement, the Deposit Agreement and the Prospectus; and (iii) the execution and delivery by the Company or the Underwriters of this Agreement and the Deposit Agreement. All payments to be made by the Company under this Agreement shall be made without withholding or deduction for or on account of any present or future taxes, levies, imposts, duties, fees, assessments or governmental charges whatsoever, imposed or levied by or on behalf of the United Kingdom or any political subdivision or taxing authority thereof or therein unless the Company is or becomes required by law to deduct or withhold such taxes, levies, imposts, fees, duties, assessments or other governmental charges. In that event, and except for any net income, capital gains or franchise taxes imposed on the Underwriters by England and Wales or other applicable jurisdiction or by any political subdivision or taxing authority thereof or therein as a result of any present or former connection (other than any connection resulting from the transactions contemplated by this Agreement) between the Underwriters and such jurisdiction, the Company shall pay such additional amounts as may be necessary in order to ensure that the net amounts received by each Underwriter after such withholding or deduction shall equal the amounts that would have been received if no withholding or deduction had been made.

(c) If the performance by the Underwriters of any of their obligations under this Agreement shall represent for VAT purposes under any applicable law the making by the Underwriters of any supply of goods or services to the Company (to the extent applicable), the Company shall pay to the Underwriters, in addition to the amounts otherwise payable by the Company pursuant to this Agreement, an amount equal to the VAT chargeable on any such supply of goods and services provided that the Underwriters have issued the Company with an appropriate VAT invoice in respect of the supply to which the payment relates. Where a sum (a “**Relevant Sum**”) is paid or reimbursed to the Underwriters pursuant to this Agreement in respect of any cost, expense or other amount and that cost, expense or other amount includes an amount in respect of irrecoverable VAT (the “**VAT Element**”) which has been certified as such by the Underwriters (acting reasonably), then the Company, to the extent applicable, shall, in addition, pay an amount equal to the VAT Element to the Underwriters. For the purposes of this Agreement, “**VAT**” means value added tax as provided for in the Value Added Tax Act 1994 (“**VATA**”) and subordinate legislation made under VATA as amended, modified or re-enacted (whether before or after the date of this Agreement) and any similar sales, consumption, use or turnover tax whether within the United Kingdom or elsewhere in the world.

6. *CONDITIONS OF UNDERWRITERS’ OBLIGATIONS.* The respective obligations of the several Underwriters hereunder are subject to the accuracy, when made and as of the Applicable Time and on each Closing Date, of the representations and warranties of the Company contained herein, to the accuracy of the statements of the Company made in any certificates pursuant to the provisions hereof, to the performance by the Company of its obligations hereunder, and to each of the following additional terms and conditions:

(a) The Registration Statement has become effective under the Securities Act, and no stop order suspending the effectiveness of the Registration Statement or any part thereof, preventing or suspending the use of any Preliminary Prospectus, the Prospectus or any Permitted Free Writing Prospectus or any part thereof shall have been issued and no proceedings for that purpose or pursuant to Section 8A under the Securities Act shall have been initiated or threatened by the Commission, and all requests for additional information on the part of the Commission (to be included in the Registration Statement or the Prospectus or otherwise) shall have been complied with to the reasonable satisfaction of the Representatives; the Rule 462(b) Registration Statement, if any, each Issuer Free Writing Prospectus and the Prospectus shall have been filed with, the Commission within the applicable time period prescribed for such filing by, and in compliance with, the Rules and Regulations and in accordance with Section 4(a) of this Agreement, and the Rule 462(b) Registration Statement, if any, shall have become effective immediately upon its filing with the Commission and FINRA shall have raised no unresolved objection to the fairness and reasonableness of the terms of this Agreement or the transactions contemplated hereby.

(b) The Underwriters shall have received on the Closing Date a certified copy of (i) the minutes or resolutions of the Board (or a duly constituted committee thereof) resolving, *inter alia*, to approve the execution by the Company of this Agreement, the Deposit Agreement, the Registration Statement, the ADS Registration Statement, the General Disclosure Package, each Issuer Free Writing Prospectus and the Prospectus, the listing of the ADSs on the Exchange and the application for admission of the Ordinary Shares to trading on AIM, and (ii) the minutes of a general meeting of the Company at which resolutions were passed to, *inter alia*, give the Board authority to allot the Ordinary Shares represented by ADSs and the Offered Securities in the form of Ordinary Shares and to disapply statutory pre-emption rights in respect of such allotment.

(c) None of the Underwriters shall have discovered and disclosed to the Company on or prior to such Closing Date that the Registration Statement or any amendment or supplement thereto contains an untrue statement of a fact which, in the opinion of counsel for the Underwriters, is material or omits to state any fact which, in the opinion of such counsel, is material and is required to be stated therein or is necessary to make the statements therein not misleading, or that the General Disclosure Package, any Issuer Free Writing Prospectus or the Prospectus or any amendment or supplement thereto contains an untrue statement of fact which, in the opinion of such counsel, is material or omits to state any fact which, in the opinion of such counsel, is material and is necessary in order to make the statements, in the light of the circumstances in which they were made, not misleading.

(d) All corporate proceedings and other legal matters incident to the authorization, form and validity of each of this Agreement, the Deposit Agreement, the Offered Securities, the Registration Statement, the ADS Registration Statement, the General Disclosure Package, each Issuer Free Writing Prospectus and the Prospectus and all other legal matters relating to this Agreement and the transactions contemplated hereby shall be reasonably satisfactory in all material respects to counsel to the Underwriters, and the Company shall have furnished to such counsel all documents and information that they may reasonably request to enable them to pass upon such matters.

(e) Latham & Watkins LLP, U.S. counsel to the Company, shall have furnished to the Representatives such counsel's written opinion and negative assurance letter, addressed to the Underwriters and dated as of such Closing Date, in form and substance reasonably satisfactory to the Representatives.

(f) Latham & Watkins (London) LLP, UK counsel to the Company, shall have furnished to the Representatives such counsel's written opinion, addressed to the Underwriters and dated as of such Closing Date, in form and substance reasonably satisfactory to the Representatives.

(g) Latham & Watkins LLP, U.S. tax counsel to the Company, shall have furnished to the Representatives such counsel's written opinion, addressed to the Underwriters and dated as of such Closing Date, in form and substance reasonably satisfactory to the Representatives.

(h) Each of Carpmaels & Ransford LLP, Gill Jennings & Every LLP, and Wolff IP, P.C., each counsel to the Company with respect to intellectual property matters, shall have furnished to the Representatives such counsel's written opinion, addressed to the Underwriters and dated as of such Closing Date, in form and substance reasonably satisfactory to the Representatives.

(i) Patterson Belknap Webb & Tyler LLP, counsel for the Depositary, shall have furnished to the Representatives such counsel's written opinion, addressed to the Underwriters and dated as of such Closing Date, in form and substance reasonably satisfactory to the Representatives.

(j) The Representatives shall have received from Cooley LLP, as U.S. counsel for the Underwriters, such opinion or opinions, dated as of such Closing Date, with respect to such matters as the Underwriters may reasonably require, and the Company shall have furnished to such counsel such documents as they request for enabling them to pass upon such matters.

(k) The Representatives shall have received from Cooley (UK) LLP, as UK counsel for the Underwriters, such opinion or opinions, dated as of such Closing Date, with respect to such matters as the Underwriters may reasonably require, and the Company shall have furnished to such counsel such documents as they request for enabling them to pass upon such matters.

(l) At the time of the execution of this Agreement, the Representatives shall have received from Ernst & Young LLP, a letter, addressed to the Underwriters, executed and dated such date, in form and substance satisfactory to the Representatives (i) confirming that they are an independent registered accounting firm with respect to the Company and its subsidiaries within the meaning of the Securities Act and the Rules and Regulations and PCAOB and (ii) stating the conclusions and findings of such firm, of the type ordinarily included in accountants' "comfort letters" to underwriters, with respect to the financial statements and certain financial information contained in the Registration Statements, the General Disclosure Package and the Prospectus.

(m) On the effective date of any post-effective amendment to the Registration Statement and on such Closing Date, the Representatives shall have received a letter (the "**bring-down letter**") from Ernst & Young LLP addressed to the Underwriters and dated such Closing Date confirming, as of the date of the bring-down letter (or, with respect to matters involving changes or developments since the respective dates as of which specified financial information is given in the General Disclosure Package and the Prospectus, as the case may be, as of a date not more than three (3) business days prior to the date of the bring-down letter), the conclusions and findings of such firm, of the type ordinarily included in accountants' "comfort letters" to underwriters, with respect to the financial information and other matters covered by its letter delivered to the Representatives concurrently with the execution of this Agreement pursuant to paragraph (l) of this Section 6.

(n) The Company shall have furnished to the Representatives a certificate, dated as of such Closing Date, of its Chief Executive Officer and its Chief Financial Officer stating in their respective capacities as officers of the Company on behalf of the Company and not in their individual capacities that (i) no stop order suspending the effectiveness of the Registration Statement (including, for avoidance of doubt, any Rule 462(b) Registration Statement), the ADS Registration Statement or any post-effective amendment thereto, shall be in effect and no proceedings for such purpose shall have been instituted or, to their knowledge, threatened by the Commission, (ii) for the period from and including the date of this Agreement through and including such Closing Date, there has not occurred a Material Adverse Effect, (iii) to their knowledge, after reasonable investigation, as of such Closing Date, the representations and warranties of the Company in this Agreement are true and correct and the Company has complied with all agreements and satisfied all conditions on its part to be performed or satisfied hereunder at or prior to such Closing Date, and (iii) there has not been, subsequent to the date of the most recent audited financial statements included in the General Disclosure Package, any material adverse change in the financial position or results of operations of the Company, or any change or development that, individually or in the aggregate, would reasonably be expected to involve a material adverse change in the financial position or results of operations of the Company, except as set forth in the General Disclosure Package and the Prospectus.

(o) Since the date of the latest audited financial statements included in the General Disclosure Package, (i) neither the Company nor any of its subsidiaries shall have sustained any loss or interference with its business from fire, explosion, flood or other calamity, whether or not covered by insurance, or from any labor dispute or court or governmental action, order or decree, otherwise than as set forth in the General Disclosure Package, and (ii) there shall not have been any change in the capital stock (other than the issuance of Ordinary Shares or other securities of the Company upon exercise, exchange, vesting, or conversion of awards granted pursuant to, and the grant of awards under, equity incentive plans described in the Registration Statement, the General Disclosure Package and the Prospectus, or the issuance of Ordinary Shares pursuant to the terms of the Novartis Notes or warrants, each as described in the Registration Statement, the General Disclosure Package and the Prospectus) or long-term debt of the Company or any of its subsidiaries, or any change, or any development involving a prospective change, in or affecting the business, properties, assets, general affairs, management, financial position, shareholders' equity or results of operations of the Company and its subsidiaries, taken as a whole, otherwise than as set forth in the General Disclosure Package or the Prospectus, the effect of which, in any such case described in clause (i) or (ii) of this paragraph 6(l), is, in the judgment of the Representatives, so material and adverse as to make it impracticable or inadvisable to proceed with the sale or delivery of the Offered Securities on the terms and in the manner contemplated in the General Disclosure Package.

(p) No action shall have been taken and no law, statute, rule, regulation or order shall have been enacted, adopted or issued by any governmental or regulatory authority that would prevent the issuance or sale of the Offered Securities or materially and adversely affect or potentially materially and adversely affect the business or operations of the Company; and no injunction, restraining order or order of any other nature by any foreign, federal or state court of competent jurisdiction shall have been issued which would prevent the issuance or sale of the Offered Securities or materially and adversely affect or potentially materially and adversely affect the business or operations of the Company.

(q) Subsequent to the execution and delivery of this Agreement there shall not have occurred any of the following: (i) trading in any of the Company's securities shall have been suspended or materially limited by the Commission, the Exchange, or trading in securities generally on the New York Stock Exchange, Nasdaq Global Select Market, Nasdaq Global Market, Nasdaq Capital Market, the NYSE MKT LLC or in the over-the-counter market, or trading in any securities of the Company on any exchange or in the over-the-counter market, shall have been suspended or materially limited, or minimum or maximum prices or maximum range for prices shall have been established on any such exchange or such market by the Commission, by such exchange or market or by any other regulatory body or governmental authority having jurisdiction, (ii) a banking moratorium shall have been declared by federal or state authorities in the United States or authorities in England and Wales or a material disruption has occurred in commercial banking or securities settlement or clearance services in the United States or England and Wales, (iii) the United States or England and Wales shall have become engaged in hostilities, or the subject of a major act of terrorism, or there shall have been an outbreak of or escalation in hostilities involving the United States or England and Wales, or there shall have been a declaration of a national emergency or war by the United States or England and Wales or (iv) there shall have occurred such a material adverse change in general economic, political or financial conditions (or the effect of international conditions on the financial markets in the United States or England and Wales shall be such) as to make it, in the judgment of the Representatives, impracticable or inadvisable to proceed with the sale or delivery of the Offered Securities on the terms and in the manner contemplated in the General Disclosure Package and the Prospectus.

(r) The Exchange shall have approved the ADSs for listing therein, subject only to official notice of issuance and evidence of satisfactory distribution; the ADSs shall have been determined to be eligible for clearance and settlement through the facilities of the DTC.

(s) The Company shall have applied to the London Stock Exchange for the Ordinary Shares represented by the ADSs and the Offered Securities in the form of Ordinary Shares to be admitted to trading on AIM at 8:00 a.m. (UK time) on the business day immediately following the Closing Date or Option Closing Date, as applicable, which application has not been rejected, and such Ordinary Shares have been allotted conditional only on receipt by the Company of funds for the Ordinary Shares represented by the ADSs and the Offered Securities in the form of Ordinary Shares and admission to AIM.

(t) The Representatives shall have received on such Closing Date satisfactory evidence of the good standing of the Company and its subsidiaries in their respective jurisdictions of organization and their good standing as foreign corporations in such other jurisdictions as the Representatives may reasonably request, in each case in writing or any standard form of telecommunication from the appropriate governmental authorities of such jurisdictions, dated no more than one business day prior to such Closing Date.

(u) The Representatives shall have received the written agreements, substantially in the form of Exhibit I hereto, of the officers, directors, and all shareholders and optionholders of the Company listed in Schedule D to this Agreement.

(v) The Company shall have furnished to the Representatives a Secretary's Certificate of the Company, in form and substance reasonably satisfactory to counsel to the Underwriters and customary for the type of offering contemplated by this Agreement.

(w) The Company shall have furnished to the Representatives a certificate, dated such Closing Date, of its Chief Financial Officer, in form and substance reasonably satisfactory to the Representatives.

(x) The Custodian shall have furnished to the Representatives a certificate satisfactory to the Representatives of one of its authorized officers with respect to the deposit with it of the Ordinary Shares represented by the Offered Securities in the form of ADSs.

(y) The Depositary shall have furnished or caused to be furnished to the Representatives a certificate satisfactory to the Representatives of one of its authorized officers with respect to the issuance of the Offered Securities in the form of ADSs, the execution, issuance, countersignature and delivery of the ADRs evidencing the Offered Securities in the form of ADSs pursuant to the Deposit Agreement, and such other customary matters related thereto as the Representatives may reasonably request.

(z) On or prior to such Closing Date, the Company shall have furnished to the Representatives such further certificates and documents as the Representatives may reasonably request.

All opinions, letters, evidence and certificates mentioned above or elsewhere in this Agreement shall be deemed to be in compliance with the provisions hereof only if they are in form and substance reasonably satisfactory to counsel for the Underwriters.

7. INDEMNIFICATION AND CONTRIBUTION.

(a) The Company shall indemnify and hold harmless each Underwriter and its affiliates, directors, officers, managers, members, employees, representatives and agents and each person, if any, who controls any Underwriter within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act (collectively the "**Underwriter Indemnified Parties**," and each, an "**Underwriter**")

Indemnified Party") against any loss, claim, damage, expense or liability whatsoever (or any action, investigation or proceeding in respect thereof), joint or several, to which such Underwriter Indemnified Party may become subject, under the Securities Act or otherwise, insofar as such loss, claim, damage, expense, liability, action, investigation or proceeding arises out of or is based upon (i) any untrue statement or alleged untrue statement of a material fact contained in any Written Testing-the-Waters Communication, any Preliminary Prospectus, any Issuer Free Writing Prospectus, the Registration Statement, the ADS Registration Statement, the Prospectus or in any amendment or supplement thereto or in any materials or information provided to investors by, or with the approval of, the Company in connection with the marketing of the offering of the Offered Securities, including any road show or investor presentations made to investors by the Company (whether in person or electronically) ("**Marketing Materials**") or (ii) the omission or alleged omission to state in any Written Testing-the-Waters Communication, any Preliminary Prospectus, any Issuer Free Writing Prospectus, the Registration Statement, the ADS Registration Statement, the Prospectus or in any amendment or supplement thereto or in any Marketing Materials, a material fact required to be stated therein or necessary to make the statements therein not misleading, and shall reimburse each Underwriter Indemnified Party promptly upon demand for any legal fees or other expenses reasonably incurred by that Underwriter Indemnified Party in connection with investigating, or preparing to defend, or defending against, or appearing as a third party witness in respect of, or otherwise incurred in connection with, any such loss, claim, damage, expense, liability, action, investigation or proceeding, as such fees and expenses are incurred; *provided, however*, that the Company shall not be liable in any such case to the extent that any such loss, claim, damage, expense or liability arises out of or is based upon an untrue statement or alleged untrue statement in, or omission or alleged omission from any Written Testing-the-Waters Communication, Preliminary Prospectus, the Registration Statement, the ADS Registration Statement, the Prospectus or any such amendment or supplement thereto, any Issuer Free Writing Prospectus or any Marketing Materials made in reliance upon and in conformity with written information furnished to the Company through the Representatives by or on behalf of any Underwriter specifically for use therein, which information the parties hereto agree is limited to the Underwriter's Information. Each indemnity agreement in this Section 7(a) is not exclusive and is in addition to each other indemnity agreement in this Section 7(a) and each other liability which the Company might have under this Agreement or otherwise, and shall not limit any rights or remedies which may otherwise be available under this Agreement, at law or in equity to any Underwriter Indemnified Party.

(b) Each Underwriter, severally and not jointly, shall indemnify and hold harmless the Company and its directors, its officers who signed the Registration Statement or the ADS Registration Statement and each person, if any, who controls the Company within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act (collectively, the "**Company Indemnified Parties**," and each, a "**Company Indemnified Party**") against any loss, claim, damage, expense or liability whatsoever (or any action, investigation or proceeding in respect thereof), joint or several, to which such Company Indemnified Party may become subject, under the Securities Act or otherwise, insofar as such loss, claim, damage, expense, liability, action, investigation or proceeding arises out of or is based upon (i) any untrue statement or alleged untrue statement of a material fact contained in any Written Testing-the-Waters Communication, any Preliminary Prospectus, any Issuer Free Writing Prospectus, the Registration Statement, the ADS Registration Statement, the Prospectus or in any amendment or supplement thereto or in any Marketing Materials, or (ii) the omission or alleged omission to state in any Written Testing-the-Waters Communication, any Preliminary Prospectus, any Issuer Free Writing Prospectus, the Registration Statement, the ADS Registration Statement, the Prospectus or in any amendment or supplement thereto or in any Marketing Materials, a material fact required to be stated therein or necessary to make the statements therein not misleading, but in each case only to the extent that the untrue statement or alleged untrue statement or omission or alleged omission was made in reliance upon and in conformity with written information furnished to the Company through the Representatives by or on behalf of that Underwriter specifically for use therein, which information the parties hereto agree is limited to the

Underwriters' Information, and shall reimburse any Company Indemnified Party promptly upon demand for any legal fees or other expenses reasonably incurred by such Company Indemnified Party in connection with investigating, or preparing to defend, or defending against, or appearing as a third-party witness in respect of, or otherwise incurred in connection with any such loss, claim, damage, expense, liability, action, investigation or proceeding, as such fees and expenses are incurred. Each indemnity agreement in this Section 7(b) is not exclusive and is in addition to each other indemnity agreement in this Section 7(b) and each other liability which the Underwriters or any single Underwriter might have under this Agreement or otherwise, and shall not limit any rights or remedies which may otherwise be available under this Agreement, at law or in equity to any Company Indemnified Party.

(c) Promptly after receipt by an indemnified party under this Section 7 of notice of the commencement of any action, the indemnified party shall, if a claim in respect thereof is to be made against an indemnifying party under this Section 7, notify such indemnifying party in writing of the commencement of that action; *provided, however*, that the failure to notify the indemnifying party shall not relieve it from any liability which it may have under this Section 7 except to the extent it has been materially prejudiced by such failure; *provided, further*, that the failure to notify an indemnifying party shall not relieve it from any liability which it may have to an indemnified party otherwise than under this Section 7. If any such action shall be brought against an indemnified party, and it shall notify the indemnifying party thereof, the indemnifying party shall be entitled to participate therein and, to the extent that it wishes, jointly with any other similarly notified indemnifying party, to assume the defense of such action with counsel reasonably satisfactory to the indemnified party (which counsel shall not, except with the written consent of the indemnified party, be counsel to the indemnifying party). After notice from the indemnifying party to the indemnified party of its election to assume the defense of such action, except as provided herein, the indemnifying party shall not be liable to the indemnified party under Section 7 for any legal or other expenses subsequently incurred by the indemnified party in connection with the defense of such action other than reasonable costs of investigation; *provided, however*, that any indemnified party shall have the right to employ separate counsel in any such action and to participate in the defense of such action but the fees and expenses of such counsel (other than reasonable costs of investigation) shall be at the expense of such indemnified party unless (i) the employment thereof has been specifically authorized in writing by the Company in the case of a claim for indemnification under Section 7(a) or the Representatives in the case of a claim for indemnification under Section 7(b), (ii) such indemnified party shall have been advised by its counsel that there may be one or more legal defenses available to it which are different from or additional to those available to the indemnifying party, or (iii) the indemnifying party has failed to assume the defense of such action and employ counsel reasonably satisfactory to the indemnified party within a reasonable period of time after notice of the commencement of the action or the indemnifying party does not diligently defend the action after assumption of the defense, in which case, if such indemnified party notifies the indemnifying party in writing that it elects to employ separate counsel at the expense of the indemnifying party, the indemnifying party shall not have the right to assume the defense of (or, in the case of a failure to diligently defend the action after assumption of the defense, to continue to defend) such action on behalf of such indemnified party and the indemnifying party shall be responsible for legal or other expenses subsequently incurred by such indemnified party in connection with the defense of such action; *provided, however*, that the indemnifying party shall not, in connection with any one such action or separate but substantially similar or related actions in the same jurisdiction arising out of the same general allegations or circumstances, be liable for the reasonable fees and expenses of more than one separate firm of attorneys at any time for all such indemnified parties (in addition to any local counsel), which firm shall be designated in writing by the Representatives if the indemnified parties under this Section 7 consist of any Underwriter Indemnified Party or by the Company if the indemnified parties under this Section 7 consist of any Company Indemnified Parties. Subject to this Section 7(c), the amount payable by an indemnifying party under Section 7 shall include, but not be limited to, (x) reasonable documented legal fees and expenses of counsel to the indemnified party and any other expenses in investigating, or

preparing to defend or defending against, or appearing as a third-party witness in respect of, or otherwise incurred in connection with, any action, investigation, proceeding or claim, and (y) all amounts paid in settlement of any of the foregoing. No indemnifying party shall, without the prior written consent of the indemnified parties (which consent shall not be unreasonably withheld or delayed), settle or compromise or consent to the entry of judgment with respect to any pending or threatened action or any claim whatsoever, in respect of which indemnification or contribution could be sought under this Section 7 (whether or not the indemnified parties are actual or potential parties thereto), unless such settlement, compromise or consent (A) includes an unconditional release of each indemnified party in form and substance reasonably satisfactory to such indemnified party from all liability arising out of such action or claim and (B) does not include a statement as to or an admission of fault, culpability or a failure to act by or on behalf of any indemnified party. Subject to the provisions of the following sentence, no indemnifying party shall be liable for settlement of any pending or threatened action or any claim whatsoever that is effected without its written consent (which consent shall not be unreasonably withheld or delayed), but if settled with its written consent, if its consent has been unreasonably withheld or delayed or if there be a judgment for the plaintiff in any such matter, the indemnifying party agrees to indemnify and hold harmless any indemnified party from and against any loss or liability by reason of such settlement or judgment. In addition, if at any time an indemnified party shall have requested that an indemnifying party reimburse the indemnified party for fees and expenses of counsel, such indemnifying party agrees that it shall be liable for any settlement of the nature contemplated by Section 7(a) effected without its written consent if (i) such settlement is entered into more than forty-five (45) days after receipt by such indemnifying party of the request for reimbursement, (ii) such indemnifying party shall have received notice of the terms of such settlement at least thirty (30) days prior to such settlement being entered into and (iii) such indemnifying party shall not have reimbursed such indemnified party in accordance with such request prior to the date of such settlement.

(d) If the indemnification provided for in this Section 7 is unavailable or insufficient to hold harmless an indemnified party under Section 7(a) or 7(b), then each indemnifying party shall, in lieu of indemnifying such indemnified party, contribute to the amount paid, payable or otherwise incurred by such indemnified party as a result of such loss, claim, damage, expense or liability (or any action, investigation or proceeding in respect thereof), as incurred, (i) in such proportion as shall be appropriate to reflect the relative benefits received by the Company on the one hand and the Underwriters on the other from the offering of the Offered Securities, or (ii) if the allocation provided by clause (i) of this Section 7(d) is not permitted by applicable law, in such proportion as is appropriate to reflect not only the relative benefits referred to in clause (i) of this Section 7(d), but also the relative fault of the Company on the one hand and the Underwriters on the other with respect to the statements, omissions, acts or failures to act which resulted in such loss, claim, damage, expense or liability (or any action, investigation or proceeding in respect thereof) as well as any other relevant equitable considerations. The relative benefits received by the Company on the one hand and the Underwriters on the other with respect to such offering shall be deemed to be in the same proportion as the total net proceeds from the offering of the Offered Securities purchased under this Agreement (before deducting expenses) received by the Company bear to the total underwriting discounts and commissions received by the Underwriters with respect to the Offered Securities purchased under this Agreement, in each case as set forth in the table on the cover page of the Prospectus. The relative fault of the Company on the one hand and the Underwriters on the other shall be determined by reference to, among other things, whether the untrue or alleged untrue statement of a material fact or the omission or alleged omission to state a material fact relates to information supplied by the Company on the one hand or the Underwriters on the other, the intent of the parties and their relative knowledge, access to information and opportunity to correct or prevent such untrue statement, omission, act or failure to act; *provided, however*, that the parties hereto agree that the written information furnished to the Company through the Representatives by or on behalf of the Underwriters for use in the Preliminary Prospectus, the Registration Statement, the ADS Registration Statement, the Prospectus or in any amendment or supplement thereto, consists solely of the Underwriters' Information.

(e) The Company and the Underwriters agree that it would not be just and equitable if contributions pursuant to Section 7(d) above were to be determined by pro rata allocation or by any other method of allocation which does not take into account the equitable considerations referred to Section 7(d) above. The amount paid or payable by an indemnified party as a result of the loss, claim, damage, expense, liability, action, investigation or proceeding referred to in Section 7(d) above shall be deemed to include, subject to the limitations set forth above, any legal or other expenses reasonably incurred by such indemnified party in connection with investigating, preparing to defend or defending against or appearing as a third party witness in respect of, or otherwise incurred in connection with, any such loss, claim, damage, expense, liability, action, investigation or proceeding. Notwithstanding the provisions of this Section 7, no Underwriter shall be required to contribute any amount in excess of the amount by which the total underwriting discounts and commissions received by such Underwriter with respect to the offering of the Offered Securities exceeds the amount of any damages which the Underwriter has otherwise paid or become liable to pay by reason of any untrue or alleged untrue statement, omission or alleged omission, act or alleged act or failure to act or alleged failure to act. No person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Securities Act) shall be entitled to contribution from any person who was not guilty of such fraudulent misrepresentation. The Underwriters' obligations to contribute as provided in this Section 7 are several in proportion to their respective underwriting obligations and not joint.

8. *TERMINATION.* The obligations of the Underwriters hereunder may be terminated by the Representatives, in their absolute discretion, by notice given to the Company prior to delivery of and payment for the Firm Securities if, prior to that time, any of the events described in Sections 6(o) or 6(q) have occurred or if the Underwriters shall decline to purchase the Offered Securities for any reason permitted under this Agreement.

9. *REIMBURSEMENT OF UNDERWRITERS' EXPENSES.* Notwithstanding anything to the contrary in this Agreement, if (a) this Agreement shall have been terminated pursuant to Section 8, (b) the Company shall fail to tender the Offered Securities for delivery to the Underwriters for any reason not permitted under this Agreement, (c) the Underwriters shall decline to purchase the Offered Securities for any reason permitted under this Agreement or (d) the sale of the Offered Securities is not consummated because any condition to the obligations of the Underwriters set forth herein is not satisfied or because of the refusal, inability or failure on the part of the Company to perform any agreement herein or to satisfy any condition or to comply with the provisions hereof, then, in addition to the payment of amounts in accordance with Section 5, the Company shall reimburse the Underwriters in accordance with this Section 9 for the fees and expenses of Underwriters' counsel and for such other documented out-of-pocket expenses as shall have been reasonably incurred by them in connection with this Agreement and the proposed purchase of the Offered Securities, including, without limitation, travel and lodging expenses of the Underwriters, and upon demand the Company shall pay the full amount thereof to the Representatives; *provided, however*, that if this Agreement is terminated pursuant to Section 10 by reason of the default of one or more Underwriters, the Company shall not be obligated to reimburse any defaulting Underwriter on account of expenses to the extent incurred by such defaulting Underwriter; *provided, further*, that the foregoing shall not limit any reimbursement obligation of the Company to any non-defaulting Underwriter under this Section 9.

10. *SUBSTITUTION OF UNDERWRITERS.* If any Underwriter or Underwriters shall default in its or their obligations to purchase the shares of Offered Securities hereunder on any Closing Date, and the aggregate number of shares which such defaulting Underwriter or Underwriters agreed but failed to purchase does not exceed ten percent (10%) of the total number of shares to be purchased by all Underwriters on such Closing Date, the other Underwriters shall be obligated severally, in proportion to their respective commitments hereunder, to purchase the shares which such defaulting Underwriter or Underwriters agreed but failed to purchase on such Closing Date. If any Underwriter or Underwriters

shall so default and the aggregate number of shares with respect to which such default or defaults occur is more than ten percent (10%) of the total number of shares to be purchased by all Underwriters on such Closing Date, and arrangements satisfactory to the Representatives and the Company for the purchase of such shares by other persons are not made within forty-eight (48) hours after such default, this Agreement shall terminate.

If the remaining Underwriters or substituted Underwriters are required hereby or agree to take up all or part of the shares of Offered Securities of a defaulting Underwriter or Underwriters on such Closing Date as provided in this Section 10, (i) the Company shall have the right to postpone such Closing Dates for a period of not more than five (5) full business days in order that the Company may effect whatever changes may thereby be made necessary in the Registration Statement, the Prospectus, or in any other documents or arrangements, and the Company agrees promptly to file any amendments to the Registration Statement or supplements to the Prospectus which may thereby be made necessary, and (ii) the respective numbers of shares to be purchased by the remaining Underwriters or substituted Underwriters shall be taken as the basis of their underwriting obligation for all purposes of this Agreement. Nothing herein contained shall relieve any defaulting Underwriter of its liability to the Company or the other Underwriters for damages occasioned by its default hereunder. Any termination of this Agreement pursuant to this Section 10 shall be without liability on the part of any non-defaulting Underwriter or the Company, except that the representations, warranties, covenants, indemnities, agreements and other statements set forth in Section 2, the obligations with respect to expenses to be paid or reimbursed pursuant to Sections 5 and 9 and the provisions of Section 7 and Sections 11 through 21, inclusive, shall not terminate and shall remain in full force and effect.

11. *ABSENCE OF FIDUCIARY RELATIONSHIP.* The Company acknowledges and agrees that:

(a) each Underwriter's responsibility to the Company is solely contractual in nature, the Representatives have been retained solely to act as underwriters in connection with the sale of the Offered Securities and no fiduciary, advisory or agency relationship between the Company and the Representatives have been created in respect of any of the transactions contemplated by this Agreement, irrespective of whether any of the Representatives has advised or is advising the Company on other matters;

(b) the price of the Offered Securities set forth in this Agreement was established by the Company following discussions and arm's-length negotiations with the Representatives, and the Company is capable of evaluating and understanding, and understands and accepts, the terms, risks and conditions of the transactions contemplated by this Agreement;

(c) it has been advised that the Representatives and their affiliates are engaged in a broad range of transactions which may involve interests that differ from those of the Company and that the Representatives have no obligation to disclose such interests and transactions to the Company by virtue of any fiduciary, advisory or agency relationship; and

(d) it waives, to the fullest extent permitted by law, any claims it may have against the Representatives for breach of fiduciary duty or alleged breach of fiduciary duty and agrees that the Representatives shall have no liability (whether direct or indirect) to the Company in respect of such a fiduciary duty claim or to any person asserting a fiduciary duty claim on behalf of or in right of the Company, including shareholders, employees or creditors of the Company.

12. *SUCCESSORS; PERSONS ENTITLED TO BENEFIT OF AGREEMENT.* This Agreement shall inure to the benefit of and be binding upon the several Underwriters, the Company and their respective successors and assigns. Nothing expressed or mentioned in this Agreement is intended or shall be

construed to give any person, other than the persons mentioned in the preceding sentence, any legal or equitable right, remedy or claim under or in respect of this Agreement, or any provisions herein contained, this Agreement and all conditions and provisions hereof being intended to be and being for the sole and exclusive benefit of such persons and for the benefit of no other person; except that the representations, warranties, covenants, agreements and indemnities of the Company contained in this Agreement shall also be for the benefit of the Underwriter Indemnified Parties, and the indemnities of the several Underwriters shall be for the benefit of the Company Indemnified Parties. It is understood that each Underwriter's responsibility to the Company is solely contractual in nature and the Underwriters do not owe the Company, or any other party, any fiduciary duty as a result of this Agreement. No purchaser of any of the Offered Securities from any Underwriter shall be deemed to be a successor or assign by reason merely of such purchase.

13. *SURVIVAL OF INDEMNITIES, REPRESENTATIONS, WARRANTIES, ETC.* The respective indemnities, covenants, agreements, representations, warranties and other statements of the Company and the several Underwriters, as set forth in this Agreement or made by them respectively, pursuant to this Agreement, shall remain in full force and effect, regardless of any investigation made by or on behalf of any Underwriter, the Company or any person controlling any of them and shall survive delivery of and payment for the Offered Securities. Notwithstanding any termination of this Agreement, including without limitation any termination pursuant to Section 8 or Section 10, the indemnities, covenants, agreements, representations, warranties and other statements forth in Sections 2, 5, 7 and 9 and Sections 11 through 21, inclusive, of this Agreement shall not terminate and shall remain in full force and effect at all times.

14. *NOTICES.* All statements, requests, notices and agreements hereunder shall be in writing, and:

(a) if to the Underwriters, shall be delivered or sent by mail, telex, facsimile transmission or email to (i) Cowen and Company, LLC, 599 Lexington Avenue, New York, New York 10022, Attention: Head of Equity Capital Markets, Fax: 646-562-1249 with a copy to the General Counsel, Fax: 646-562-1124; (ii) BMO Capital Markets Corp., 3 Times Square, New York, New York 10036, Attention: Legal Department, Fax: 212-702-1205; (iii) RBC Capital Markets, LLC, 200 Vesey Street, 8th Floor, New York, New York 10281, Attention: Equity Capital Markets, Fax: 212-428-6260 and (iv) Divakar Gupta, Cooley LLP, 1114 Avenue of the Americas, New York, New York 10036-7798, Fax: 212-479-6275 and

(b) if to the Company shall be delivered or sent by mail, telex, facsimile transmission or email to Mereo BioPharma Group plc, Attention: Charles Sermon, with a copy to Latham & Watkins LLP, 140 Scott Drive, Menlo Park, CA 94025, Attention: Mark Roeder;

provided, however, that any notice to an Underwriter pursuant to Section 7 shall be delivered or sent by mail, or facsimile transmission to such Underwriter at its address set forth in its acceptance telex to the Representatives, which address will be supplied to any other party hereto by the Representatives upon request. Any such statements, requests, notices or agreements shall take effect at the time of receipt thereof.

15. *DEFINITION OF CERTAIN TERMS.* For purposes of this Agreement, (i) "**affiliate**" has the meaning set forth in Rule 405 under the Rules and Regulations, (ii) "**business day**" means any day on which The Nasdaq Stock Market is open for trading and (iii) "**subsidiary**" has the meaning set forth in Rule 405 of the Rules and Regulations.

16. **GOVERNING LAW.** This Agreement shall be governed by and construed in accordance with the laws of the State of New York, including without limitation Section 5-1401 of the New York General Obligations. The Company irrevocably (i) submits to the non-exclusive jurisdiction of the Federal and state courts in the Borough of Manhattan in The City of New York for the purpose of any suit, action or other proceeding arising out of this Agreement or the transactions contemplated by this Agreement, the Registration Statement, the ADS Registration Statement and any Preliminary Prospectus or the Prospectus, (ii) agrees that all claims in respect of any such suit, action or proceeding may be heard and determined by any such court, (iii) waives to the fullest extent permitted by applicable law, any immunity from the jurisdiction of any such court or from any legal process, (iv) agrees not to commence any such suit, action or proceeding other than in such courts, (v) waives, to the fullest extent permitted by applicable law, any claim that any such suit, action or proceeding is brought in an inconvenient forum and (vi) appoints Cogency Global Inc. as its agent to receive service of process or other legal summons for purposes of any such suit, action or proceeding that may be instituted in any state or federal court in the City and County of New York.

17. **UNDERWRITERS' INFORMATION.** The parties hereto acknowledge and agree that, for all purposes of this Agreement, the Underwriters' Information consists solely of the following information in the Prospectus: the statements concerning the Underwriters contained in the second sentence of the eighth paragraph and the ninth paragraph under the heading "Underwriting."

18. **AUTHORITY OF THE REPRESENTATIVES.** In connection with this Agreement, the Representatives will act for and on behalf of the several Underwriters, and any action taken under this Agreement by the Representatives, will be binding on all of the Underwriters.

19. **PARTIAL UNENFORCEABILITY.** The invalidity or unenforceability of any section, paragraph, clause or provision of this Agreement shall not affect the validity or enforceability of any other section, paragraph, clause or provision hereof. If any section, paragraph, clause or provision of this Agreement is for any reason determined to be invalid or unenforceable, there shall be deemed to be made such minor changes (and only such minor changes) as are necessary to make it valid and enforceable.

20. **GENERAL.** This Agreement constitutes the entire agreement of the parties to this Agreement and supersedes all prior written or oral and all contemporaneous oral agreements, understandings and negotiations with respect to the subject matter hereof. In this Agreement, the masculine, feminine and neuter genders and the singular and the plural include one another. The section headings in this Agreement are for the convenience of the parties only and will not affect the construction or interpretation of this Agreement. This Agreement may be amended or modified, and the observance of any term of this Agreement may be waived, only by a writing signed by the Company and the Representatives.

21. **COUNTERPARTS.** This Agreement may be signed in any number of counterparts, including by facsimile or other electronic transmission, each of which shall be an original, with the same effect as if the signatures thereto and hereto were upon the same instrument.

22. **JUDGMENT CURRENCY.** The obligations of the Company pursuant to this Agreement in respect of any sum due to any Underwriter shall, notwithstanding any judgment in a currency other than United States dollars, not be discharged until the first (1st) business day, following receipt by such Underwriter of any sum adjudged to be so due in such other currency, on which (and only to the extent that) such Underwriter may in accordance with normal banking procedures purchase United States dollars with such other currency; if the United States dollars so purchased are less than the sum originally due to such Underwriter hereunder, the Company agrees, as a separate obligation and notwithstanding any such judgment, to indemnify such Underwriter against such loss.

(Signature page follows)

If the foregoing is in accordance with your understanding of the agreement between the Company and the several Underwriters, kindly indicate your acceptance in the space provided for that purpose below.

Very truly yours,

MEREO BIOPHARMA GROUP PLC

By: _____
Name: Denise Scots-Knight
Title: Chief Executive Officer

Accepted as of
the date first above written:
COWEN AND COMPANY, LLC
BMO CAPITAL MARKETS CORP.
RBC CAPITAL MARKETS, LLC

Acting on their own behalf
and as Representatives of several
Underwriters listed in Schedule A to this Agreement.

By: COWEN AND COMPANY, LLC

By: _____
Name:
Title:

By: BMO CAPITAL MARKETS CORP.

By: _____
Name:
Title:

By: RBC CAPITAL MARKETS, LLC

By: _____
Name:
Title:

(Signature Page to Mereo BioPharma Group plc Underwriting Agreement)

SCHEDULE A

Name	Number of Firm Securities		Number of Optional ADSs
	Ordinary Shares	ADSs	ADSs
Cowen and Company, LLC			
BMO Capital Markets Corp.			
RBC Capital Markets, LLC			
JMP Securities LLC			
Cantor Fitzgerald & Co.			
Total			

SCHEDULE B

General Use Free Writing Prospectuses

Sch. B

SCHEDULE C

Pricing Information

Firm Securities:	[•] Ordinary Shares
	[•] ADSs, representing [•] Ordinary Shares
Offering Price:	£[•] per Ordinary Share
	\$[•] per ADS
Optional ADSs:	[•] ADSs, representing [•] Ordinary Shares

SCHEDULE D

Lock-Up Parties

- 1. Denise Scots-Knight
- 2. Richard Jones
- 3. Alastair MacKinnon
- 4. John Richard
- 5. Charles Sermon
- 6. Peter Fellner
- 7. Frank Armstrong
- 8. Peter Bains
- 9. Paul Blackburn
- 10. Anders Ekblom
- 11. Kunal Kashyap
- 12. Novartis Pharma AG

Sch. D

SCHEDULE E

Subsidiaries

- Mereo BioPharma 1 Limited
- Mereo BioPharma 2 Limited
- Mereo BioPharma 3 Limited
- Mereo BioPharma 4 Limited

Sch. E

Exhibit I

Form of Lock-Up Agreement

COWEN AND COMPANY, LLC

BMO CAPITAL MARKETS CORP.

As Representatives of the several Underwriters

c/o Cowen and Company, LLC
599 Lexington Avenue
New York, New York 10022

c/o BMO Capital Markets Corp.
3 Times Square, 25th Floor
New York, New York 10036

Re: Mereo BioPharma Group plc – Registration Statement on Form F-1

Dear Sir or Madam:

This agreement is being delivered to you in connection with the proposed Underwriting Agreement (the “Underwriting Agreement”) by and among Mereo BioPharma Group plc, a public limited company incorporated under the laws of England and Wales (together with any successor thereto, the “Company”), and Cowen and Company, LLC (“Cowen”) and BMO Capital Markets Corp. (“BMO”), as representatives of a group of underwriters (collectively, the “Underwriters”), to be named therein, and the other parties thereto (if any), relating to the proposed public offering (the “Offering”) of ordinary shares, nominal value £0.003 per share (the “Ordinary Shares”), and/or American Depositary Shares representing a certain number of Ordinary Shares to be determined (the “ADSs” and, together with the Ordinary Shares, the “Securities”) of the Company.

In order to induce you and the other Underwriters to enter into the Underwriting Agreement, and in light of the benefits that the offering of the Securities will confer upon the undersigned in its capacity as a securityholder and/or an officer, director or employee of the Company, and for good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the undersigned agrees with each Underwriter that, during the period beginning on the date hereof through and including the date that is the 180th day after the date of the Underwriting Agreement (the “Lock-Up Period”), the undersigned will not, without the prior written consent of Cowen and BMO, directly or indirectly, (i) offer, sell, assign, transfer, pledge, contract to sell, or otherwise dispose of, or announce the intention to otherwise dispose of, any Securities (including, without limitation, Securities which may be deemed to be beneficially owned by the undersigned in accordance with the rules and regulations promulgated under the Securities Act of 1933, as amended (such Securities, the “Beneficially Owned Securities,” and such act, the “Securities Act”)), or securities convertible into or exercisable or exchangeable for Securities, (ii) enter into any swap, hedge or similar agreement or arrangement that transfers in whole or in part, the economic risk of ownership of the Beneficially Owned Securities or securities convertible into or exercisable or exchangeable for Securities, whether now owned or hereafter acquired by the undersigned or with respect to which the undersigned has or hereafter acquires the power of disposition, or (iii) engage in any short selling of the Securities or securities convertible into or exercisable or exchangeable for Securities.

Ex. I

If the undersigned is an officer or director of the Company, (i) Cowen and BMO agree that, at least three (3) business days before the effective date of any release or waiver of the foregoing restrictions in connection with a transfer of Securities, Cowen and BMO will notify the Company of the impending release or waiver, and (ii) the Company will agree in the Underwriting Agreement to announce the impending release or waiver by press release through a major news service at least two (2) business days before the effective date of the release or waiver. Any release or waiver granted by Cowen and BMO hereunder to any such officer or director shall only be effective two (2) business day after the publication date of such press release. The provisions of this paragraph will not apply if (a) the release or waiver is effected solely to permit a transfer not for consideration and (b) the transferee has agreed in writing to be bound by the same terms described in this agreement that are applicable to the transferor to the extent and for the duration that such terms remain in effect at the time of the transfer.

The restrictions set forth in the second paragraph shall not apply to (i) the registration of the offer and sale of the ADSs and the sale of such ADSs to the Underwriters, in each case, as contemplated by the Underwriting Agreement or (ii) the deposit of Ordinary Shares with the Depositary, in exchange for the issuance of ADSs, or the cancellation of ADSs in exchange for the issuance of Ordinary Shares, *provided* that such ADSs or Ordinary Shares issued pursuant to this clause (ii) shall remain subject to the terms of this agreement. In addition, the restrictions set forth in the second paragraph shall not apply to:

- (1) if the undersigned is a natural person, any transfers made by the undersigned (a) as a bona fide gift to any member of the immediate family (as defined below) of the undersigned or to a trust the beneficiaries of which are exclusively the undersigned or members of the undersigned's immediate family, (b) by will or intestate succession upon the death of the undersigned or (c) as a bona fide gift to a charity or educational institution;
- (2) if the undersigned is a corporation, partnership, limited liability company or other business entity, any transfers to any stockholder, partner or member of, or owner of a similar equity interest in, the undersigned, as the case may be, if, in any such case, such transfer is not for value;
- (3) if the undersigned is a corporation, partnership, limited liability company or other business entity, any transfer made by the undersigned (a) in connection with the sale or other bona fide transfer in a single transaction of all or substantially all of the undersigned's capital stock, partnership interests, membership interests or other similar equity interests, as the case may be, or all or substantially all of the undersigned's assets, in any such case not undertaken for the purpose of avoiding the restrictions imposed by this agreement or (b) to another corporation, partnership, limited liability company or other business entity so long as the transferee is an affiliate (as defined below) of the undersigned and such transfer is not for value;
- (4) any transfers made by operation of law, including pursuant to a court or regulatory agency order, a domestic order or a negotiated divorce settlement;
- (5) any transfers of Securities acquired on the open market following the Offering; and
- (6) any transfers of Securities pursuant to a bona fide third-party tender offer for all outstanding shares of the Company, merger, consolidation or other similar transaction made to all holders of the Company's Securities involving a change of control of the Company (including, without limitation, the entering into any lock-up, voting or similar agreement pursuant to which the undersigned may agree to transfer, sell, tender or otherwise dispose of Securities in connection with such transaction, or vote any Securities in favor of any such transaction), *provided* that, in the event that such tender offer, merger, consolidation or other such transaction is not completed, such Securities held by the undersigned shall remain subject to the restrictions contained in this agreement;

provided that, (A) in the case of any transfer described in clause (1), (2) or (3) above, it shall be a condition to the transfer that the transferee executes and delivers to Cowen and BMO, acting on behalf of the Underwriters, not later than one (1) business day prior to such transfer, a written agreement, in substantially the form of this agreement (it being understood that any references to “immediate family” in the agreement executed by such transferee shall expressly refer only to the immediate family of the undersigned and not to the immediate family of the transferee) and otherwise satisfactory in form and substance to Cowen and BMO and (B) in the case of any transfer described in clause (1), (2), (3) or (5) above, prior to the expiration of the Lock-Up Period, no public disclosure or filing, including under the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or applicable rules and regulations of the Alternative Investment Market (the “AIM”) operated by the London Stock Exchange plc, by any party to the transfer (transferor or transferee) shall be required, or made voluntarily, in connection with such transfer. For purposes of this paragraph, “immediate family” shall mean a spouse, child, grandchild or other lineal descendant (including by adoption), father, mother, brother or sister of the undersigned; and “affiliate” shall have the meaning set forth in Rule 405 under the Securities Act.

Notwithstanding anything herein to the contrary, nothing herein shall prevent the undersigned from establishing a 10b5-1 trading plan that complies with Rule 10b5-1 under the Exchange Act (a “10b5-1 Trading Plan”) or from amending an existing 10b5-1 Trading Plan; *provided* that, there are no sales of Securities under such plan during the Lock-Up Period; and *provided further* that the establishment of a 10b5-1 Trading Plan or the amendment of a 10b5-1 Trading Plan, in either case, providing for sales of Securities shall only be permitted if, prior to the expiration of the Lock-Up Period, no public disclosure or filing, including under applicable rules and regulations of the Securities and Exchange Commission or the AIM, or otherwise, by any party shall be required, or made voluntarily, in connection with such 10b5-1 Trading Plan.

For avoidance of doubt, nothing in this agreement prohibits the undersigned from exercising any options or warrants to purchase Securities (which exercises may be effected on a cashless basis to the extent the instruments representing such options or warrants permit exercises on a cashless basis) or converting any debt securities of the Company existing as of the date hereof and described in the final prospectus relating to the Offering (the “Prospectus”) into Securities, it being understood that any Securities issued upon such exercises or conversions will be subject to the restrictions of this agreement. Further, nothing in this agreement prohibits the undersigned from transferring Securities to the Company as forfeitures to satisfy tax withholding obligations of the undersigned in connection with the vesting or exercise of equity awards by the undersigned pursuant to the Company’s equity incentive plans existing as of the date hereof and described in the Prospectus, insofar as such equity awards are outstanding as of the date of the Underwriting Agreement.

In order to enable this covenant to be enforced, the undersigned hereby consents to the placing of legends or stop transfer instructions with the Company’s transfer agent or the account holding institution of the undersigned with respect to any Securities or securities convertible into or exercisable or exchangeable for Securities.

The undersigned further agrees that it will not, during the Lock-Up Period, make any demand or request for or exercise any right with respect to the registration under the Securities Act, of any Securities or other Beneficially Owned Securities or any securities convertible into or exercisable or exchangeable for Securities or other Beneficially Owned Securities.

In addition, the undersigned hereby irrevocably waives any and all rights to any antidilution adjustments, preemptive rights, participation rights, resale rights, rights of first refusal and similar rights that the undersigned may have in connection with the Offering, except for any such rights as have been heretofore duly exercised.

The undersigned hereby represents and warrants that the undersigned has full power and authority to enter into this agreement and that this agreement has been duly authorized (if the undersigned is not a natural person), executed and delivered by the undersigned and is a valid and binding agreement of the undersigned. This agreement and all authority herein conferred are irrevocable and shall survive the death or incapacity of the undersigned (if a natural person) and shall be binding upon the heirs, personal representatives, successors and assigns of the undersigned.

This agreement shall be governed by and construed in accordance with the internal laws of the State of New York applicable to agreements made and to be performed in such state.

If (i) the Company notifies Cowen and BMO in writing that it does not intend to proceed with the Offering, (ii) the Underwriting Agreement is not executed by May 31, 2018, or (iii) the Underwriting Agreement (other than the provisions thereof which survive termination) shall terminate or be terminated for any reason prior to payment for and delivery of any Securities, then this agreement shall immediately be terminated and the undersigned shall automatically be released from all of his or her obligations under this agreement. The undersigned acknowledges and agrees that whether or not any public offering of Securities actually occurs depends on a number of factors, including market conditions.

Ex. I-4

Exhibit II

Form of Press Release

Mereo BioPharma Group plc

[Date]

Mereo BioPharma Group plc announced today that Cowen and Company, LLC, BMO Capital Markets Corp. and RBC Capital Markets, LLC, the lead book-running managers in the Company’s recent public sale of [•] ordinary shares and [•] American Depositary Shares, each representing [•] ordinary shares, is [waiving][releasing] a lock-up restriction with respect to [•] shares of the Company’s ordinary shares [and [•] shares of the Company’s American Depositary Shares] held by [certain officers or directors][an officer or director] of the Company. The [waiver][release] will take effect on , 20 , and the shares may be sold on or after such date.

This press release is not an offer for sale of the securities in the United States or in any other jurisdiction where such offer is prohibited, and such securities may not be offered or sold in the United States absent registration or exemption from registration under the United States Securities Act of 1933, as amended.

Ex. II

Articles of Association
of Mereo BioPharma Group plc

The Companies Act 2006
Public Company

(as adopted by special resolution passed on
6 April 2018)

**New Articles of Association
of
Mereo BioPharma Group plc (the “Company”)**

(as adopted by special resolution passed on 6 April 2018)

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PART 1

INTERPRETATION AND LIMITATION OF LIABILITY

1 Preliminary

No regulations or articles set out in any statute, or in any statutory instrument or other subordinate legislation made under any statute, concerning companies (including the regulations in the Companies (Model Articles) Regulations 2008 (SI 2008/3229)) shall apply as the articles of the Company except in so far as they are repeated or contained in these Articles. The following shall be the articles of association of the Company.

1.1. In the Articles, unless the context requires otherwise, the following words and expressions will have the meanings set out below:

Appointed Number	has the meaning given in Article 135
Appointed Proxy	has the meaning given in Article 136
Appointed Proxy Record Date	has the meaning given in Article 140.1
Approved Depositary	means a custodian or some other person appointed in Writing by the Directors whereby such custodian or other person holds or is interested in Ordinary Shares and issues securities or other documents of title or otherwise evidencing the entitlement of the Holder thereof to receive such shares, provided and to the extent that the terms and conditions of the custodian or other person acting as such have been approved by the Directors for the purpose of these Articles
Articles	means these articles of association as altered from time to time
Associated Undertaking	has the meaning given in Article 20.1
Bankruptcy	includes individual insolvency proceedings in a jurisdiction other than England and Wales or Northern Ireland which have an effect similar to that of bankruptcy
Board	means the Board of Directors of the Company as appointed from time to time in accordance with the Articles

Call	has the meaning given in Article 79.1
Call Notice	has the meaning given in Article 79.1
Call Payment Date	has the meaning given in Article 82.2(a)
Capitalised Sum	has the meaning given in Article 111.1(b)
Certificate	means a paper certificate (other than a Share warrant) evidencing a person's title to specified Shares or other securities
Certificated	in relation to a Share, means that it is not an Uncertificated Share or a Share in respect of which a Share warrant has been issued and is current
Chairman	has the meaning given in Article 16.2
Chairman of the Meeting	has the meaning given in Article 42.3
Companies Acts	means the Companies Acts (as defined in section 2 of the Companies Act 2006), in so far as they apply to the Company
Company's Lien	has the meaning given in Article 77.1
Default Shares	has the meaning given in Article 95.5
Depository Shares	has the meaning given in Article 135
Direction Notice	has the meaning given in Article 95.5
Director	means a Director of the Company, and includes any person occupying the position of Director, by whatever name called
Distribution Recipient	has the meaning given in Article 100.2
Document	includes, unless otherwise specified, any document sent or supplied in Electronic Form
Elected Ordinary Shares	has the meaning given in Article 110(d)
Electronic Form	has the meaning given in section 1168 of the Companies Act 2006

Fully Paid	in relation to a Share, means that the nominal value and any premium to be Paid to the Company in respect of that Share have been Paid to the Company
Group	means the Company and its subsidiaries
Hard Copy Form	has the meaning given in section 1168 of the Companies Act 2006
Holder	in relation to Shares means the person whose name is entered in the register of Members as the holder of the Shares, or, in the case of a Share in respect of which a Share warrant has been issued (and not cancelled), the person in possession of that warrant
Instrument	means a Document in Hard Copy Form
Invesco Fund	the Invesco Perpetual High Income Fund
Invesco UK Strategic	the Invesco Perpetual UK Strategic Income Fund
Lien Enforcement Notice	has the meaning given in Article 78
London Stock Exchange	means London Stock Exchange plc
Member	has the meaning given in section 112 of the Companies Act 2006
Nasdaq	means the market known as Nasdaq operated by The Nasdaq OMX Group, Inc.
Nasdaq Rules	means the rules of Nasdaq
Novartis	Novartis Pharma AG Lichtstrasse 35, CH-4002, Basel, Switzerland
Ordinary Resolution	has the meaning given in section 282 of the Companies Act 2006
Ordinary Shares	means ordinary shares of £0.003 each in the Company
Paid	means paid or credited as paid
Partly Paid	in relation to a Share means that part of that Share's nominal value or any premium at which it was issued has not been Paid to the Company

Persons Entitled	has the meaning given in Article 111.1(b)
Proxy Notice	has the meaning given in Article 58
Proxy Notification Address	has the meaning given in Article 59.1
Proxy Register	has the meaning given in Article 135
Regulations	means the Uncertificated Securities Regulations 2001 (SI 2001 No. 3755)
Relevant Director	has the meaning given in Article 132.4(b)
Relevant Loss	has the meaning given in Article 133.2(a)
Relevant Price	has the meaning given in Article 110(b)
Relevant Rate	has the meaning given in Article 82.2(b)
Relevant Rules	has the meaning given in Article 75.1
Relevant Situation	has the meaning given in Article 20.3
Relevant System	means the computer-based system, and procedures, which enable title to units of a security to be evidenced and transferred without a written instrument, and which facilitate supplementary and incidental matters in accordance with the Regulations
Retiring Directors	has the meaning given in Article 31.1
Shares	means shares in the Company
Special Resolution	has the meaning given in section 283 of the Companies Act 2006
Specified Place	has the meaning given in Article 45.2
Subsidiary	has the meaning given in section 1159 of the Companies Act 2006
Transmittee	means a person entitled to a Share by reason of the death or Bankruptcy of a shareholder or otherwise by operation of law

Uncertificated	in relation to a Share means that, by virtue of legislation (other than section 778 of the Companies Act 2006) permitting title to Shares to be evidenced and transferred without a Certificate, title to that Share is evidenced and may be transferred without a Certificate
WEIF	LF Woodford Equity Income Fund
WPCT	Woodford Patient Capital Trust plc
Writing	means the representation or reproduction of words, symbols or other information in a visible form by any method or combination of methods, whether sent or supplied in Electronic Form or otherwise

- 1.2. Unless the context otherwise requires, other words or expressions contained in these Articles bear the same meaning as in the Companies Act 2006 as in force on the date when these Articles become binding on the Company.
- 1.3. In accordance with section 31(1) of the Companies Act 2006, the objects of the Company are unrestricted.

2 Liability of Members

The liability of the Members is limited to the amount, if any, unpaid on the Shares held by them.

PART 2

DIRECTORS, DIRECTORS' POWERS AND RESPONSIBILITIES

3 Directors' general authority

- 3.1. Subject to the Articles, the Directors are responsible for the management of the Company's business, for which purpose they may exercise all the powers of the Company other than those required by law or these Articles to be exercised by the Company at a general meeting.
- 3.2. All acts done by a meeting of Directors, or of a committee of Directors, or by a person acting as a Director or as a member of any such committee, shall, notwithstanding that it be afterwards discovered that there was a defect in the appointment of any such person or that any of them were disqualified from holding office, or had vacated office, or were not entitled to vote, be as valid as if every such person had been duly appointed and was qualified and had continued to be a Director or member of the committee and had been entitled to vote.

4 Directors' authority to allot

The Company may from time to time pass an Ordinary Resolution authorising, in accordance with section 551 of the Companies Act 2006, the Board to exercise all the powers of the Company to allot Shares or to grant rights to subscribe for, or to convert any security into, any Shares.

5 Pari passu issues

If new Shares are created or issued which rank equally with any other existing Shares, or the Company purchases any of its own Shares, the rights of the existing Shares will not be regarded as changed or abrogated unless the terms of the existing Shares expressly say otherwise.

6 Members' reserve power

6.1. The Members may, by Special Resolution, direct the Directors to take, or refrain from taking, specified action.

6.2. No such Special Resolution invalidates anything which the Directors have done before the passing of the resolution.

7 Directors may delegate

7.1. Subject to the Articles, the Directors may delegate any of the powers which are conferred on them under the Articles:

- (a) to such person or committee;
- (b) by such means (including by power of attorney);
- (c) to such an extent;
- (d) in relation to such matters or territories; and
- (e) on such terms and conditions;

as they think fit.

7.2. If the Directors so specify, any such delegation may authorise further delegation of the Directors' powers by any person to whom they are delegated.

7.3. The Directors may revoke any delegation in whole or part, or alter its terms and conditions.

8 Committees

8.1. Committees to which the Directors delegate any of their powers must follow procedures which are based as far as they are applicable on those provisions of the Articles which govern the taking of decisions by Directors.

- 8.2. The Directors may make rules of procedure for all or any committees, which prevail over rules derived from the Articles if they are not consistent with them.

9 Observer rights

For as long as Novartis holds not less than one per cent. (1%) of the issued share capital of the Company, Novartis may appoint one observer of the Board who may attend but not participate or vote in any meeting of the Directors.

10 Power to establish local boards

- 10.1. The Directors may establish any local boards or agencies for managing any of the affairs of the Company, either in the United Kingdom or elsewhere, and may appoint any persons to be members of such local boards and may determine their remuneration. The Directors may delegate to any local board, manager or agent any of the powers, authorities and discretions vested in the Directors with power to subdelegate, and may authorise the members of any local board, or any of them, to fill any vacancies therein and to act despite vacancies. Any such appointment or delegation may be made upon such terms and subject to such conditions as the Directors may think fit, and either collaterally with or to the exclusion of its own powers, and the Directors may remove any person so appointed, and may annul or vary any such delegation, but no person dealing in good faith and without notice of any such annulment or variation shall be affected by it. Subject to this, the proceedings of any local board shall be governed by such of these Articles as regulate the proceedings of the Directors so far as they are capable of applying.

DECISION-MAKING BY DIRECTORS

11 Directors to take decisions collectively

- 11.1. Decisions of the Directors may be taken:

- (a) at a Directors' meeting; or
- (b) in the form of a Directors' written resolution.

12 Calling a Directors' meeting

- 12.1. Any Director may call a Directors' meeting.
- 12.2. The Company secretary must call a Directors' meeting if a Director so requests.
- 12.3. A Directors' meeting is called by giving notice of the meeting to the Directors.
- 12.4. Notice of any Directors' meeting must indicate:
- (a) its proposed date and time;

- (b) where it is to take place; and
 - (c) if it is anticipated that Directors participating in the meeting will not be in the same place, how it is proposed that they should communicate with each other during the meeting.
- 12.5. Notice of a Directors' meeting must be given to each Director, but need not be in Writing.
- 12.6. Any Director may waive their right to notice of any meeting and any such waiver may be retroactive.
- 12.7. Notice of a Directors' meeting need not be given to Directors who waive their entitlement to notice of that meeting, by giving notice to that effect to the Company not more than seven (7) days after the date on which the meeting is held. Where such notice is given after the meeting has been held, that does not affect the validity of the meeting, or of any business conducted at it.

13 Participation in Directors' meetings

- 13.1. Subject to the Articles, Directors participate in a Directors' meeting, or part of a Directors' meeting, when:
- (a) the meeting has been called and takes place in accordance with the Articles; and
 - (b) they can each communicate to the others any information or opinions they have on any particular item of the business of the meeting.
- 13.2. In determining whether Directors are participating in a Directors' meeting, it is irrelevant where any Director is or how they communicate with each other.
- 13.3. If all the Directors participating in a meeting are not in the same place, they may decide that the meeting is to be treated as taking place wherever any of them is.

14 Quorum for Directors' meetings

- 14.1. At a Directors' meeting, unless a quorum is participating, no proposal is to be voted on, except a proposal to call another meeting.
- 14.2. The quorum for Directors' meetings may be fixed from time to time by a decision of the Directors, but it must never be less than two, and unless otherwise fixed it is two.

15 Meetings where total number of Directors less than quorum

- 15.1. This Article applies where the total number of Directors for the time being is less than the quorum for Directors' meetings.
- 15.2. If there is only one Director, that Director may appoint sufficient Directors to make up a quorum or call a general meeting to do so but not for any other purpose.

- 15.3. If there is more than one Director:
- (a) a Directors' meeting may take place, if it is called in accordance with the Articles and at least two Directors participate in it, with a view to appointing sufficient Directors to make up a quorum or calling a general meeting to do so; and
 - (b) if a Directors' meeting is called but only one Director attends at the appointed date and time to participate in it, that Director may appoint sufficient Directors to make up a quorum or call a general meeting to do so.

16 Chairing Directors' meetings

- 16.1. The Directors may appoint a Director to chair their meetings.
- 16.2. The person so appointed for the time being is known as the Chairman.
- 16.3. The Directors may appoint other Directors as deputy or assistant chairmen to chair Directors' meetings in the Chairman's absence.
- 16.4. The Directors may terminate the appointment of the Chairman, deputy or assistant Chairman at any time.
- 16.5. If neither the Chairman nor any Director appointed generally to chair Directors' meetings in the Chairman's absence is participating in a meeting within ten minutes of the time at which it was to start, the participating Directors must appoint one of themselves to chair it.

17 Voting at Directors' meetings: general rules

- 17.1. Subject to the Articles, a decision is taken at a Directors' meeting by a majority of the votes of the participating Directors.
- 17.2. Subject to the Articles, each Director participating in a Directors' meeting has one vote.

18 Chairman's casting vote at Directors' meetings

- 18.1. If the numbers of votes for and against a proposal are equal, the Chairman or other Director chairing the meeting has a casting vote.
- 18.2. But 18.1 above does not apply if, in accordance with the Articles, the Chairman or other Director is not to be counted as participating in the decision-making process for quorum or voting purposes.

19 Transactions with the Company

- 19.1. Provided that a Director has declared at a Directors' meeting or in such other manner as the Directors may resolve to the other Directors the nature and extent of any interest of his, a Director notwithstanding his office may be a party to, or otherwise directly or indirectly interested in, any proposed or existing transaction or arrangement with the Company.

- 19.2. Except as provided by the terms of any authorisation of a Relevant Situation (as defined in Article 20.3) or if Article 19.3 applies, a Director will not count in the quorum or be entitled to vote:
- (a) on a proposal under consideration concerning his appointment to an office or employment with the Company; or
 - (b) on any undertaking or proposal in which the Director (or a person connected with the Director) is interested.
- 19.3. This Article 19.3 applies when:
- (a) the Director's interest arises solely through an interest in shares, debentures or other securities of or otherwise in or through the Company;
 - (b) the Company by Ordinary Resolution applies the provision of these Articles which would otherwise prevent a Director from being counted as participating in, or voting at, a meeting of the Board;
 - (c) the Director's interest cannot reasonably be regarded as likely to give rise to a material conflict of interest; or
 - (d) the Director's conflict of interest arises from a permitted cause as set out in Article 19.4.
- 19.4. For the purposes of Article 19.3, the following are permitted causes:
- (a) a guarantee, security or indemnity given, or to be given, by or to a Director in respect of an obligation incurred by or on behalf of the Company or any of its Subsidiaries;
 - (b) subscription, or an agreement to subscribe, for shares or other securities of the Company or any of its Subsidiaries, or to underwrite, sub-underwrite, or guarantee an offer of any such shares or securities by the Company or any of its Subsidiaries for subscription, purchase or exchange;
 - (c) arrangements pursuant to which benefits are made available to employees and Directors or former employees and Directors of the Company or any of its Subsidiaries which do not provide special benefits for Directors or former Directors;
 - (d) the purchase or maintenance of insurance which the Company is empowered to purchase or maintain for any person who is a Director or other officer of the Company under which he may benefit;

- (e) the giving to a Director of an indemnity against liabilities incurred or to be incurred by that Director in the execution and discharge of his duties;
 - (f) the provision to a Director of funds to meet expenditure incurred or to be incurred by that Director in defending criminal or civil proceedings against him or in connection with any application under any of the provisions mentioned in section 205(5) of the Companies Act 2006 or otherwise enabling him to avoid incurring that expenditure; or
 - (g) proposals concerning another company in which he is interested directly or indirectly (whether as officer, shareholder or otherwise), if he and any other persons connected with him do not to his knowledge hold an interest in shares (as that term is used in sections 820 to 825 of the Companies Act 2006) representing one per cent or more of the issued shares of any class of the equity share capital of that company (or of any third company through which his or their interest is derived) or of the voting rights available to members of the relevant company (and that interest is deemed for the purposes of this Article to be a material interest).
- 19.5. Where proposals under Article 19.2(a) are under consideration concerning the appointment of two or more Directors to any such offices or employments the proposals may be divided and considered in relation to each Director separately and (provided he is not for another reason precluded from voting) each of the Directors concerned will be entitled to participate in the decision-making process and count in the quorum and vote in respect of each decision except that concerning his own appointment.
- 19.6. Subject to the immediately preceding Article 19.5 and provided that he has declared to the other Directors the nature and extent of any interest of his and provided that a majority of the other Directors consent, a Director may participate in the decision-making process and count in the quorum and vote if a proposed decision of the Directors is concerned with an actual or proposed transaction or arrangement with the Company in which the Director is interested.
- 20 Conflicts of interest**
- 20.1. A Director may be a director or other officer of, or employed by, or otherwise interested in, any company in the Group, any undertaking promoted by or advised by or managed by a company in the Group and any undertaking in which a company in the Group is otherwise interested (each, an “**Associated Undertaking**”), or be a party to, or otherwise interested in, any contract, transaction or arrangement in which an Associated Undertaking is interested, provided that the Director declares to the other Directors the nature and extent of his interest as soon as practicable after such interest arises.
- 20.2. A Director may make full disclosure of any information relating to the Company to another company in the Group (or anyone acting on behalf of any such company in the Group, including its advisers).

- 20.3. If a situation (a “**Relevant Situation**”) arises in which a Director has, or can have, a direct or indirect interest that conflicts, or possibly may conflict, with the interests of the Company (other than a situation that cannot reasonably be regarded as likely to give rise to a conflict of interest or a conflict of interest arising in relation to a transaction or arrangement with the Company), the Directors may authorise in accordance with the Companies Act a Relevant Situation in respect of any Director and the continuing performance by the relevant Director of his duties as a Director of the Company on such terms as they may determine. Such terms may permit the interested Director to continue to participate in the decision-making process and vote and count in the quorum at a meeting of the Directors or of a committee of the Directors in respect of resolutions relating to the subject matter of the Relevant Situation. Authorisation of a Relevant Situation may be withdrawn, and the terms of authorisation may be varied or subsequently imposed, at any time. Any resolution of the Directors for the purposes of providing, varying the terms of or withdrawing such authorisation will not be effective unless:
- (a) the requirement as to the quorum at the meeting at which the resolution is proposed is met without counting the interested Director or any other interested Director (and for these purposes any other provisions of these Articles that would require the interested Director or any other interested Director to be present during such part of the meeting for the quorum requirement to be met will not apply); and
 - (b) the resolution is passed without the interested Director or any other interested Director voting or would have been passed if their votes had not been counted.
- 20.4. Notwithstanding the foregoing, if a Relevant Situation arises and the matter has not previously been duly authorised, a Director may elect to deal with the Relevant Situation in the following manner:
- (a) he will declare to the other Directors the nature and extent of his interest in the Relevant Situation (except as set forth in paragraph (d) below);
 - (b) he will not vote (and will not be counted in the quorum at a meeting of the Directors or of a committee of the Directors) in respect of a resolution of the Directors relating to the subject matter of the Relevant Situation; and/or
 - (c) he may elect to be excluded from all information and discussion by the Company relating to the subject matter of the Relevant Situation; and
 - (d) if he obtains (other than through his position as a Director of the Company) information that is confidential to a third party, or in respect of which he owes a duty of confidentiality to a third party, or the disclosure of which would amount to a breach of applicable law or regulation, he may elect not to disclose it to the Company or to use it in relation to the Company’s affairs in circumstances where to do so would amount to a breach of that confidence or a breach of applicable law or regulation, and the provisions of the Articles that would require him to be present for the quorum requirement for meetings of the Directors to be met will not apply.

- 20.5. If a Relevant Situation has been duly authorised by the Directors or the Company (or is otherwise permitted or dealt with in accordance with the Articles, as described above) and its nature and extent has been disclosed to the other Directors, a Director may participate in the decision making process and count in the quorum and vote if a proposed decision of the Directors is concerned with such situation (subject to any restrictions imposed under the terms on which it was authorised).

21 Directors permitted to retain benefits

- 21.1. A Director is not required, by reason of being a Director (or because of the fiduciary relationship established by reason of being a Director), to account to the Company for any remuneration or other benefit which he derives from or in connection with a relationship involving a conflict of interest or possible conflict of interest which has been authorised by the Directors (whether pursuant to Article 20.3 or otherwise) or by the Company in a general meeting (subject in each case to any terms, limits or conditions attaching to that authorisation).
- 21.2. If he has disclosed to the Board the nature and extent of his interest to the extent required by the Companies Act 2006, a Director is not required, by reason of being a Director (or because of the fiduciary relationship established by reason of being a Director), to account to the Company for any remuneration or other benefit which he derives from or in connection with:
- (a) being a party to, or otherwise interested in, any transaction or arrangement with:
 - (i) the Company or in which the Company is interested; or
 - (ii) a body corporate in which the Company is interested;
 - (b) acting (otherwise than as auditor) alone or through his organisation in a professional capacity for the Company (and he or that organisation is entitled to remuneration for professional services as if he were not a Director); or
 - (c) being a director or other officer of, or employed by, or otherwise interested in the Company's Subsidiaries or any other body corporate in which the Company is interested.
- 21.3. A Director's receipt of any remuneration or other benefit referred to in Article 21.1 or 21.2 does not constitute an infringement of his duty under section 176 of the Companies Act 2006; and
- 21.4. A transaction or arrangement referred to in Article 21.1 or 21.2 is not liable to be avoided on the ground of any remuneration, benefit or interest referred to in that Article.

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- 22 Board's ruling is final**
- 22.1. If a question arises at any meeting of the Board or committee or sub-committee of the Board as to the materiality of a Director's interest or as to the entitlement of a Director to vote or count in the quorum and the question is not resolved by his voluntarily agreeing to abstain from voting, the question shall be decided by a resolution of the Board or such committee (such Director being excluded from voting on the resolution), and such decision shall be final and conclusive except in a case where the nature or extent of the interests of such Director have not been fairly disclosed.
- 23 Proposing Directors' written resolutions**
- 23.1. Any Director may propose a Directors' written resolution.
- 23.2. The Company secretary must propose a Directors' written resolution if a Director so requests.
- 23.3. A Directors' written resolution is proposed by giving notice of the proposed resolution to the Directors.
- 23.4. Notice of a proposed Directors' written resolution must indicate:
- (a) the proposed resolution; and
 - (b) the time by which it is proposed that the Directors should adopt it.
- 23.5. Notice of a proposed Directors' written resolution must be given in Writing to each Director.
- 23.6. Any decision which a person giving notice of a proposed Directors' written resolution takes regarding the process of adopting that resolution must be taken reasonably in good faith.
- 24 Adoption of Directors' written resolutions**
- 24.1. A proposed Directors' written resolution is adopted when all the Directors who would have been entitled to vote on the resolution at a Directors' meeting have signed one or more copies of it, provided that those Directors would have formed a quorum at such a meeting.
- 24.2. It is immaterial whether any Director signs the resolution before or after the time by which the notice proposed that it should be adopted.
- 24.3. Once a Directors' written resolution has been adopted, it must be treated as if it had been a decision taken at a Directors' meeting in accordance with the Articles.
- 24.4. The Company secretary must ensure that the Company keeps a record, in Writing, of all Directors' written resolutions for at least ten years from the date of their adoption.

- 25 Directors' discretion to make further rules**
- 25.1. Subject to the Articles, the Directors may make any rule which they think fit about how they take decisions, and about how such rules are to be recorded or communicated to Directors.
- 26 Directors' power relating to other companies**
- 26.1. The Board may exercise the voting power conferred by the shares in any company held or owned by the Company in any way that it decides (including voting in favour of any resolution appointing any of them directors of that company, or voting or providing for the payment of remuneration to the directors of that company).

APPOINTMENT OF DIRECTORS

- 27 Number of Directors**
- Unless otherwise determined by Ordinary Resolution the Directors of the Company shall number no less than two and not more than nine.
- 28 Methods of appointing Directors**
- 28.1. Any person who is willing to act as a Director, and is permitted by law to do so, may be appointed to be a Director either to fill a casual vacancy or as an addition to the existing Board:
- (a) by Ordinary Resolution; or
 - (b) by a decision of the Directors,
- but the total number of Directors shall not exceed the maximum number fixed in accordance with Article 27.
- 28.2. No person shall be elected as a Director unless such person is recommended by the Board or the Company has received from such person confirmation in Writing of that person's willingness to be elected as a Director, no later than seven days before the general meeting at which the relevant resolution is proposed.
- 29 Retiring Directors**
- 29.1. At each annual general meeting of the Company any Director then in office:
- (a) who has been appointed by the Board since the previous annual general meeting in accordance with Article 28.1; or
 - (b) for whom it is the third annual general meeting following the annual general meeting at which he was elected or last re-elected;
- shall retire from office but shall be eligible for re-appointment.

30 Deemed re-appointment

- 30.1. A Director who retires at an annual general meeting shall (unless he is removed from office or his office is vacated in accordance with these Articles) retain office until the close of the meeting at which he retires or (if earlier) when a resolution is passed at that meeting not to fill the vacancy or to elect another person in his place or the resolution to re-appoint him is put to the meeting and lost.
- 30.2. If the Company, at any meeting at which a Director retires in accordance with these Articles does not fill the office vacated by such Director, the retiring Director, if willing to act, shall be deemed to be re-appointed unless at that meeting a resolution is passed not to fill the vacancy or elect another person in his place or unless the resolution to re-appoint him is put to the meeting and lost.

31 Procedure if insufficient Directors appointed

- 31.1. If:
- (a) at the annual general meeting in any year any resolution or resolutions for the appointment or re-appointment of the persons eligible for appointment or re-appointment as Directors are put to the meeting and lost; and
 - (b) at the end of that meeting the number of Directors is fewer than any minimum number of Directors required under Article 27,
- all retiring Directors who stood for re-appointment at that meeting (“**Retiring Directors**”) shall be deemed to have been re-appointed as Directors and shall remain in office but the Retiring Directors may only act for the purpose of filling vacancies, convening general meetings of the Company and performing such duties as are essential to maintain the Company as a going concern, and not for any other purpose.
- 31.2. The Retiring Directors shall convene a general meeting as soon as reasonably practicable following the meeting referred to in Article 31.1 and they shall retire from office at that meeting. If at the end of any meeting convened under this Article the number of Directors is fewer than any minimum number of Directors required under Article 27, the provisions of this Article shall also apply to that meeting.

32 Removal of Directors

In addition to any power of removal conferred by the Companies Acts, the Company may by Special Resolution, or by Ordinary Resolution of which special notice has been given in accordance with section 312 of the Companies Act 2006, remove a Director before the expiry of his period of office (without prejudice to a claim for damages for breach of contract or otherwise) and may (subject to these Articles) by Ordinary Resolution appoint another person who is willing to act to be a Director in his place.

33 Termination of Director's appointment

33.1. A person ceases to be a Director as soon as:

- (a) that person ceases to be a Director by virtue of any provision of the Companies Act 2006 or is prohibited from being a Director by law or (if applicable) the Nasdaq Rules;
- (b) a Bankruptcy order is made against that person;
- (c) a composition is made with that person's creditors generally in satisfaction of that person's debts or any analogous event occurs in the United Kingdom or another country;
- (d) a registered medical practitioner who is treating that person gives a written opinion to the Company stating that that person has become physically or mentally incapable of acting as a Director and may remain so for more than three months;
- (e) by reason of that person's mental health, a court makes an order which wholly or partly prevents that person from personally exercising any powers or rights which that person would otherwise have;
- (f) he is absent from meetings of the Directors for six successive months without the permission of the Directors and the Directors resolve that his office is vacated;
- (g) he is removed from office by notice in Writing served upon him signed by all his co-Directors (without prejudice to any claims for damages which he may have for breach of any contract between him and the Company); or
- (h) notification is received by the Company from the Director that the Director is resigning from office as Director, and such resignation has taken effect in accordance with its terms.

34 Directors' remuneration

34.1. Directors may undertake any services for the Company that the Directors decide.

34.2. Directors are entitled to such remuneration as the Directors determine:

- (a) for their services to the Company as Directors; and
- (b) for any other service which they undertake for the Company.

34.3. A Director's remuneration may:

- (a) take any form; and
- (b) include any arrangements in connection with the payment of a pension, allowance or gratuity, or any death, sickness or disability benefits, to or in respect of that Director.

- 34.4. Unless the Directors decide otherwise, Directors' remuneration accrues from day to day.
- 34.5. Unless the Directors decide otherwise, Directors are not accountable to the Company for any remuneration which they receive as Directors or other officers or employees of the Company's Subsidiaries or of any other body corporate in which the Company is interested.

35 Directors' expenses

The Company may pay any reasonable expenses which the Directors properly incur in connection with their attendance at:

- (a) meetings of Directors or committees of Directors;
- (b) general meetings; or
- (c) separate meetings of the Holders of any class of Shares or of debentures of the Company,
- (d) or otherwise in connection with the exercise of their powers and the discharge of their responsibilities in relation to the Company.

36 Authentication of Documents

Any Director or the company secretary or any person appointed by the Directors for the purpose shall have power to authenticate any Documents affecting the constitution of the Company and any resolutions passed by the Company or the Directors or any committee of the Directors and any books, records, Documents and accounts relating to the business of the Company and to certify copies of them or extracts from them as true copies or extracts, and where any books, records, Documents or accounts are elsewhere than at the Office the local manager or other officer of the Company having the custody of them shall be deemed to be a person appointed by the Directors for the above purposes. A Document purporting to be a copy of a resolution or an extract from the minutes of a meeting of the Company or of the Directors or any committee, which is certified as described in this Article, shall be conclusive evidence in favour of all persons dealing with the Company upon the faith of such resolution or extract of minutes, that such resolution has been duly passed or, as the case may be, that such minutes or extract is a true and accurate record of proceedings at a duly constituted meeting.

SECRETARY

37 Appointment, remuneration and removal

- 37.1. Subject to the Companies Acts and any other provisions of law, the company secretary shall be appointed by the Directors for such term, at such remuneration and upon such conditions as they may think fit, and any company secretary so appointed may be removed from office by the Directors but at any time without prejudice to any claim for damages for breach of any contract of service between the company secretary and the Company. If thought fit, two or more persons may be appointed as joint company secretaries and the Directors may also appoint from time to time on such terms as they think fit one or more assistant or deputy company secretaries.

- 37.2. Any provision of the Companies Acts or these Articles requiring or authorising a thing to be done by or to a Director and a company secretary shall not be satisfied by it being done by or to the same person acting both as Director and as, or in the place of, the company secretary.

PART 3

DECISION-MAKING BY MEMBERS ORGANISATION OF GENERAL MEETINGS

38 Frequency of meetings and quorum

- 38.1. An annual general meeting shall be held in accordance with the applicable statutory provisions or on the requisition of shareholders in accordance with the Companies Act. An annual general meeting shall be called by not less than such minimum notice period as is permitted by the applicable statutory provisions.
- 38.2. The requisite quorum for general meetings of the Company shall be two qualifying persons, as determined in accordance with the Companies Act 2006.

39 Calling general meetings

- 39.1. Two or more Members holding 5% or more of the voting share capital of the Company may require the Directors to call a general meeting (or instruct the Company secretary to do so).
- 39.2. The Directors may call a general meeting.

40 Attendance and speaking at general meetings

- 40.1. A person is able to exercise the right to speak at a general meeting when that person is in a position to communicate to all those attending the meeting, during the meeting, any information or opinions which that person has on the business of the meeting.
- 40.2. A person is able to exercise the right to vote at a general meeting when:
- (a) that person is able to vote, during the meeting, on resolutions put to the vote at the meeting; and
 - (b) that person's vote can be taken into account in determining whether or not such resolutions are passed at the same time as the votes of all the other persons attending the meeting.

- 40.3. The Directors may make whatever arrangements they consider appropriate to enable those attending a general meeting to exercise their rights to speak or vote at it.
- 40.4. In determining attendance at a general meeting, it is immaterial whether any two or more Members attending it are in the same place as each other.
- 40.5. Two or more persons who are not in the same place as each other attend a general meeting if their circumstances are such that if they have (or were to have) rights to speak and vote at that meeting, they are (or would be) able to exercise them.
- 40.6. The Directors may direct that any person wishing to attend a general meeting should provide evidence of identity and submit to such searches or other security arrangements or restrictions as the Directors shall consider appropriate in the circumstances and shall be entitled in its absolute discretion to refuse entry to any meeting to any person who fails to provide such evidence of identity or to submit to such searches or to otherwise comply with such security arrangements or restrictions. The Chairman of the Meeting shall take such action or give direction as he thinks fit to promote the orderly conduct of the business of the meeting as laid down in the notice of general meeting and to ensure the security of the meeting and the safety of the people attending the meeting. The Chairman of the Meeting's decision on matters of procedure or arising incidentally from the business of the meeting shall be final as shall be his determination as to whether any matter is of such a nature.

41 Quorum for general meetings

No business other than the appointment of the Chairman of the Meeting is to be transacted at a general meeting if the persons attending it do not constitute a quorum.

42 Chairing general meetings

- 42.1. If the Directors have appointed a Chairman, the Chairman shall chair general meetings if present and willing to do so.
- 42.2. If the Directors have not appointed a Chairman, or if the Chairman is unwilling to chair the meeting or is not present within ten minutes of the time at which a meeting was due to start:
- (a) the Directors present; or
- (b) (if no Directors are present), the meeting,
- must appoint a Director or Member to chair the meeting, and the appointment of the Chairman of the Meeting must be the first business of the meeting.
- 42.3. The person chairing a meeting in accordance with this Article is referred to as the “**Chairman of the Meeting**”.

43 Attendance and speaking by Directors and non-Members

- 43.1. Directors may attend and speak at general meetings, whether or not they are Members.
- 43.2. The Chairman of the Meeting may permit other persons who are not:
- (a) Members of the Company; or
 - (b) otherwise entitled to exercise the rights of Members in relation to general meetings, to attend and speak at a general meeting.

44 Adjournment

- 44.1. If the persons attending a general meeting within half an hour of the time at which the meeting was due to start do not constitute a quorum, or if during a meeting a quorum ceases to be present, the Chairman of the Meeting must adjourn it.
- 44.2. The Chairman of the Meeting may adjourn a general meeting at which a quorum is present if:
- (a) the meeting consents to an adjournment; or
 - (b) it appears to the Chairman of the Meeting that an adjournment is necessary to protect the safety of any person attending the meeting or ensure that the business of the meeting is conducted in an orderly manner.
- 44.3. The Chairman of the Meeting must adjourn a general meeting if directed to do so by the meeting.
- 44.4. When adjourning a general meeting, the Chairman of the Meeting must:
- (a) either specify the time and place to which it is adjourned or state that it is to continue at a time and place to be fixed by the Directors; and
 - (b) have regard to any directions as to the time and place of any adjournment which have been given by the meeting.
- 44.5. If the continuation of an adjourned meeting is to take place more than fourteen (14) days after it was adjourned, the Company must give at least seven (7) clear days' notice of it (that is, excluding the day of the adjourned meeting and the day on which the notice is given):
- (a) to the same persons to whom notice of the Company's general meetings is required to be given; and
 - (b) containing the same information which such notice is required to contain.
- 44.6. No business may be transacted at an adjourned general meeting which could not properly have been transacted at the meeting if the adjournment had not taken place.

45 Procedure where meetings held at more than one place

- 45.1. The provisions of this Article shall apply if any general meeting is held at or adjourned to more than one place.
- 45.2. The notice of such a Meeting or adjourned meeting shall specify the place at which the Chairman of the Meeting shall preside (for the purposes of this Article 45 the “**Specified Place**”) and the Directors shall make arrangements for simultaneous attendance and participation at the Specified Place and at other places by Members, provided that persons attending at any particular place shall be able to see and hear and be seen and heard by means of audio visual links by persons attending the Specified Place and at the other places at which the meeting is held.
- 45.3. The Directors may from time to time make such arrangements for the purpose of controlling the level of attendance at any such place (whether involving the issue of tickets or the imposition of some geographical or regional means of selection or otherwise) as they shall in their absolute discretion consider appropriate, and may from time to time vary any such arrangements or make new arrangements in place of them, provided that a Member who is not entitled to attend, in person or by proxy, at any particular place shall be entitled so to attend at one of the other places, and the entitlement of any Member so to attend the meeting or adjourned meeting at such place shall be subject to any such arrangements as may from time to time be in force and by the notice of meeting or adjourned meeting stated to apply to the meeting.
- 45.4. For the purposes of all other provisions of these Articles, any such meeting shall be treated as being held at the Specified Place.
- 45.5. If a meeting is adjourned to more than one place, not less than seven days’ notice of the adjourned meeting shall be given despite any other provision of these Articles.

VOTING AT GENERAL MEETINGS

46 Voting: general

- 46.1. A resolution put to the vote of a general meeting must be decided on a show of hands unless a poll is duly demanded in accordance with the Articles.
- 46.2. Notwithstanding Article 46.1, on a poll, any Shares held by WEIF, Invesco Fund, Invesco UK Strategic and Novartis will each have one vote per Share, provided that if at any time:
- (a) WEIF’s Shares constitute more than 19.5% of the total voting share capital of the Company, WEIF’s Shares shall be limited in aggregate to 19.5% of the total number of votes, such votes to be split equally on a fractional basis amongst WEIF’s Shares;

- (b) Invesco Fund's Shares constitute more than 19.5% of the total voting share capital of the Company, Invesco Fund's Shares shall be limited in aggregate to 19.5% of the total number of votes, such votes to be split equally on a fractional basis amongst Invesco Fund's Shares; and
- (c) Invesco UK Strategic's Shares constitute more than 19.5% of the total voting share capital of the Company, Invesco UK Strategic's Shares shall be limited in aggregate to 19.5% of the total number of votes, such votes to be split equally on a fractional basis amongst Invesco UK Strategic's Shares,

provided further that any votes which would, but for the operation of this Article 46.2, be exercisable by WEIF, Invesco Fund or Invesco UK Strategic shall be deemed to be held and exercisable by the Holders of Shares, other than WEIF, WPCT, Invesco Fund, Invesco UK Strategic and Novartis, pro rata in proportion to the number of Shares held by them.

- 46.3. A Special Resolution shall be effective for any purpose for which an Ordinary Resolution is expressed to be required under any provision of the Articles.

47 Errors and disputes

- 47.1. No objection may be raised to the qualification of any person voting at a general meeting except at the meeting or adjourned meeting at which the vote objected to is tendered, and every vote not disallowed at the meeting is valid.
- 47.2. Any such objection must be referred to the Chairman of the Meeting whose decision is final.

48 Demanding a poll

- 48.1. A poll on a resolution may be demanded:

- (a) in advance of the general meeting where it is to be put to the vote; or
- (b) at a general meeting, either before a show of hands on that resolution or immediately after the result of a show of hands on that resolution is declared.

- 48.2. A poll may be demanded by:

- (a) the Chairman of the Meeting;
- (b) the Directors;
- (c) two or more persons having the right to vote on the resolution; or
- (d) a person or persons representing not less than one tenth of the total voting rights of all the Members having the right to vote on the resolution.

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- 48.3. A demand for a poll may be withdrawn if:
- (a) the poll has not yet been taken; and
 - (b) the Chairman of the Meeting consents to the withdrawal.

49 Procedure on a poll

- 49.1. Subject to the Articles, polls at general meetings must be taken when, where and in such manner as the Chairman of the Meeting directs.
- 49.2. The Chairman of the Meeting may appoint scrutineers (who need not be Members) and decide how and when the result of the poll is to be declared.
- 49.3. The result of a poll shall be the decision of the meeting in respect of the resolution on which the poll was demanded.
- 49.4. A poll on:
- (a) the election of the Chairman of the Meeting; or
 - (b) a question of adjournment,
- must be taken immediately.
- 49.5. Other polls must be taken within thirty (30) days of their being demanded.
- 49.6. A demand for a poll does not prevent a general meeting from continuing, except as regards the question on which the poll was demanded.
- 49.7. No notice need be given of a poll not taken immediately if the time and place at which it is to be taken are announced at the meeting at which it is demanded.
- 49.8. In any other case, at least seven (7) days' notice must be given specifying the time and place at which the poll is to be taken.

50 Votes of Members

- 50.1. Subject to any other provision of these Articles and without prejudice to any special rights, privileges or restrictions as to voting attached to any Shares for the time being forming part of the capital of the Company:
- (a) on a show of hands:
 - (i) each Member present in person has one vote;
 - (ii) except as otherwise provided in these Articles, each proxy present in person who has been duly appointed by one or more Members entitled to vote on a resolution has one vote;

- (iii) each proxy present in person has one vote for and one vote against a resolution if the proxy has been duly appointed by more than one Member entitled to vote on the resolution and the proxy has been instructed by one or more of those Members to vote for the resolution and by one or more other of those Members to vote against it;
- (iv) each proxy present in person has one vote for and one vote against a resolution if the proxy has been duly appointed by more than one Member entitled to vote on the resolution and either:
 - (A) the proxy has been instructed by one or more of those Members to vote for the resolution and has been given any discretion by one or more other of those Members to vote and the proxy exercises that discretion to vote against it; or
 - (B) the proxy has been instructed by one or more of those Members to vote against the resolution and has been given any discretion by one or more other of those Members to vote and the proxy exercises that discretion to vote for it; and
- (v) each duly authorised representative present in person of a Member that is a corporation has one vote; and
- (b) subject always to the provisions of Article 46.2, on a poll each Member present in person or by proxy or (being a corporation) by a duly authorised representative has one vote for each Share held by the Member.

50.2. For the avoidance of doubt, the Company itself is prohibited (to the extent specified by the Companies Acts or other provisions of law) from exercising any rights to attend or vote at meetings in respect of any Shares held by it as treasury shares.

51 **Votes on a show of hands or on a poll**

On a show of hands or on a poll, votes may be given either personally or by proxy or (in the case of a corporate Member) by a duly authorised representative and on a poll a person entitled to more than one vote need not, if he votes, use all his votes or cast all the votes he uses in the same way.

52 **Votes of joint holders**

In the case of joint holders of a Share only the vote of the senior holder who votes, whether in person or by proxy, may be counted by the Company and for this purpose the senior holder is determined by the order in which the names of the joint holders appear in the register in respect of the Share.

53 Voting on behalf of incapable Member

A Member in respect of whom an order has been made by any court having jurisdiction (whether in the United Kingdom or elsewhere) in matters concerning mental disorder may vote, whether on a show of hands or on a poll, by any person authorised in that behalf by that court, and any such person may vote by proxy. Evidence to the satisfaction of the Directors of the authority of the person claiming to exercise the right to vote shall be deposited at or delivered to the registered office of the Company (or such other place or address as is specified in accordance with these Articles for the deposit or delivery of appointments of proxy) not later than the last time at which an appointment of a proxy should have been deposited or delivered in order to be valid for use at that meeting or on the holding of that poll.

54 No right to vote where sums overdue on Shares

No Member (whether in person or by proxy or in the case of a corporate Member, by a duly authorised representative) shall (unless the Directors otherwise determine) be entitled to vote or to exercise any other right of membership at any general meeting or at any separate meeting of the holders of any class of Shares in the Company in respect of any Share held by him unless all Calls or other sums presently payable by him in respect of that Share in the Company have been Paid.

55 A proxy's obligations to vote

The Company is entitled to assume without enquiry that a proxy has complied with any obligation to vote in accordance with instructions given by the Member by whom the proxy is appointed. The validity of anything done at a meeting is not affected by any failure by a proxy to comply with such an obligation.

56 Appointment of proxies

56.1. A Member is entitled to appoint a proxy to exercise all or any of such Member's rights to attend and to speak and vote at a general meeting.

56.2. A proxy need not be a Member of the Company.

57 Multiple Proxies

A Member may appoint more than one proxy in relation to a meeting provided that each proxy is appointed to exercise the rights attached to a different Share or Shares held by such Member.

58 Content of Proxy Notices

58.1. Proxies may only validly be appointed by a notice in Writing (a "**Proxy Notice**") which:

- (a) states the name and address of the Member appointing the proxy;
- (b) identifies the person appointed to be that Member's proxy and the general meeting in relation to which that person is appointed;

- (c) is signed by or on behalf of the Member appointing the proxy, or is authenticated in such manner as the Directors may determine; and
 - (d) is delivered to the Company in accordance with the Articles and any instructions contained in the notice of the general meeting to which they relate.
- 58.2. The Company may require Proxy Notices to be delivered in a particular form, and may specify different forms for different purposes.
- 58.3. Proxy Notices may specify how the proxy appointed under them is to vote (or that the proxy is to abstain from voting) on one or more resolutions. The Company is entitled to assume without enquiry that a proxy has complied with any obligation to vote in accordance with instructions given by the Member by whom the proxy is appointed. The validity of anything done at a meeting is not affected by any failure by a proxy to comply with such an obligation.
- 58.4. Unless a Proxy Notice indicates otherwise, it must be treated as:
- (a) allowing the person appointed under it as a proxy discretion as to how to vote on any ancillary or procedural resolutions put to the meeting; and
 - (b) appointing that person as a proxy in relation to any adjournment of the general meeting to which it relates as well as the meeting itself.
- 58.5. No appointment of a proxy shall be valid after the expiration of 12 months from the date stated in it as its date of execution except at an adjourned meeting or on a poll demanded at a meeting or an adjourned meeting where the meeting was originally held within 12 months from such date.
- 59 Delivery of Proxy Notices**
- 59.1. Any notice of a general meeting must specify the address or addresses (“**Proxy Notification Address**”) at which the Company or its agents will receive Proxy Notices relating to that meeting, or any adjournment of it, delivered in Hard Copy Form or Electronic Form.
- 59.2. A person who is entitled to attend, speak or vote (either on a show of hands or on a poll) at a general meeting remains so entitled in respect of that meeting or any adjournment of it, even though a valid Proxy Notice has been delivered to the Company by or on behalf of that person.
- 59.3. Subject to Articles 59.4 and 59.5, a Proxy Notice must be delivered to a Proxy Notification Address not less than 48 hours before the general meeting or adjourned meeting to which it relates.
- 59.4. In the case of a poll taken more than 48 hours after it is demanded, the notice must be delivered to a Proxy Notification Address not less than 24 hours before the time appointed for the taking of the poll.

- 59.5. In the case of a poll not taken during the meeting but taken not more than 48 hours after it was demanded, the Proxy Notice must be delivered:
- (a) in accordance with Article 59.3; or
 - (b) at the meeting at which the poll was demanded to the Chairman, secretary or any Director.
- 59.6. An appointment under a Proxy Notice may only be revoked by delivering a notice in Writing given by or on behalf of the person by whom or on whose behalf the Proxy Notice was given to a Proxy Notification Address.
- 59.7. A notice revoking a proxy appointment only takes effect if it is delivered before:
- (a) the start of the meeting or adjourned meeting to which it relates (and the termination of the authority of a person to act as proxy does not affect whether that person counts in deciding whether there is a quorum at a meeting or adjourned meeting, the validity of anything that person does as Chairman of a Meeting or adjourned meeting or the validity of a poll demanded by that person at a meeting or adjourned meeting unless the Company receives notice of termination before the commencement of the meeting or adjourned meeting, as applicable); or
 - (b) (in the case of a poll not taken on the same day as the meeting or adjourned meeting) the time appointed for taking the poll to which it relates (and the termination of the authority of a person to act as proxy does not affect the validity of a vote given by that person unless the Company receives the notice of termination before the time appointed for taking the poll).

60 Proxy and Uncertificated Shares

- 60.1. The Directors may allow a proxy for a Holder of any Uncertificated Shares to be appointed by electronic means or by means of a website in the form of an uncertificated proxy instruction. The Directors may also allow any supplement to the uncertificated proxy instruction or any amendment or revocation of any uncertificated proxy instruction to be made by a further uncertificated proxy instruction.
- 60.2. The Directors may decide what method should be used to determine at what time the instruction or notification is treated as being received by the Company. The Directors may treat any notification purporting to or expressed to be sent on behalf of a Holder of an Uncertificated Share as sufficient evidence of the authority of the person sending the instruction to send it on behalf of that Holder.
- 60.3. For the purposes of this Article 60, an uncertificated proxy instruction is a properly authenticated dematerialised instruction and/or other instruction or notification, sent through a Relevant System to a participant in that system chosen by the Directors to act for the Company. The uncertificated proxy instruction may be in any form and subject to any terms and conditions that the Directors deem appropriate, but always subject to the facilities and requirements of the Relevant System.

61 Corporations acting by representatives

A corporation which is a Member of the Company may by resolution of its directors or other governing body authorise a person or persons to act as its representative or representatives at any meeting of the Company or at any separate general meeting of the Holders of any class of Shares. Such a corporation is for the purposes of these Articles deemed to be present in person at any meeting if a person or persons so authorised is or are present at it.

62 Amendments to resolutions

62.1. An Ordinary Resolution to be proposed at a general meeting may be amended by Ordinary Resolution if:

- (a) notice of the proposed amendment is given to the Company secretary in Writing by a person entitled to vote at the general meeting at which it is to be proposed not less than 48 hours before the meeting is to take place (or such later time as the Chairman of the Meeting may determine); and
- (b) the proposed amendment does not, in the reasonable opinion of the Chairman of the Meeting, materially alter the scope of the resolution.

62.2. A Special Resolution to be proposed at a general meeting may be amended by Ordinary Resolution, if:

- (a) the Chairman of the Meeting proposes the amendment at the general meeting at which the resolution is to be proposed; and
- (b) the amendment does not go beyond what is necessary to correct a grammatical or other non-substantive error in the resolution.

62.3. If the Chairman of the Meeting, acting in good faith, wrongly decides that an amendment to a resolution is out of order, the Chairman's error does not invalidate the vote on that resolution.

RESTRICTIONS ON MEMBERS' RIGHTS**63 No voting of Shares on which money owed to Company**

No voting rights attached to a Share may be exercised at any general meeting, at any adjournment of it, or on any poll called at or in relation to it, unless all amounts payable to the Company in respect of that Share have been Paid.

64 Class meetings

The provisions of the Articles relating to general meetings apply, with any necessary modifications, to meetings of the Holders of any class of Shares.

PART 4

**SHARES AND DISTRIBUTIONS
ISSUE OF SHARES**

65 Powers to issue different classes of Share

- 65.1. Subject to the Articles, but without prejudice to the rights attached to any existing Share, the Company may issue Shares with the rights and restrictions set out in the Articles and any other Shares with such rights or restrictions as may be determined by Ordinary Resolution (or failing such determination, as the Directors may determine).
- 65.2. The Company may issue Shares which are to be redeemed, or are liable to be redeemed at the option of the Company or the Holder, and the Directors may determine the terms, conditions and manner of redemption of any such Shares and must do so before the Shares are allotted.
- 65.3. Subject to the Articles and to any direction given by the Company in a general meeting, the Directors may allot, grant options over, or otherwise dispose of Shares to such persons (including the Directors themselves) at such times and on such terms as the Directors may think proper.

66 Payment of commissions on subscription for Shares

- 66.1. The Company may pay any person a commission in consideration for that person:
- (a) subscribing, or agreeing to subscribe, for Shares;
 - (b) procuring, or agreeing to procure, subscriptions for Shares;
 - (c) purchasing, or agreeing to purchase, treasury shares for cash; or
 - (d) procuring, or agreeing to procure, purchases of treasury shares for cash.
- 66.2. Any such commission may be Paid:
- (a) in cash, or in Fully Paid or Partly Paid Shares or other securities, or partly in one way and partly in the other; and
 - (b) in respect of a conditional or an absolute subscription.

INTERESTS IN SHARES

67 Company not bound by less than absolute interests

Except as required by law, no person is to be recognised by the Company as holding any Share upon any trust, and except as otherwise required by law or the Articles, the Company is not in any way to be bound by or recognise any interest in a Share other than the Holder's absolute ownership of it and all the rights attaching to it.

68 Renunciation

The Directors may at any time after the allotment of any Share but before any person has been entered into the register as the Holder recognise a renunciation of such allotment by the allottee in favour of some other person and may accord to any allottee of a Share a right to effect such renunciation upon and subject to such terms and conditions as the Directors may think fit to impose.

69 Rights attaching to Shares

69.1. Each Share is entitled to one vote per Share at a meeting of the Members of the Company.

VARIATION OF RIGHTS

70 Variation of rights

Whenever the capital of the Company is divided into different classes of Shares, the rights or privileges attached to any class may (unless otherwise provided by the terms of issue of the Shares of that class) be varied or abrogated, either whilst the Company is a going concern or during or in contemplation of a winding-up, either with the consent in Writing of the Holders of 75% in nominal value of the issued Shares of the class (excluding any Shares of that class held as treasury shares), or with the sanction of a Special Resolution passed at a separate general meeting of such Holders (but not otherwise).

SHARE CERTIFICATES

71 Certificates to be issued except in certain cases

71.1. The Company must issue each Member with one or more Certificates in respect of the Shares which that Member holds.

71.2. This Article does not apply to:

- (a) Uncertificated Shares;
- (b) Shares in respect of which a Share warrant has been issued;

- (c) Shares in respect of which the Company is not required by law to issue a Certificate; or
- 71.3. Except as otherwise specified in the Articles, all Certificates must be issued free of charge.
- 71.4. No Certificate may be issued in respect of Shares of more than one class.
- 71.5. If more than one person holds a Share, only one Certificate may be issued in respect of it.

72 Contents and execution of Share Certificates

- 72.1. Every Certificate must specify:
 - (a) in respect of how many Shares, of what class, it is issued;
 - (b) the nominal value of those Shares;
 - (c) the amount Paid up on them; and
 - (d) any distinguishing numbers assigned to them.
- 72.2. Certificates must: be executed in accordance with the Companies Acts.

73 Consolidated Share Certificates

- 73.1. When a Member's holding of Shares of a particular class increases, the Company may issue that Member with:
 - (a) a single, consolidated Certificate in respect of all the Shares of a particular class which that Member holds; or
 - (b) a separate Certificate in respect of only those Shares by which that Member's holding has increased.
- 73.2. When a Member's holding of Shares of a particular class is reduced, the Company must ensure that the Member is issued with one or more Certificates in respect of the number of Shares held by the Member after that reduction. But the Company need not (in the absence of a request from the Member) issue any new Certificate if:
 - (a) all the Shares which the Member no longer holds as a result of the reduction; and
 - (b) none of the Shares which the Member retains following the reduction, were, immediately before the reduction, represented by the same Certificate.
- 73.3. A Member may request the Company, in Writing, to replace:
 - (a) the Member's separate Certificates with a consolidated Certificate; or

- (b) the Member's consolidated Certificate with two or more separate Certificates representing such proportion of the Shares as the Member may specify.
- 73.4. When the Company complies with such a request it may charge such reasonable fee as the Directors may decide for doing so.
- 73.5. A consolidated Certificate must not be issued unless any Certificates which it is to replace have first been returned to the company secretary for cancellation.
- 74 Replacement Share Certificates**
- 74.1. If a Certificate issued in respect of a Member's Shares is:
 - (a) damaged or defaced; or
 - (b) said to be lost, stolen or destroyed,that Member is entitled to be issued with a replacement Certificate in respect of the same Shares.
- 74.2. A Member exercising the right to be issued with such a replacement Certificate:
 - (a) may at the same time exercise the right to be issued with a single Certificate or separate Certificates;
 - (b) must return the Certificate which is to be replaced to the Company if it is damaged or defaced; and
 - (c) must comply with such conditions as to evidence, indemnity and the payment of a reasonable fee as the Directors decide.

SHARES NOT HELD IN CERTIFIED FORM

- 75 Uncertificated Shares**
- 75.1. In this Article, the "**Relevant Rules**" means:
 - (a) any applicable provision of the Companies Acts about the holding, evidencing of title to, or transfer of Shares other than in Certificated form; and
 - (b) any applicable legislation, rules or other arrangements made under or by virtue of such provision.
- 75.2. The provisions of this Article have effect subject to the Relevant Rules.
- 75.3. Any provision of the Articles which is inconsistent with the Relevant Rules must be disregarded, to the extent that it is inconsistent, whenever the Relevant Rules apply.

- 75.4. Any Share or class of Shares of the Company may be issued or held on such terms, or in such a way, that:
- (a) title to it or them is not, or must not be, evidenced by a Certificate; or
 - (b) it or they may or must be transferred wholly or partly without a Certificate.
- 75.5. The Directors have power to take such steps as they think fit in relation to:
- (a) the evidencing of and transfer of title to Uncertificated Shares (including in connection with the issue of such Shares);
 - (b) any records relating to the holding of Uncertificated Shares;
 - (c) the conversion of Certificated Shares into Uncertificated Shares; or
 - (d) the conversion of Uncertificated Shares into Certificated Shares.
- 75.6. The Company may by notice to the Holder of a Share require that Share:
- (a) if it is Uncertificated, to be converted into Certificated form; and
 - (b) if it is Certificated, to be converted into Uncertificated form,
- to enable it to be dealt with in accordance with the Articles.
- 75.7. If:
- (a) the Articles give the Directors power to take action, or require other persons to take action, in order to sell, transfer or otherwise dispose of Shares; and
 - (b) Uncertificated Shares are subject to that power, but the power is expressed in terms which assume the use of a Certificate or other written Instrument,
- the Directors may take such action as is necessary or expedient to achieve the same results when exercising that power in relation to Uncertificated Shares.
- 75.8. In particular, the Directors may take such action as they consider appropriate to achieve the sale, transfer, disposal, forfeiture, re-allotment or surrender of an Uncertificated Share or otherwise to enforce a lien in respect of it.
- 75.9. Unless the Directors otherwise determine, Shares which a Member holds in Uncertificated form must be treated as separate holdings from any Shares which that Member holds in Certificated form.
- 75.10. A class of Shares must not be treated as two classes simply because some Shares of that class are held in Certificated form and others are held in Uncertificated form.

76 Share warrants

- 76.1. The Directors may issue a Share warrant in respect of any Fully Paid Share.
- 76.2. Share warrants must be:
- (a) issued in such form; and
 - (b) executed in such manner,
- as the Directors decide.
- 76.3. A Share represented by a Share warrant may be transferred by delivery of the warrant representing it.
- 76.4. The Directors may make provision for the payment of dividends in respect of any Share represented by a Share warrant.
- 76.5. Subject to the Articles, the Directors may decide the conditions on which any Share warrant is issued. In particular, they may:
- (a) decide the conditions on which new warrants are to be issued in place of warrants which are damaged or defaced, or said to have been lost, stolen or destroyed;
 - (b) decide the conditions on which bearers of warrants are entitled to attend and vote at general meetings;
 - (c) decide the conditions subject to which bearers of warrants may surrender their warrant so as to hold their Shares in Certificated or Uncertificated form instead; and
 - (d) vary the conditions of issue of any warrant from time to time,
- and the bearer of a warrant is subject to the conditions and procedures in force in relation to it, whether or not they were decided or specified before the warrant was issued.
- 76.6. Subject to the conditions on which the warrants are issued from time to time, bearers of Share warrants have the same rights and privileges as they would if their names had been included in the register as Holders of the Shares represented by their warrants.
- 76.7. The Company must not in any way be bound by or recognise any interest in a Share represented by a Share warrant other than the absolute right of the bearer of that warrant to that warrant.

PARTLY PAID SHARES

77 Company's Lien over Partly Paid Shares

- 77.1. The Company has a lien (the “**Company's Lien**”) over every Share which is Partly Paid for any part of:

-
- (a) that Share's nominal value; and
- (b) any premium at which it was issued,
- which has not been Paid to the Company, and which is payable immediately or at some time in the future, whether or not a Call Notice has been sent in respect of it.
- 77.2. The Company's Lien over a Share:
- (a) takes priority over any third party's interest in that Share; and
- (b) extends to any dividend or other money payable by the Company in respect of that Share and (if the lien is enforced and the Share is sold by the Company) the proceeds of sale of that Share.
- 77.3. The Directors may at any time decide that a Share which is or would otherwise be subject to the Company's Lien shall not be subject to it, either wholly or in part.
- 78 Enforcement of the Company's Lien**
- 78.1. Subject to the provisions of this Article, if:
- (a) a Lien Enforcement Notice has been given in respect of a Share; and
- (b) the person to whom the notice was given has failed to comply with it,
- the Company may sell that Share in such manner as the Directors decide.
- 78.2. A "**Lien Enforcement Notice**":
- (a) may only be given in respect of a Share which is subject to the Company's Lien, in respect of which a sum is payable and the due date for payment of that sum has passed;
- (b) must specify the Share concerned;
- (c) must require payment of the sum payable within fourteen (14) days of the notice;
- (d) must be addressed either to the Holder of the Share or to a person entitled to it by reason of the Holder's death, Bankruptcy or otherwise; and
- (e) must state the Company's intention to sell the Share if the notice is not complied with.
- 78.3. Where Shares are sold under this Article:
- (a) the Directors may authorise any person to execute an Instrument of transfer of the Shares to the purchaser or a person nominated by the purchaser; and

- (b) the transferee is not bound to see to the application of the consideration, and the transferee's title is not affected by any irregularity in or invalidity of the process leading to the sale.
- 78.4. The net proceeds of any such sale (after payment of the costs of sale and any other costs of enforcing the lien) must be applied:
- (a) *first*, in payment of so much of the sum for which the lien exists as was payable at the date of the Lien Enforcement Notice; and
- (b) *second*, to the Holder of the Shares at the time of the sale, but only after the Certificate for the Shares sold has been surrendered to the Company for cancellation or a suitable indemnity has been given for any lost Certificates, and subject to a lien equivalent to the Company's Lien over the Shares before the sale for any money payable in respect of the Shares after the date of the Lien Enforcement Notice.
- 78.5. A statutory declaration by a Director or the Company secretary that the declarant is a Director or the Company secretary and that a Share has been sold to satisfy the Company's Lien on a specified date:
- (a) is conclusive evidence of the facts stated in it as against all persons claiming to be entitled to the Share; and
- (b) subject to compliance with any other formalities of transfer required by the Articles or by law, constitutes a good title to the Share.
- 79 Call Notices**
- 79.1. Subject to the Articles and the terms on which Shares are allotted, the Directors may send a notice (a "**Call Notice**") to a Member requiring the Member to pay the Company a specified sum of money (a "**Call**") which is payable in respect of Shares (whether on account of the nominal value of the Shares or by way of premium) which that Member holds at the date when the Directors decide to send the Call Notice.
- 79.2. A Call Notice:
- (a) may not require a Member to pay a Call which exceeds the total sum unpaid on that Member's Shares (whether as to the Share's nominal value or any amount payable to the Company by way of premium);
- (b) must state when and how any Call to which it relates it is to be Paid; and
- (c) may permit or require the Call to be Paid by instalments.
- 79.3. A Member must comply with the requirements of a Call Notice, but no Member is obliged to pay any Call before 14 days have passed since the notice was sent.

- 79.4. Before the Company has received any Call due under a Call Notice the Directors may:
- (a) revoke it wholly or in part; or
 - (b) specify a later time for payment than is specified in the notice,
- by a further notice in Writing to the Member in respect of whose Shares the Call is made.

80 Liability to pay Calls

- 80.1. Liability to pay a Call is not extinguished or transferred by transferring the Shares in respect of which it is required to be Paid.
- 80.2. Joint Holders of a Share are jointly and severally liable to pay all Calls in respect of that Share.
- 80.3. Subject to the terms on which Shares are allotted, the Directors may, when issuing Shares, provide that Call Notices sent to the Holders of those Shares may require them:
- (a) to pay Calls which are not the same; or
 - (b) to pay Calls at different times.

81 When Call Notice need not be issued

- 81.1. A Call Notice need not be issued in respect of sums which are specified, in the terms on which a Share is issued, as being payable to the Company in respect of that Share (whether in respect of nominal value or premium):
- (a) on allotment;
 - (b) on the occurrence of a particular event; or
 - (c) on a date fixed by or in accordance with the terms of issue.
- 81.2. But if the due date for payment of such a sum has passed and it has not been Paid, the Holder of the Share concerned is treated in all respects as having failed to comply with a Call Notice in respect of that sum, and is liable to the same consequences as regards the payment of interest and forfeiture.

82 Failure to comply with Call Notice: automatic consequences

- 82.1. If a person is liable to pay a Call and fails to do so by the Call payment date:
- (a) the Directors may issue a notice of intended forfeiture to that person; and
 - (b) until the Call is Paid, that person must pay the Company interest on the Call from the Call payment date at the Relevant Rate together with all expenses that may have been incurred by the Company by reason of such non-payment.

- 82.2. For the purposes of this Article:
- (a) the “**Call Payment Date**” is the time when the Call Notice states that a Call is payable, unless the Directors give a notice specifying a later date, in which case the Call Payment Date is that later date; and
 - (b) the “**Relevant Rate**” is:
 - (i) the rate fixed by the terms on which the Share in respect of which the Call is due was allotted;
 - (ii) such other rate as was fixed in the Call Notice which required payment of the Call, or has otherwise been determined by the Directors; or
 - (iii) if no rate is fixed in either of these ways, five (5) per cent. per annum.
- 82.3. The Relevant Rate must not exceed by more than five (5) percentage points the base lending rate most recently set by the Monetary Policy Committee of the Bank of England in connection with its responsibilities under Part 2 of the Bank of England Act 1998.
- 82.4. The Directors may waive any obligation to pay interest on or expenses in respect of a Call wholly or in part.

83 Notice of intended forfeiture

A notice of intended forfeiture:

- (a) may be sent in respect of any Share in respect of which a Call has not been Paid as required by a Call Notice;
- (b) must be sent to the Holder of that Share or to a person entitled to it by reason of the Holder’s death, Bankruptcy or otherwise;
- (c) must require payment of the Call and any accrued interest by a date which is not less than fourteen (14) days after the date of the notice;
- (d) must state how the payment is to be made; and
- (e) must state that if the notice is not complied with, the Shares in respect of which the Call is payable will be liable to be forfeited.

84 Directors’ power to forfeit Shares

If a notice of intended forfeiture is not complied with before the date by which payment of the Call is required in the notice of intended forfeiture, the Directors may decide that any Share in respect of which it was given is forfeited, and the forfeiture is to include all dividends or other moneys payable in respect of the forfeited Shares and not Paid before the forfeiture.

85 Effect of forfeiture

85.1. Subject to the Articles, the forfeiture of a Share extinguishes:

- (a) all interests in that Share, and all claims and demands against the Company in respect of it; and
- (b) all other rights and liabilities incidental to the Share as between the person whose Share it was prior to the forfeiture and the Company.

85.2. Any Share which is forfeited in accordance with the Articles:

- (a) is deemed to have been forfeited when the Directors decide that it is forfeited;
- (b) is deemed to be the property of the Company; and
- (c) may be sold, re-allotted or otherwise disposed of upon such terms and in such manner as the Board shall decide either to the person who was before the forfeiture the holder of the Share or to any other person and whether with or without all or any part of the amount previously Paid up on the Share being credited as so Paid up,

provided that any Share not disposed of in accordance with this Article 85.2 within a period of 3 years from the date of forfeiture shall, at the expiry of that period, be cancelled in accordance with the provisions of the Companies Acts and any other applicable laws.

85.3. If a person's Shares have been forfeited:

- (a) the Company must send that person notice that forfeiture has occurred and record it in the register of Members;
- (b) that person ceases to be a Member in respect of those Shares;
- (c) that person must surrender the Certificate for the Shares forfeited to the Company for cancellation;
- (d) that person remains liable to the Company for all sums payable by that person under the Articles at the date of forfeiture in respect of those Shares, including any interest and expenses (whether accrued before or after the date of forfeiture) and that person shall remain liable to satisfy all (if any) of the claims and demands which the Company might have enforced in respect of the time of the forfeiture without any reduction or allowance for the value of the Shares at the time of forfeiture or for any consideration received on this disposal, but that person's liability shall cease if and when the Company shall have received payment in full of all such moneys in respect of the Shares; and

- (e) the Directors may waive payment of such sums wholly or in part or enforce payment without any allowance for the value of the Shares at the time of forfeiture or for any consideration received on their disposal.
- 85.4. At any time before the Company disposes of a forfeited Share, the Directors may decide to cancel the forfeiture on payment of all Calls and interest due in respect of it and on such other terms as they think fit.
- 86 Procedure following forfeiture**
- 86.1. If a forfeited Share is to be disposed of by being transferred, the Company may receive the consideration for the transfer and the Directors may authorise any person to execute the Instrument of transfer.
- 86.2. A statutory declaration by a Director or the Company secretary that the declarant is a Director or the Company secretary and that a Share has been forfeited on a specified date:
- (a) is conclusive evidence of the facts stated in it as against all persons claiming to be entitled to the Share, and
- (b) subject to compliance with any other formalities of transfer required by the Articles or by law, constitutes a good title to the Share.
- 86.3. A person to whom a forfeited Share is transferred is not bound to see to the application of the consideration (if any) nor is that person's title to the Share affected by any irregularity in or invalidity of the process leading to the forfeiture or transfer of the Share.
- 86.4. If the Company sells a forfeited Share, the person who held it prior to its forfeiture is entitled to receive from the Company the proceeds of such sale, net of any commission, and excluding any amount which:
- (a) was, or would have become, payable; and
- (b) had not, when that Share was forfeited, been Paid by that person in respect of that Share,
- but no interest is payable to such a person in respect of such proceeds and the Company is not required to account for any money earned on them.
- 86.5. The forfeiture of a Share shall involve the extinction at the time of the forfeiture or surrender of all interest in and all claims and demands against the Company in respect of the Share and all other rights and liabilities incidental to the Share as between the holder whose Share is forfeited or surrendered and the Company, except only such of those rights and liabilities as are by the Articles expressly saved, or as are by the Companies Act and any other applicable laws given or imposed in the case of past Members.

87 Surrender of Shares

- 87.1. A Member may surrender any Share:
- (a) in respect of which the Directors may issue a notice of intended forfeiture;
 - (b) which the Directors may forfeit; or
 - (c) which has been forfeited.
- 87.2. The Directors may accept the surrender of any such Share.
- 87.3. The effect of surrender on a Share is the same as the effect of forfeiture on that Share.
- 87.4. A Share which has been surrendered may be dealt with in the same way as a Share which has been forfeited.

88 Power to sell Shares of untraced Members

- 88.1. The Company shall be entitled to sell at the best price reasonably obtainable any Share of a Member or any Share to which a person is entitled by transmission if and provided that:
- (a) during a period of 12 years (provided that in that period at least three dividends, whether interim or final, shall have been declared and paid) no cheque or warrant sent by the Company to the Member or person entitled by transmission in the manner authorised by these Articles has been cashed and no communication has been received by the Company from the Member or person entitled by transmission;
 - (b) the Company has at the expiration of that period given notice by advertisement in both a national newspaper and a newspaper circulating in the area in which the last known address of the Member or the address at which service of notices may be effected in the manner authorised by these Articles is located of its intention to sell such Share; and
 - (c) the Company has not during the further period of three months after the date of the advertisement (or, if published on different dates, the later of the two advertisements) and prior to the date of sale received any communication from the Member or person entitled by transmission.
- 88.2. To give effect to the sale of any Share pursuant to Article 88.1, the Company may appoint any person to execute as transferor any necessary Instrument of transfer of such Share and such Instrument of transfer shall be as effective as if it had been executed by the holder or person entitled by transmission to the Share. The transferee shall not be bound to see to the application of the purchase moneys nor shall his title to the Shares be affected by any irregularity or invalidity in the proceedings relating to the sale. The net proceeds of sale shall belong to the Company and on receipt the Company shall be indebted to the Member or other person entitled to such Share for an amount equal to the

net proceeds of such sale but no trust shall be created and no interest shall be payable in respect of the proceeds of sale which may either be employed in the business of the Company or invested in such investment (other than Shares of the Company or its holding company, if any) as the Directors may from time to time think fit.

TRANSFER AND TRANSMISSION OF SHARES

89 Transfers of Shares

- 89.1. Shares may be transferred by means of an Instrument of transfer in any usual form or any other form approved by the Directors or the Articles, which is executed by or on behalf of:
- (a) the transferor; and
 - (b) (if any of the Shares is Partly Paid) the transferee.
- 89.2. No fee may be charged for registering any Instrument of transfer or other Document relating to or affecting the title to any Share.
- 89.3. The Company may retain any Instrument of transfer which is registered.
- 89.4. The transferor remains the Holder of a Share until the transferee's name is entered in the register of Members as Holder of it.
- 89.5. The Directors may refuse to register the transfer of a Share if:
- (a) the Share is not Fully Paid;
 - (b) the transfer is not lodged at the Company's registered office or such other place as the Directors have appointed;
 - (c) the transfer is not accompanied by the Certificate for the Shares to which it relates, or such other evidence as the Directors may reasonably require to show the transferor's right to make the transfer, or evidence of the right of someone other than the transferor to make the transfer on the transferor's behalf;
 - (d) the transfer is in respect of more than one class of Share; or
 - (e) the transfer is in favour of more than four transferees.
- 89.6. If the Directors refuse to register the transfer of a Share, the Instrument of transfer must be returned to the transferee with the notice of refusal unless they suspect that the proposed transfer may be fraudulent.

90 Transfer of Uncertificated Shares

- 90.1. A transfer of an Uncertificated Share must not be registered if it is in favour of more than four transferees.

91 Transmission of Shares

- 91.1. If title to a Share passes to a Transmittree, the Company may only recognise the Transmittree as having any title to that Share.
- 91.2. Nothing in these Articles releases the estate of a deceased Member from any liability in respect of a Share solely or jointly held by that Member.

92 Transmittrees' rights

- 92.1. A Transmittree who produces such evidence of entitlement to Shares as the Directors may properly require:
- (a) may, subject to the Articles, choose either to become the Holder of those Shares or to have them transferred to another person; and
- (b) subject to the Articles, and pending any transfer of the Shares to another person, has the same rights as the Holder had.
- 92.2. But Transmittrees do not have the right to attend or vote at a general meeting in respect of Shares to which they are entitled, by reason of the Holder's death or Bankruptcy or otherwise, unless they become the Holders of those Shares.

93 Exercise of Transmittrees' rights

- 93.1. Transmittrees who wish to become the Holders of Shares to which they have become entitled must notify the Company in Writing of that wish.
- 93.2. If the Share is a Certificated Share and a Transmittree wishes to have it transferred to another person, the Transmittree must execute an Instrument of transfer in respect of it.
- 93.3. If the Share is an Uncertificated Share and the Transmittree wishes to have it transferred to another person, the Transmittree must:
- (a) procure that all appropriate instructions are given to effect the transfer; or
- (b) procure that the Uncertificated Share is changed into Certificated form and then execute an Instrument of transfer in respect of it.
- 93.4. Any transfer made or executed under this Article is to be treated as if it were made or executed by the person from whom the Transmittree has derived rights in respect of the Share, and as if the event which gave rise to the transmission had not occurred.

94 Transmittrees bound by prior notices

If a notice is given to a Member in respect of Shares and a Transmittree is entitled to those Shares, the Transmittree is bound by the notice if it was given to the Member before the Transmittree's name has been entered in the register of Members.

95.1. If any Member, or any other person appearing to be interested in Shares held by such Member, has been duly served with a notice under section 793 of the Companies Act 2006 and is in default for the prescribed period in supplying to the Company the information thereby required, then at any time after that the Directors may in their absolute discretion by notice to such Member or such other person direct:

- (a) that in respect of the Default Shares, the Member shall not be entitled to vote either personally or by proxy at a general meeting of the Company or a meeting of the holders of any class of Shares of the Company or to exercise any other right conferred by membership in relation to general meetings of the Company or meetings of the holders of any class of Shares of the Company; and/or
- (b) where the Default Shares represent at least 0.25 per cent of the issued Shares of any class of Shares of the Company (excluding any Shares of that class held as treasury shares), that:
 - (i) any dividend or other money which would otherwise be payable in respect of the Default Shares shall (in whole or any part thereof) be retained by the Company without any liability to pay interest thereon when such money is finally paid to the Member and, in circumstances where an option to elect to receive Ordinary Shares instead of cash in respect of any dividend shall be or has been given to Members, any notice of election made under such an option in respect of the Default Shares shall not be effective; and/or
 - (ii) no transfer, other than an approved transfer, of any of the Shares held by such Member shall be registered unless (A) the Member is not himself in default as regards supplying the information required, and (B) the transfer is of part only of the Member's holding and, when presented for registration, is accompanied by a certificate from the Member, in a form satisfactory to the Directors, to the effect that after due and careful enquiry the Member is satisfied that none of the Shares the subject of the transfer are Default Shares; and/or
 - (iii) any Shares held by such Member in Uncertificated form shall forthwith be converted in a Certificated form (and the Directors shall be entitled to direct the operator of any Relevant System applicable to those Shares to effect that conversion immediately) and that Member shall not after that be entitled to convert all or any Shares held by him in Uncertificated form (except with the authority of the Directors) unless (A) the Member is not himself in default as regards supplying the information required, and (B) the Shares which the Member wishes to convert are part only of his holding and he has issued a certificate, in a form satisfactory to the Directors, to the effect that after due and careful enquiry the Member is satisfied that none of the Shares he is proposing to convert into Uncertificated form are Default Shares.

- 95.2. The Company shall send to each other person appearing to be interested in the Shares the subject of any Direction Notice a copy of the notice, but the failure or omission by the Company to do so shall not invalidate such notice. Neither the Company nor the Directors shall in any event be liable to any person as a result of the Directors having imposed any restrictions pursuant to Article 95.1 if the Directors have acted in good faith.
- 95.3. Any Direction Notice shall have effect in accordance with its terms until seven days (or such shorter period as the Directors may resolve) after the earlier of the date on which:
- (a) the Company is satisfied that the default in respect of which the Direction Notice was issued has been rectified; and
 - (b) notification shall be received by the Company that the Default Shares shall have been transferred to a third party by means of an approved transfer.
- 95.4. The Directors may at any time give notice cancelling a Direction Notice, in whole or in part, or suspending, in whole or in part, the imposition of any restrictions contained in the Direction Notice for a given period. If dividends or other moneys payable in respect of any Default Shares shall be withheld as a result of any restrictions imposed by a Direction Notice, such dividends or other money shall accrue and shall be payable (without interest) upon the relevant restrictions ceasing to apply.
- 95.5. For the purposes of this Article 95:
- (a) **“Default Shares”** means Shares in relation to which a default has occurred entitling the Company to issue a Direction Notice and any further Shares which are issued in respect of those Shares;
 - (b) a **“Direction Notice”** means a notice issued by the Company pursuant to Article 95.1;
 - (c) a person shall be treated as appearing to be interested in any Shares if the Member holding such Shares or any other person has given to the Company information under section 793 of the Companies Act 2006 which either names such person as being so interested, or fails to establish the identities of those interested in the Shares and (after taking into account the said information and any other information given under section 793 of the Companies Act 2006) the Company knows or has reasonable cause to believe that the person in question is or may be interested in the Shares;
 - (d) **“interested”** shall be construed as it is for the purpose of section 793 of the Companies Act 2006;
 - (e) the prescribed period is fourteen days from the date of service of the notice under section 793 of the Companies Act 2006;

- (f) a transfer of Shares is an approved transfer if and only if:
 - (i) it is a transfer of Shares to an offeror by way or in pursuance of acceptance of a takeover offer for the Company;
 - (ii) the Directors are satisfied that the transfer is made pursuant to a bona fide sale of the whole of the beneficial ownership of the Shares to a party unconnected with the Member or with other persons appearing to be interested in such Shares; or
 - (iii) the transfer results from a sale made through a recognised investment exchange as defined in the Financial Services and Markets Act 2000 or any other stock exchange outside the United Kingdom on which the Company's Shares are normally traded; and
- (g) reference to a person being in default in supplying to the Company the information required by a notice under the said section 793 of the Companies Act 2006 includes:
 - (i) reference to his having failed or refused to give all or any part of it; and
 - (ii) reference to his having given information which he knows to be false in a material particular or having recklessly given information which is false in a material particular.

95.6. Nothing in this Article 95 shall limit the powers of the Company under section 794 of the Companies Act 2006 or any other powers whatsoever.

CONSOLIDATION AND SUBDIVISION OF SHARES

96 Procedure for disposing of fractions of Shares

96.1. This Article applies where:

- (a) there has been a consolidation or division of Shares, and
- (b) as a result, Members are entitled to fractions of Shares.

96.2. The Directors may deal with such fractions as they think fit and in particular (but without prejudice to the foregoing):

- (a) sell the Shares representing the fractions to any person including the Company for the best price reasonably obtainable;
- (b) in the case of a Certificated Share, authorise any person to execute an Instrument of transfer of the Shares to the purchaser or a person nominated by the purchaser; and

- (c) distribute the net proceeds of sale in due proportion among the Holders of the Shares.
- 96.3. Where any Holder's entitlement to a portion of the proceeds of sale amounts to less than a minimum figure determined by the Directors, that Member's portion may be distributed to an organisation which is a charity for the purposes of the law of England and Wales, Scotland or Northern Ireland.
- 96.4. The person to whom the Shares are transferred is not obliged to ensure that any purchase money is received by the person entitled to the relevant fractions.
- 96.5. The transferee's title to the Shares is not affected by any irregularity in or invalidity of the process leading to their sale.
- 96.6. The Directors may, without prejudice to Article 96.2 and subject to the Companies Acts and any other applicable laws, in each case where the number of Shares held by the Holder is not an exact multiple of the number of Shares to be consolidated into a single Share, issue to such Holder credited as Fully Paid by way of capitalisation the minimum number of Shares required to round up his holdings to a multiple (such issue being deemed to have been effected immediately prior to consolidation) and the amount required to pay up such Shares shall be appropriated at its discretion from any sums standing to the credit of any of the Company's reserve accounts (including, subject to the Companies Act 2006, share premium account and capital redemption reserve) or to the credit of the profit and loss account and capitalised by applying the same in paying up such Shares.

DISTRIBUTIONS

97 Procedure for declaring dividends

- 97.1. The Company may by Ordinary Resolution declare dividends and may fix the time for payment of such dividend, and the Directors may decide to pay interim dividends as appear to the Board to be justified by the financial position of the Company. For the avoidance of doubt, no dividend shall be payable to the Company itself in respect of any Shares held by it as treasury shares (except to the extent permitted by the Companies Acts or any other provision of law).
- 97.2. A dividend must not be declared unless the Directors have made a recommendation as to its amount. Such a dividend must not exceed the amount recommended by the Directors.
- 97.3. No dividend may be declared or Paid unless it is in accordance with Members' respective rights.
- 97.4. If the Company's Share capital is divided into different classes, no interim dividend may be Paid on Shares carrying deferred or non-preferred rights if, at the time of payment, any preferential dividend is in arrears.

- 97.5. The Directors may pay at intervals any dividend payable at a fixed rate if it appears to them that the profits available for distribution justify the payment.
- 97.6. If the Directors act in good faith, they do not incur any liability to the Holders of Shares conferring preferred rights for any loss they may suffer by the lawful payment of an interim dividend on Shares with deferred or non-preferred rights.

98 Currency of dividends

Dividends may be declared or paid in any currency and the Directors may decide the rate of exchange for any currency conversions that may be required, and how any costs involved are to be met, in relation to the currency of any dividend.

99 Calculation of dividends

- 99.1. Except as otherwise provided by the Articles, by Members' resolution, the Directors' decision to pay a dividend, the rights attached to, or the terms of issue of any Shares, all dividends must be apportioned and Paid proportionately to the amounts Paid up on the Shares in respect of which the dividend is paid during any portion or portions of the period in respect of which the dividend is Paid.
- 99.2. If any Share is issued on terms providing that it ranks for dividend as from a particular date, that Share ranks for dividend accordingly.
- 99.3. For the purposes of calculating dividends, no account is to be taken of any amount which has been Paid up on a Share in advance of the due date for payment of that amount.

100 Payment of dividends and other distributions

- 100.1. Where a dividend or other sum which is a distribution is payable in respect of a Share, it must be Paid by one or more of the following means:
- (a) transfer to a bank or building society account specified by the Distribution Recipient either in Writing or as the Directors may otherwise decide;
 - (b) sending a cheque made payable to the Distribution Recipient by post to the Distribution Recipient at the Distribution Recipient's registered address (if the Distribution Recipient is a Holder of the Share), or (in any other case) to an address specified by the Distribution Recipient either in Writing or as the Directors may otherwise decide;
 - (c) sending a cheque made payable to such person by post to such person at such address as the Distribution Recipient has specified either in Writing or as the Directors may otherwise decide;
 - (d) in relation to any dividend or other sum payable in respect of Shares held in Uncertificated form, by means of a Relevant System; or

- (e) any other means of payment as the Directors agree with the Distribution Recipient either in Writing or by such other means as the Directors decide,

and subject always, in the case of Shares held in Uncertificated form, to the facilities and requirements of the Relevant System concerned where payment is to be made by means of such system.

100.2. In the Articles, the “**Distribution Recipient**” means, in respect of a Share in respect of which a dividend or other sum is payable:

- (a) the Holder of the Share;
- (b) if the Share has two or more joint Holders, whichever of them is named first in the register of Members; or
- (c) if the Holder is no longer entitled to the Share by reason of death or Bankruptcy, or otherwise by operation of law, the Transmitttee.

101 Uncashed dividends and other distributions

The Company may cease to send any cheque or warrant through the post or may stop the transfer of any sum by any bank or other funds transfer system or may stop any other means of payment, as the case may be, for any dividend payable on any Shares which is normally paid in that manner on those Shares if either in respect of at least two consecutive dividends payable on those Shares the cheques or warrants have been returned undelivered or remain uncashed or the transfer of other means of payment has failed or in respect of one dividend payable on those Shares the cheques or warrants have been returned undelivered or remain uncashed or the transfer or other means of payment has failed and reasonably enquiries made by the Company have failed to establish any new address of the Holder of those Shares but, subject to the provisions of these Articles, the Company shall recommence sending cheques or warrants or transferring funds or using the other means of payment, as the case may be, in respect of dividends payable on those Shares if the Holder or person entitled by transmission claims the arrears of the dividend in which event the Company shall resume payment of dividend (and arrears) as notified by the claimant or, in the absence of such notification, in the same manner in which payment was effected prior to the suspension of the payment of dividend. If any such cheque, warrant or order has or is alleged to have been lost, stolen or destroyed, the Directors may, on request of the person entitled to it, issue a replacement cheque, warrant or order subject to compliance with such conditions as to evidence and indemnity and the payment of out of pocket expenses of the Company in connection with the request as the Directors may think fit.

102 Deductions from distributions in respect of sums owed to the Company

102.1. If:

- (a) a Share is subject to the Company’s Lien; and

- (b) the Directors are entitled to issue a Lien Enforcement Notice in respect of it, they may, instead of issuing a Lien Enforcement Notice, deduct from any dividend or other sum payable in respect of the Share any sum of money which is payable to the Company in respect of that Share to the extent that they are entitled to require payment under a Lien Enforcement Notice.
- 102.2. Money so deducted must be used to pay any of the sums payable in respect of that Share.
- 102.3. The Company must notify the Distribution Recipient in Writing of:
- (a) the fact and amount of any such deduction;
- (b) any non-payment of a dividend or other sum payable in respect of a Share resulting from any such deduction; and
- (c) how the money deducted has been applied.
- 103 No interest on distributions**
- 103.1. The Company may not pay interest on any dividend or other sum payable in respect of a Share unless otherwise provided by:
- (a) the rights attached to the Share; or
- (b) the provisions of another agreement between the Holder of that Share and the Company.
- 104 Unclaimed distributions**
- 104.1. All dividends or other sums which are:
- (a) payable in respect of Shares; and
- (b) unclaimed after having been declared or become payable, may be invested or otherwise made use of by the Directors for the benefit of the Company until claimed.
- 104.2. The payment of any such dividend or other sum into a separate account does not make the Company a trustee in respect of it.
- 104.3. If:
- (a) twelve (12) years have passed from the date on which a dividend or other sum became due for payment; and
- (b) the Distribution Recipient has not claimed it, the Distribution Recipient is no longer entitled to that dividend or other sum and it ceases to remain owing by the Company.

105 Non-cash distributions

- 105.1. Subject to the terms of issue of the Share in question, the Company may, by Ordinary Resolution on the recommendation of the Directors, decide to pay all or part of a dividend or other distribution payable in respect of a Share by transferring non-cash assets of equivalent value (including, without limitation, Shares or other securities in any company).
- 105.2. If the Shares in respect of which such a non-cash distribution is Paid are Uncertificated, any Shares in the Company which are issued as a non-cash distribution in respect of them must be Uncertificated.
- 105.3. For the purposes of paying a non-cash distribution, the Directors may make whatever arrangements they think fit, including, where any difficulty arises regarding the distribution:
- (a) fixing the value of any assets;
 - (b) paying cash to any Distribution Recipient on the basis of that value in order to adjust the rights of recipients; and
 - (c) vesting any assets in trustees.

106 Waiver of distributions

- 106.1. Distribution Recipients may waive their entitlement to a dividend or other distribution payable in respect of a Share by giving the Company notice in Writing to that effect, but if:
- (a) the Share has more than one Holder; or
 - (b) more than one person is entitled to the Share, whether by reason of the death or Bankruptcy of one or more joint Holders, or otherwise,
- the notice is not effective unless it is expressed to be given, and signed, by all the Holders or persons otherwise entitled to the Share.

107 Record dates

- 107.1. All dividends and interest shall belong and be paid (subject to any Company's Lien) to those Members whose names shall be on the register at the Record Date despite any subsequent transfer or transmission of Shares.

107.2. Subject to any provision of the Companies Acts or any other provision of law, the “**Record Date**” is such date specified by the Company or the Directors by resolution as the date at the close of business (or such other time as the Directors may determine) on which persons registered as the Holders of Shares shall be entitled to receipt of any dividend, distribution, allotment, issue, notice, information, Document or circular and such record date may be on or before the date the same is made, paid or despatched or (in the case of any dividend, interest, allotment or issue) after the date on which the same is recommended, resolved, declared or announced but without prejudice to the rights inter se in respect of the same of the transferors and transferees of any such Shares.

108 Return of capital

108.1. If the Company is in liquidation, the liquidator may, if they are so authorised by a Special Resolution of the Members of the Company and any other authority required by any applicable statutory provision:

- (a) divide among the Holder(s) of the Shares (excluding the Company itself to the extent that it is a Member by virtue only of its holding any Shares as treasury Shares) in specie or in kind the whole or any part of the assets of the Company whether or not the assets shall consist of property of one kind or shall consist of properties of different kinds and may for such purpose set such value as the liquidator deems fair upon any one or more class or classes of property and may determine how such division shall be carried out as between the Members or different classes of Members; or
- (b) vest the whole or any part of the assets in trustees upon such trusts for the benefit of the Holder(s) of the Shares as the liquidator determines, and the liquidation of the Company may be closed and the Company dissolved, provided that no Member shall be compelled to accept any assets upon which there is any liability.

109 Distribution of Shares or other consideration on a transfer or sale

A Special Resolution sanctioning a transfer or sale to another company duly passed pursuant to section 110 of the Insolvency Act 1986 may authorise the distribution of any Shares or other consideration receivable by the liquidator among the Members (whether or not in accordance with the existing rights of Members) and any such distribution shall be binding on all Members subject to the right of dissent and consequential rights conferred by section 111 of the Insolvency Act 1986.

110 Scrip dividends

With the prior approval of an Ordinary Resolution of the Company passed at any general meeting, the Directors may, in respect of any dividend specified by the Ordinary Resolution, offer any Holders of Ordinary Shares (excluding, for the avoidance of doubt, the Company itself to the extent that it is such a Holder by virtue only of its holding any Shares as treasury shares) the right to elect to receive in lieu of that dividend (or part of any of that dividend) an allotment of Ordinary Shares credited as Fully Paid. In any such case, the following provisions shall apply:

- (a) the Ordinary Resolution may authorise the Directors to make such offer in respect of a particular dividend (whether or not already declared or recommended) and/or in respect of all or any dividends declared, proposed to be paid or made within a period specified by that Ordinary Resolution;
- (b) the basis of allotment shall be determined by the Directors so that the value (calculated at the Relevant Price) of the additional Ordinary Shares each holder of Ordinary Shares who elects to receive the same shall be allotted in lieu of any amount of dividend shall equal as nearly as possible the net cash amount of the dividend that such holder elects to forgo and may (with the sanction of a Special Resolution) exceed such amount. For the purposes of this Article 110, the “**Relevant Price**” of an Ordinary Share shall be equal to the average middle market quotation for the Ordinary Shares as derived from the Daily Official List of London Stock Exchange, or the middle-market quotation of American Depositary Shares in Nasdaq (adjusted as the Directors shall determine to reflect the number of Ordinary Shares represented by each American Depositary Share), on such five consecutive dealing days as the Directors shall determine, provided the first of such days shall be on or after the day on which such Ordinary Shares are first quoted “ex” the relevant dividend, or shall be calculated in such other manner as the Directors may determine and is set out in the announcement of the availability of the election in respect of the relevant dividend. A certificate or report by the auditors of the Company as to the amount of the Relevant Price in respect of any dividend shall be conclusive evidence of that amount and in giving such a certificate or report, the auditors of the Company may rely on advice or information from brokers or other sources of information as they think fit;
- (c) if the Directors determine to allow such right of election on any occasion, they shall give notice in Writing to the holders of Ordinary Shares of the right of election offered to them and shall specify the procedure to be followed (which, for the avoidance of doubt, may include an election by means of a Relevant System). The Directors may also establish or vary a procedure for election mandates under which shareholders may elect to receive Ordinary Shares instead of cash both in respect of the relevant dividend and (until they notify the Company that such mandate is revoked) in respect of future dividends not yet declared or resolved (and, accordingly, in respect of which the basis of allotment shall not have been determined) and the Directors may include in the procedure the right to make and revoke such election by means of a Relevant System;
- (d) the dividend (or that part of the dividend in respect of which a right of election has been offered) shall not be payable in cash on Ordinary Shares in respect of which the share election has been duly exercised (for the purposes of this Article 110, the “**Elected Ordinary Shares**”), and in the place of that dividend, additional Shares (subject to paragraph (e)) shall be allotted to the holders of the Elected Ordinary Shares on the basis of allotment determined as already described. For this purpose, the Directors shall capitalise, out of such of the sums standing to the credit of any reserve (including any share premium account or capital redemption reserve and/or profit and loss account) as the Directors may

determine, whether or not the same is available for distribution, a sum equal to the aggregate nominal amount of additional Ordinary Shares to be allotted on such basis and shall apply the same in paying up in full the appropriate number of Ordinary Shares for allotment and distribution to and amongst the holders of the Elected Ordinary Shares on such basis;

- (e) no fraction of any Share shall be allotted. The Directors may make provisions as they think fit for any fractional entitlements including provisions whereby, in whole or in part, the benefit of any fractions accrues to the Company and/or under which fractional entitlements are accrued and/or retained and in each case accumulated on behalf of any shareholder and such accruals or retentions are applied to the allotment by way of bonus to or cash subscription on behalf of such shareholder of Fully Paid Shares and/or provisions whereby cash payments may be made to Members in respect of their fractional entitlements;
- (f) the additional Ordinary Shares so allotted shall rank *pari passu* in all respects with the Fully Paid Ordinary Shares then in issue, save only as regards participation in the relevant dividend;
- (g) Article 111 shall apply (*mutatis mutandis*) to any capitalisation made pursuant to this Article;
- (h) the Directors may on any occasion determine that rights of election shall not be made available in respect of Ordinary Shares represented by depositary receipts or to any holders of Ordinary Shares with registered addresses in any territory where in the absence of a registration statement or other special formalities the circulation of an offer of rights of election would or might be unlawful, undesirable or impracticable and in such event the provisions of this Article shall be read and construed subject to such determination;
- (i) in relation to any particular proposed dividend, the Directors may in their absolute discretion amend, suspend or withdraw the offer previously made to holders of Ordinary Shares to elect to receive additional Ordinary Shares in lieu of the cash dividend (or any part of it) at any time prior to the allotment of the additional Ordinary Shares; and
- (j) unless the Directors otherwise determine, or unless the Regulations and/or the rules of the Relevant System concerned otherwise require, the new Ordinary Share(s) which a shareholder has elected to receive instead of cash in respect of the whole (or some part) of the specified dividend declared in respect of his Elected Ordinary Shares shall be Uncertificated (in respect of the shareholder's Elected Ordinary Shares which were in Uncertificated form on the date of his election) and Certificated (in respect of the shareholder's Elected Ordinary Shares which were Certificated on the date of his election).

111 Authority to capitalise and appropriation of Capitalised Sums

111.1. Subject to the Articles, the Directors may, if they are so authorised by an Ordinary Resolution:

- (a) decide to capitalise any profits of the Company (whether or not they are available for distribution) which are not required for paying a preferential dividend, or any sum standing to the credit of the Company's Share premium account or capital redemption reserve; and
- (b) appropriate any sum which they so decide to capitalise (a "**Capitalised Sum**") to the persons who would have been entitled to it if it were distributed by way of dividend (the "**Persons Entitled**") and in the same proportions.

111.2. Capitalised Sums must be applied:

- (a) on behalf of the Persons Entitled; and
- (b) in the same proportions as a dividend would have been distributed to them.

111.3. Any Capitalised Sum may be applied in paying up new Shares of a nominal amount equal to the Capitalised Sum which are then allotted credited as Fully Paid to the Persons Entitled or as they may direct.

111.4. A Capitalised Sum may be applied:

- (a) in or towards paying up any amounts unpaid on existing Shares held by the Persons Entitled; or
- (b) in paying up new debentures of the Company which are then allotted credited as Fully Paid to the Persons Entitled or as they may direct.

111.5. Subject to the Articles the Directors may:

- (a) apply Capitalised Sums in accordance with Articles 111.3 and 111.4 partly in one way and partly in another;
- (b) make such arrangements as they think fit to deal with Shares or debentures becoming distributable in fractions under this Article (including the issuing of fractional Certificates or the making of cash payments); and
- (c) authorise any person to enter into an agreement with the Company on behalf of all the Persons Entitled which is binding on them in respect of the allotment of Shares and debentures to them under this Article.

**MISCELLANEOUS PROVISIONS
COMMUNICATIONS**

112 Means of communication to be used

- 112.1. Subject to the Articles, anything sent or supplied by or to the Company under the Articles may be sent or supplied in any way in which the Companies Act 2006 provides for Documents, information or notices which are authorised or required by any provision of that Act to be sent or supplied by or to the Company.
- 112.2. Subject to the Articles, any notice or Document to be sent or supplied to a Director in connection with the taking of decisions by Directors may also be sent or supplied by the means by which that Director has asked to be sent or supplied with such notices or Documents for the time being.
- 112.3. Subject to the Articles, a Director may agree with the Company that notices or Documents sent to that Director in a particular way are to be deemed to have been received within a specified time of their being sent, and for the specified time to be less than 48 hours.

113 Hard Copy Form

Any Document, information or notice is validly sent or supplied by the Company in Hard Copy Form if it is handed to the intended recipient or sent or supplied by hand or through the post in a prepaid envelope:

- (a) to an address specified for the purpose by the intended recipient;
- (b) if the intended recipient is a company, to its registered office;
- (c) to the address shown in the Company's register of Members;
- (d) to any address to which any provision of the Companies Acts authorises it to be sent or supplied; or
- (e) if the Company is unable to obtain an address falling within paragraphs (a) to (d), to the last address known to the Company of the intended recipient.

114 Electronic form

Any Document, information or notice is validly sent or supplied by the Company in Electronic Form:

- (a) to a person if that person has agreed (generally or specifically) that the Document, information or notice may be sent or supplied in that form and has not revoked that agreement; or

- (b) to a company that is deemed to have so agreed by the Companies Acts.

115 Electronic means

Any Document, information or notice is validly sent or supplied by the Company by electronic means if it is sent or supplied:

- (a) to an address specified for the purpose by the intended recipient (generally or specifically); or
- (b) where the intended recipient is a company, to an address deemed by the Companies Acts to have been so specified.

116 Website

Any Document, information or notice is validly sent or supplied by the Company to a person by being made available on a website if:

- (a) the person has agreed (generally or specifically) that the Document, information or notice may be sent or supplied to him in that manner, or he is taken to have so agreed under Schedule 5 of the Companies Act 2006, and in either case he has not revoked that agreement;
- (b) the Company has notified the intended recipient of:
 - (i) the presence of the Document, information or notice on the website,
 - (ii) the address of the website;
 - (iii) the place on the website where it may be accessed;
 - (iv) how to access the Document, information or notice; and
 - (v) any other information prescribed by the Companies Acts or any other provisions of law including, when the Document, information or notice is a notice of meeting, that fact, the place, date and time of the meeting and whether the meeting is an annual general meeting; and
- (c) the Document, information or notice is available on the website throughout the period specified by any applicable provision of the Companies Acts or, if no such period is specified, the period of 28 days starting on the date on which the notification referred to in paragraph (b) above is sent to the relevant person.

117 Sending or supplying any Document, information or notice by any other means

Any Document, information or notice that is sent or supplied otherwise than in hard copy or Electronic Form or by means of a website is validly sent or supplied if it is sent or supplied in a form or manner that has been agreed by the intended recipient.

118 Joint holders

In respect of joint holdings all Documents, notices and information shall be sent or supplied to the joint holder whose name stands first in the register in respect of such joint holding, and notice so sent or supplied shall be sufficient notice to all the joint holders. A joint holder whose name stands first in the register but who has no specified or registered address in the United Kingdom for the service of notices shall be disregarded for this purpose except to the extent that the Company intends to send or supply a notice by electronic means and the joint holder whose name stands first in the register has agreed (generally or specifically) to the sending or supply of that Document, information or notice by electronic means and has not revoked that agreement and he has notified the Company of an address for that purpose. Anything to be agreed or specified in respect of a joint holding may be agreed or specified by the joint holder whose name stands first in the register. Paragraphs 16(2) and 16(3) of Schedule 5 of the Companies Acts shall not apply.

119 Members resident abroad

A Member who (having no registered address within the United Kingdom) has not supplied to the Company an address within the United Kingdom for the service of notices shall not be entitled to receive any Document, information or notice from the Company except to the extent that the Directors decide to send a Document, information or a notice to that Member by electronic means and that Member has consented (or is deemed to have consented) to the sending of that Document, information or notice by electronic means and he has, where necessary, notified the Company of an address for that purpose.

120 Presence at meeting evidence in itself of receipt of notice

A Member present either in person or by proxy, or in the case of a corporate Member by a duly authorised representative, at any meeting of the Company or of the Holders of any class of Shares shall be deemed to have received notice of the meeting and, where required, of the purposes for which it was called.

121 Document, information or notice given by advertisement in certain circumstances

Unless the Companies Acts or any other provisions of law require a notice, Document or information to be sent or supplied in a different way, any notice, information or Document shall be sufficiently sent or supplied if published by advertisement inserted once in at least one national newspaper published in the United Kingdom.

122 When Document, information or notice is deemed served

- 122.1. Where a Document, information or a notice is sent by post it shall be deemed to have been received by the intended recipient 48 hours after it was posted. In proving such service, it shall be sufficient to prove that the letter containing the notice or Document was properly addressed, prepaid and posted.

- 122.2. A notice given by advertisement shall be deemed to have been given or served on the day on which the advertisement appears.
- 122.3. Where a Document, information or notice is sent or supplied by electronic means it shall be deemed to have been received by the intended recipient on the day on which the Document, information or notice was sent or supplied by or on behalf of the Company. In proving such service, it shall be sufficient to prove that the Document, information or notice was properly addressed.
- 122.4. Where a Document, information or notice is sent or supplied by means of a website, it is deemed to have been received by the recipient when the material was first made available on the website or, if later, when the recipient received (or is deemed to have received) notice of the fact that the material was available on the website.
- 122.5. In calculating a period of hours for the purposes of this Article, it is immaterial whether a day is a working day (as defined in the Companies Act 2006) or not.
- 122.6. Where a Document, information or a notice to be given or sent by electronic means has failed to be transmitted after three attempts, then that notice or other Document shall nevertheless be deemed to have been sent for the purposes of Article 122.3 and, without prejudice to Article 124, that failure shall not invalidate any meeting or other proceeding to which the notice or Document relates.

123 Manner of giving notice of general meetings

Notice of every general meeting shall, subject to the provisions of these Articles, be given in any manner authorised in these Articles to:

- (a) every Member entitled to notice under Articles 118, 119 or otherwise;
- (b) all Persons Entitled to a Share in consequence of death or Bankruptcy of a Member, if the Company has been notified in accordance with Article 125;
- (c) the auditors for the time being of the Company; and
- (d) the Directors of the Company.

No other person shall be entitled to receive notices of general meetings.

124 Omission or non-receipt of Document, notice or information.

Without prejudice to any other Articles, the accidental failure to send any Document, notice or information to or the non-receipt of any Document, notice or information by any person entitled to any Document, notice or information relating to any meeting or other proceeding shall not invalidate the relevant meeting or other proceeding.

125 Service of Document, notice or information on person entitled by transmission

A person entitled to a Share in consequence of the death or Bankruptcy of a Member upon supplying to the Company such evidence as the Directors may reasonably require to show his title to the Share, and upon supplying also an address within the United Kingdom for the sending or supply of Documents, notices or information (or, in relation to any Document, notice or information which that person agrees (generally or specifically) to receive and which the Company intends to send or supply using electronic means, an address for that purpose), shall be entitled to have sent or supplied to him at such address any Document, notice or information to which the Member (but for his death or Bankruptcy) would have been entitled, and that sending or supply shall for all purposes be deemed a sufficient sending or supply of that Document, notice or information on all persons interested (whether jointly with or as claiming through or under him) in the Share. Except as already provided, any Document, information or notice sent by post to, left at, or sent or supplied using electronic means to the address of any Member in pursuance of these Articles shall, even if the Member is then dead or bankrupt, and whether or not the Company has notice of his death or Bankruptcy, be deemed to have been duly sent or supplied in respect of any Share registered in the name of such Member as sole or first-named joint holder.

126 Notice when post not available

If at any time by reason of the suspension or curtailment of postal services within the United Kingdom the Company desires to but is unable effectively to convene a general meeting by notices sent through the post then, despite the availability of any other method of sending or supplying notices under Articles 114, 115, 116 and 117, a general meeting may be convened by a notice advertised on the same date in at least one national newspaper published in the United Kingdom and such notice shall be deemed to have been duly sent or supplied to all Members entitled to it to whom the Company would otherwise have sent the relevant notice by post at noon on the day on which the advertisement appears. In any such case the Company shall send confirmatory copies of the notice by post to all Members to whom it would otherwise have sent the original notice by post if at least seven days prior to the meeting the posting of notices to addresses throughout the United Kingdom again becomes practicable.

127 Failure to notify contact details

127.1. If:

- (a) the Company sends two consecutive Documents to a Member over a period of at least twelve (12) months; and
 - (b) each of those Documents is returned undelivered, or the Company receives notification that it has not been delivered,
- that Member ceases to be entitled to receive notices from the Company.

127.2. A Member who has ceased to be entitled to receive notices from the Company becomes entitled to receive such notices again by sending the Company:

- (a) a new address to be recorded in the register of Members; or
- (b) if the Member has agreed that the Company should use a means of communication other than sending things to such an address, the information that the Company needs to use that means of communication effectively.

128 Reference to Documents being served etc.

The provisions of Article 112 through to 127 apply to any notice, Document or information to be sent or supplied under these Articles whether the Articles require the notice, Document or information to be “sent” or “supplied” or any other word such as “given”, “delivered” or “served”.

ADMINISTRATIVE ARRANGEMENTS

129 Destruction of Documents

129.1. The Company is entitled to destroy:

- (a) all Instruments of transfer of Shares which have been registered, and all other Documents on the basis of which any entries are made in the register of Members, from six (6) years after the date of registration;
- (b) all dividend mandates, variations or cancellations of dividend mandates, and notifications of change of address, from two years after they have been recorded;
- (c) all Share Certificates which have been cancelled from one year after the date of the cancellation;
- (d) all Paid dividend warrants and cheques from one year after the date of actual payment; and
- (e) all Proxy Notices from one year after the end of the meeting to which the Proxy Notice relates.

129.2. If the Company destroys a Document in good faith, in accordance with the Articles, and without notice of any claim to which that Document may be relevant, it is conclusively presumed in favour of the Company that:

- (a) entries in the register purporting to have been made on the basis of an Instrument of transfer or other Document so destroyed were duly and properly made;
- (b) any Instrument of transfer so destroyed was a valid and effective Instrument duly and properly registered;
- (c) any Share Certificate so destroyed was a valid and effective Certificate duly and properly cancelled; and

- (d) any other Document so destroyed was a valid and effective Document in accordance with its recorded particulars in the books or records of the Company.
- 129.3. This Article does not impose on the Company any liability which it would not otherwise have if it destroys any Document before the time at which this Article permits it to do so.
- 129.4. In this Article, references to the destruction of any Document include a reference to its being disposed of in any manner.
- 130 No right to inspect accounts and other records**
- 130.1. Except as provided by law or authorised by the Directors or an Ordinary Resolution of the Company, no person is entitled to inspect any of the Company's accounting or other records or Documents merely by virtue of being a Member.
- 131 Provision for employees on cessation of business**
- The Directors may decide to make provision for the benefit of persons employed or formerly employed by the Company or any of its Subsidiaries (other than a Director or former Director or shadow Director) in connection with the cessation or transfer to any person of the whole or part of the undertaking of the Company or that Subsidiary.

DIRECTORS' INDEMNITY AND INSURANCE

- 132 Indemnity**
- 132.1. Subject to Article 132.3, a Relevant Director of the Company or an associated company may be indemnified out of the Company's assets against:
- (a) any liability incurred by that Director in connection with any negligence, default, breach of duty or breach of trust in relation to the Company or an associated company;
 - (b) any liability incurred by that Director in connection with the activities of the Company or an associated company in its capacity as a trustee of an occupational pension scheme (as defined in section 235(6) of the Companies Act 2006); and
 - (c) any other liability incurred by that Director in the actual or purported execution or discharge of his duties, the exercise or purported exercise of his powers or otherwise in relation to his duties or powers as an officer of the Company or an associated company.
- 132.2. Where a Relevant Director is indemnified against a liability in accordance with this Article, the indemnity extends to each cost, charge, loss, expense and liability incurred by him in relation to that liability.
- 132.3. This Article does not authorise any indemnity which would be prohibited or rendered void by any provision of the Companies Acts or by any other provision of law.

- 132.4. In this Article and Article 133:
- (a) companies are associated if one is a Subsidiary of the other or both are subsidiaries of the same body corporate, and
 - (b) a “**Relevant Director**” means any Director or former Director, or other officer or former officer, of the Company or an associated company.

133 Insurance

133.1. Subject to and so far as may be permitted by the Companies Acts and any other provision of law, the Directors may decide to purchase and maintain insurance, at the expense of the Company, for the benefit of any Relevant Director in respect of any Relevant Loss.

133.2. In this Article:

- (a) a “**Relevant Loss**” means any loss or liability which has been or may be incurred by a Relevant Director in connection with that Relevant Director’s actual or purported execution and/or discharge of his duties or powers in relation to the Company, any associated company or any pension fund or employees’ Share scheme of the Company or associated company; and
- (b) companies are associated if one is a Subsidiary of the other or both are subsidiaries of the same body corporate.

134 Defence expenditure

134.1. Subject to and so far as may be permitted by the provisions of the Companies Acts and any other provision of law, the Company may:

- (a) provide a Director or other officer of the Company or of its associated companies with funds to meet expenditure incurred or to be incurred by him:
 - (i) in defending any criminal or civil proceedings in connection with any alleged negligence, default, breach of duty or breach of trust by him in relation to the Company or an associated company or in connection with any application for relief under any of the provisions referred to in section 205(5) of the Companies Acts; and
 - (ii) in defending himself in an investigation by a regulatory authority or against action proposed to be taken by a regulatory authority in connection with any alleged negligence, default, breach of duty or breach of trust by him in relation to the Company or an associated company; and
- (b) do anything to enable such a Director or other officer to avoid incurring such expenditure.

135 Maintenance of register by Approved Depositary

An Approved Depositary shall maintain a register or system(s) (the “**Proxy Register**”) in which shall be recorded the aggregate number of Ordinary Shares which for the time being are registered in the name of the Approved Depositary or its nominee (the “**Depositary Shares**”) as well as the name and address of each person who is for the time being appointed as an Appointed Proxy pursuant to Article 136 below and, against his name and address, the number of Depositary Shares in respect of which that Appointed Proxy’s appointment for the time being subsists (his “**Appointed Number**”). The Proxy Register shall be open to inspection by any person authorised by the Company during usual business hours and the Approved Depositary shall furnish to the Company or its agents upon demand all such information as to the contents of the Proxy Register, or any part of it, as may be requested.

136 Appointment of Approved Proxies

Without prejudice to the right of an Approved Depositary or its nominee to exercise any rights conferred in these Articles, an Approved Depositary or its nominee may appoint as its proxy or proxies such person or persons as it thinks fit (each such person being an “**Appointed Proxy**”) and may determine the method by which and the terms upon which, such appointments are made, save that each such appointment shall specify the Appointed Number in respect of which that appointment is made and the aggregate Appointed Numbers of all the Appointed Proxies subsisting at any one time shall not exceed the aggregate number of Depositary Shares.

137 Rights of Appointed Proxies

Subject to the Companies Acts and any other provisions of law and subject to the provisions of this Article 137, and so long as the Depositary Shares shall be of a sufficient number so as to include his Appointed Number, an Appointed Proxy:

- (a) shall upon production to the Company at a general meeting of written evidence of his appointment (which shall be in such form as the Company and the Approved Depositary shall determine from time to time) be entitled to the same rights, and subject to the same restrictions, in relation to his Appointed Number as though the Ordinary Shares represented by the Appointed Number were registered in the name of the Approved Depositary (or its nominee) and the Appointed Proxy was a person validly appointed as proxy by the Approved Depositary (or its nominee) in accordance with Article 56 to Article 60 (inclusive); and
- (b) shall himself be entitled, by an Instrument of proxy duly signed by him and deposited with the Company in accordance with Article 59, to appoint another person as his proxy in relation to his Appointed Number so that the provisions of these paragraphs shall apply (*mutatis mutandis*) in relation to such an appointment as though the Ordinary Shares represented by the Appointed Number were registered in the name of the Appointed Proxy and the appointment by the Appointed Proxy was made in accordance with Articles 56 through to Article 60.

138 Notices to Appointed Proxies

The Company may send an Appointed Proxy at his address as is shown in the Proxy Register all notices and other Documents which are sent to the Holders of Ordinary Shares.

139 Payment of dividends to Appointed Proxies

The Company may pay to an Appointed Proxy at his address as shown in the Proxy Register all dividends payable on the Ordinary Shares in respect of which he has been appointed as Appointed Proxy, and payment of any such dividend shall be a good discharge to the Company of its obligation to make payment to the Approved Depositary or its nominee in respect of the Ordinary Shares concerned.

140 Determination of entitlement of Appointed Proxies

140.1. For the purposes of determining which persons are entitled as Appointed Proxies:

- (a) to exercise the rights conferred by Article 137;
- (b) to receive notices and other Documents sent pursuant to Article 138; and
- (c) to be paid dividends pursuant to Article 139,

and each Appointed Proxy's Appointed Number, the Approved Depositary may determine that the Appointed Proxies who are so entitled shall be the persons entered in the Proxy Register at the close of business on a date (an "**Appointed Proxy Record Date**") determined by the Approved Depositary in consultation with the Company.

140.2. When an Appointed Proxy Record Date is determined for a particular purpose:

- (a) the number of Depositary Shares in respect of which a person entered in the Proxy Register as an Appointed Proxy is to be treated as having been appointed for that purpose shall be the number appearing against his name in the Proxy Register as at the close of business on the Appointed Proxy Record Date; and
- (b) changes to entities in the Proxy Register after the close of business on the Appointed Proxy Record Date shall be disregarded in determining the entitlement of any person for the purpose concerned.

141 No interest in Shares

Except as required by law, no Appointed Proxy shall be recognised by the Company as holding any interest in Shares upon any trust and subject to the recognition of the rights conferred in relation to general meetings by appointments made by Appointed Proxies pursuant to Article 137(b) the Company shall be entitled to treat any person entered in the Proxy Register as an Appointed Proxy as the only person (other than the Approved Depositary) who has any interest in the Ordinary Shares in respect of which the Appointed Proxy has been appointed.

142 Questions as to validity to vote Depositary Shares

If any question shall arise as to whether any particular person or persons has or have been validly appointed to vote (or exercise any other right) in respect of any Depositary Shares (whether by reason of the aggregate number of Shares in respect of which appointments are recorded in the Proxy Register exceeding the aggregate number of Depositary Shares or for any other reason) such question shall if arising at or in relation to a general meeting be determined by the Chairman of the Meeting (and if arising in any other circumstances shall be determined by the Directors) whose determination (which may include declining to recognise a particular appointment or appointments as valid) shall if made in good faith be conclusive and binding on all persons interested.

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption “Experts” and to the use of our reports dated February 27, 2018, in the Registration Statement (Form F-1) and related Prospectus of Mereo BioPharma plc dated April 9, 2018.

/s/ Ernst & Young LLP

London, United Kingdom

April 9, 2018