As filed with the Securities and Exchange Commission on June 3, 2019.

Registration Statement No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form F-1

REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

Orchard Therapeutics plc

(Exact name of registrant as specified in its charter)

England and Wales	2836	Not applicable
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification Number)

108 Cannon Street
London EC4N 6EU
United Kingdom
Tel: +44 (0) 20 3808 8286
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Cogency Global Inc.
10 East 40th Street 10th Floor
New York, New York 10016
+1 212 947 7200
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Mitchell S. Bloom Michael H. Bison Goodwin Procter LLP 100 Northern Avenue Boston, MA 02210 (617) 570-1000	Andrew Harrow Goodwin Procter (UK) LLP 100 Cheapside London EC2V 6DY United Kingdom +44 20 7447 4200	Deanna L. Kirkpatrick Marcel R. Fausten Davis Polk & Wardwell LLP 450 Lexington Avenue New York, NY 10017 (212) 450-4000

Approximate date of commencement of proposed sale to 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.

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. ☐

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

CALCULATION OF REGISTRATION FEE

Title of each class of securities being registered	Amount to be registered(1)	Proposed maximum offering price per share(2)	Proposed maximum aggregate offering price(2)	Amount of registration fee
Ordinary shares, nominal value £0.10 per share(3)	10,350,000	$18.71	$193,648,500	$23,471

(1) Includes shares represented by American Depositary Shares, or ADSs, that are issuable upon exercise of the underwriters' option to purchase additional shares.

(2) Estimated solely for the purpose of computing the amount of the registration fee pursuant to Rule 457(c) under the Securities Act of 1933, as amended, based on the average of the high and low prices of the registrant's ADSs as reported on the Nasdaq Global Select Market on May 31, 2019.

(3) These ordinary shares are represented by ADSs, each of which represents one ordinary share of the registrant. ADSs issuable upon deposit of the ordinary shares registered hereby have been registered pursuant to a separate registration statement on Form F-6 (File No. 333-227905).

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, as amended, or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), shall determine.

The information contained in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and we are not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated June 3, 2019

Preliminary prospectus

9,000,000 American depositary shares
Representing 9,000,000 ordinary shares

We are offering 9,000,000 American Depositary Shares, or ADSs. Each ADS represents one ordinary share. The ADSs may be evidenced by American Depositary Receipts, or ADRs.

The public offering price is $ per ADS. Our ADSs are listed on the Nasdaq Global Select Market under the symbol "ORTX." On May 31, 2019, the last reported sale price of our ADSs on the Nasdaq Global Select Market was $18.91 per share.

Investing in our ADSs involves a high degree of risk. Before buying any ADSs, you should carefully read the discussion of material risks of investing in our ADSs in "Risk factors" beginning on page 21 of this prospectus.

We are an "emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012 and a "foreign private issuer" under applicable U.S. federal securities laws. As such, we have elected to comply with certain reduced public company reporting requirements. See "Prospectus summary—implications of being an emerging growth company and a foreign private issuer" for additional information.

Neither the U.S. Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

	Per ADS	Total
Public offering price	$	$
Underwriting discount(1)	$	$
Proceeds to Orchard Therapeutics plc, before expenses	$	$

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

Delivery of the ADSs is expected to be made on or about , 2019. We have granted the underwriters an option for a period of 30 days to purchase an additional 1,350,000 ADSs. If the underwriters exercise the option in full, the total underwriting discounts payable by us will be $ million, and the total proceeds available to us, before expenses, will be $ million, assuming a midpoint of the range.

J.P. Morgan **Goldman Sachs & Co. LLC** **Cowen** **Barclays**

Lead Manager

Guggenheim Securities

Co-Manager

Wedbush PacGrow

Prospectus dated , 2019

Table of contents

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 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.

For investors outside the United States: Neither we nor the underwriters have done anything that would permit this 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 offering of the ADSs and the distribution of this prospectus outside the United States.

We are incorporated under the laws of England and Wales. Under the rules of the U.S. Securities and Exchange Commission, or the SEC, we are currently considered a “foreign private issuer.” As a foreign private issuer, we are not 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, or the Exchange Act.

Market, industry and other data

This prospectus contains estimates, projections and other information concerning our industry, our business, and the markets for our product candidates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties, and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from our own internal estimates and research as well as from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.

In addition, assumptions and estimates of our and our industry's future performance are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those described in the section titled "Risk factors." These and other factors could cause our future performance to differ materially from our assumptions and estimates. See "Special note regarding forward-looking statements."

About this prospectus

In connection with our initial public offering, we completed a corporate reorganization, pursuant to which Orchard Therapeutics Limited (now known as Orchard Therapeutics (Europe) Limited) became a wholly-owned subsidiary of Orchard Rx Limited (now known as Orchard Therapeutics plc), a newly formed holding company with nominal assets and no liabilities, contingencies, or commitments, which was formed to effect the corporate reorganization. Orchard Rx Limited was re-registered as a public limited company and changed its name from Orchard Rx Limited to Orchard Therapeutics plc. For more details on the corporate reorganization, see Note 7 to our audited consolidated financial statements included in our Annual Report on Form 20-F for the year ended December 31, 2018 incorporated herein by reference.

Unless otherwise indicated or the context otherwise requires, all references in this prospectus to the terms “Orchard Therapeutics Limited,” “Orchard Rx Limited,” “Orchard Therapeutics plc,” “the company,” “we,” “us” and “our” refer to (i) Orchard Therapeutics Limited and its wholly-owned U.S. subsidiary prior to the completion of our corporate reorganization, (ii) Orchard Rx Limited and its subsidiaries after the completion of our corporate reorganization and (iii) Orchard Therapeutics plc and its subsidiaries after the re-registration of Orchard Rx Limited as a public limited company on October 29, 2018. See Note 7 to our audited consolidated financial statements included in our Annual Report on Form 20-F for the fiscal year ended December 31, 2018 incorporated herein by reference.

We own various trademark registrations and applications, and unregistered trademarks, including Orchard Therapeutics plc and our corporate logo. All other trade names, trademarks and service marks of other companies appearing in this prospectus are the property of their respective holders. Solely for convenience, the trademarks and trade names in this prospectus may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend to use or display other companies’ trademarks and trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

Presentation of financial information

Although we are a UK company, the functional currency of our reporting entity is the U.S. Dollar and we prepare our consolidated financial statements in accordance with generally accepted accounting principles in the United States, or U.S. GAAP, as issued by the Financial Accounting Standards Board. All references in this prospectus to "$" are to U.S. Dollars and all references to "£" are to pounds sterling. Unless otherwise indicated, certain pounds sterling amounts contained in this prospectus have been translated into U.S. Dollars at the rate of $1.2687 to £1.00, which was the noon buying rate of the Federal Reserve Bank of New York on December 31, 2018, the last business day of the fiscal year ended December 31, 2018. These translations should not be considered representations that any such amounts have been, could have been or could be converted into pounds sterling at that or any other exchange rate as of that or any other date.

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. We have historically conducted our business through Orchard Therapeutics Limited and our U.S. subsidiary, and therefore our historical consolidated financial statements previously presented the consolidated results of operations of Orchard Therapeutics Limited. Following our reorganization that we completed in connection with our initial public offering, our consolidated financial statements present the consolidated results of operations of Orchard Therapeutics plc.

Prospectus summary

The following summary highlights information contained elsewhere in this prospectus and in the documents we incorporate herein by reference. This summary does not contain all of the information you should consider before investing in our ADSs. You should read the entire prospectus carefully, including the section titled "Risk factors" contained in this prospectus, any related free writing prospectus and the section titled "Risk Factors" in our Annual Report on Form 20-F for the fiscal year ended December 31, 2018 along with our consolidated financial statements and notes to those consolidated financial statements and the other information incorporated by reference in this prospectus.

Overview

We are a commercial-stage, fully-integrated biopharmaceutical company dedicated to transforming the lives of patients with serious and life-threatening rare diseases through *ex vivo* autologous hematopoietic stem cell, or HSC, based gene therapies. Our gene therapy approach seeks to transform a patient's own, or autologous, HSCs into a gene-modified drug product to treat the patient's disease through a single administration. We achieve this outcome by utilizing a viral vector to introduce a functional copy of a missing or faulty gene into the patient's autologous HSCs through an *ex vivo* process, resulting in a drug product that can then be administered to the patient at the bedside.

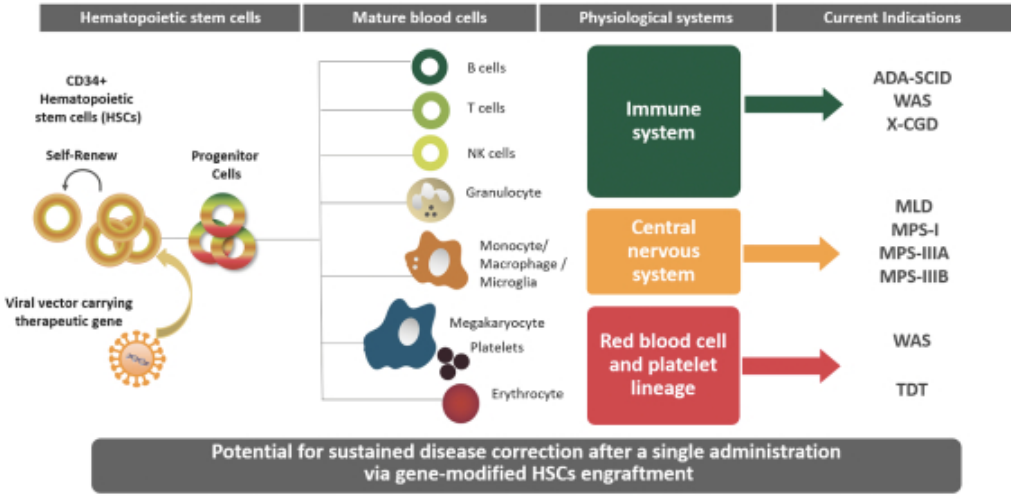
To date, over 150 patients have been treated with our commercial product and clinical-stage product candidates across six different diseases, with follow-up periods of up to 18 years following a single administration. We believe the data observed across these programs, in combination with our deep expertise in the development, manufacturing and commercialization of gene and cell therapies, position us to provide potentially transformative therapies to patients suffering from a broad range of rare diseases.

We are initially focusing our *ex vivo* autologous HSC gene therapy approach on three therapeutic rare disease franchise areas: primary immune deficiencies, neurometabolic disorders and hemoglobinopathies. Our portfolio currently includes Strimvelis, our commercial-stage gammaretroviral-based product for the treatment of adenosine deaminase-severe combined immunodeficiency, or ADA-SCID, six lentiviral-based product candidates in clinical-stage development and several other product candidates in preclinical development. We anticipate making near-term regulatory submissions for approval of three of our most advanced clinical-stage product candidates. These include OTL-101 for the treatment of ADA-SCID, OTL-200 for the treatment of metachromatic leukodystrophy, or MLD, and OTL-103 for the treatment of Wiskott-Aldrich syndrome, or WAS. For each of these lead product candidates, we are in ongoing discussions with the applicable regulatory authorities with respect to the clinical and other data required for regulatory submission. We plan to submit a biologics license application, or BLA, for OTL-101 with the United States Food and Drug Administration, or the FDA, in 2020, followed by a marketing authorization application, or MAA, submission with the European Medicines Agency, or the EMA. We plan to submit an MAA for OTL-200 with the EMA in the first half of 2020, followed approximately one year later by a BLA with the FDA, and we plan to submit an MAA with the EMA and a BLA with the FDA for OTL-103 in 2021. In addition, we plan to meet with appropriate regulatory officials during 2019 regarding the design of a registrational trial for OTL-102 for the treatment of X-linked chronic granulomatous disease, or X-CGD. We also plan to

meet with appropriate regulatory officials in the next twelve months regarding the design of a registrational trial for OTL-300 for the treatment of transfusion-dependent betathalassemia, or TDT.

We intend to bring potentially transformative therapies to the broadest number of patients suffering from rare diseases. The indications we are initially targeting in our primary immune deficiencies and neurometabolic franchises (ADA-SCID, MLD, WAS, X-CGD, mucopolysaccharidosis type IIIA, or MPS-IIIA, and mucopolysaccharidosis type I, or MPS-I) have a combined annual incidence rate of between 1,200 and 2,600 patients in markets around the world where treatments for rare diseases are often reimbursed. We believe the total market opportunity in the disease areas underlying these six programs could be greater than $3 billion annually based on incidence alone. The indication we are initially targeting in our hemoglobinopathies franchise is TDT, which is a more common genetic disease with a global incidence estimated to be approximately 25,000 symptomatic individuals born each year, thereby providing additional revenue potential in this indication. In addition, each of our indications have prevalent populations made up of people living with diseases who could be eligible for our treatments upon receiving marketing approval, which could significantly increase the size of our market opportunity, particularly with X-CGD, WAS and TDT.

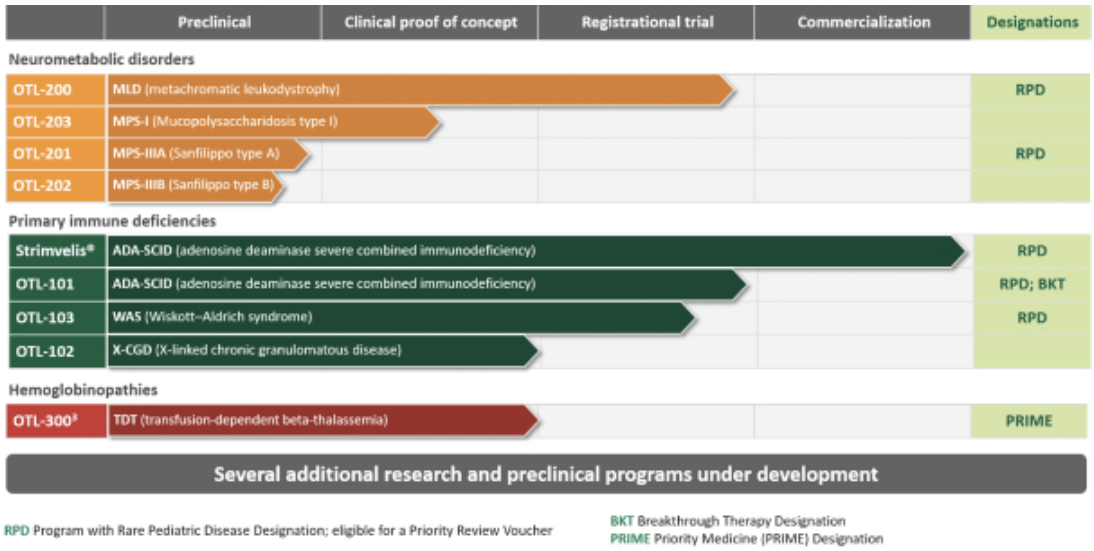
We believe our approach of using lentiviral vectors to genetically modify HSCs has wide-ranging applicability to a large number of indications. The ability of HSCs to differentiate into multiple cell types allows us to deliver gene-modified cells to multiple physiological systems, including the central nervous system, immune system and red blood cell lineage, thereby potentially enabling the correction of a wide range of diseases. By leveraging the innate self-renewing capability of HSCs that are engrafted in the bone marrow as well as the ability of lentiviral vectors to achieve stable integration of a modified gene into the chromosomes of HSCs, our gene therapies have the potential to provide a durable effect following a single administration.



We have a broad and advanced portfolio of commercial- and development-stage products and product candidates. In April 2018, we strengthened our portfolio with our acquisition of Strimvelis for ADA-SCID, OTL-200 for MLD, OTL-103 for WAS and OTL-300 for TDT from Glaxo Group Limited and GlaxoSmithKline Intellectual Property Development LTD, or, together, GSK.

Our neurometabolic disorders franchise consists of one advanced registrational clinical program, OTL-200 for MLD, one clinical proof of concept-stage program, OTL-203 for MPS-I and two preclinical programs, OTL-201 for MPS-IIIA and OTL-202 for MPS-IIIB. Our primary immune deficiencies franchise consists of our commercial program, Strimvelis for ADA-SCID, two advanced registrational clinical programs, OTL-101 for ADA-SCID and OTL-103 for WAS, and one clinical proof of concept-stage program, OTL-102 for X-CGD. Our hemoglobinopathies franchise consists of one clinical proof of concept-stage program, OTL-300 for TDT.

The status of the lead pipeline programs is outlined below:



Due to the nature of our gene therapy product candidates and the indications our product candidates are intended to treat, which are rare or ultra-rare indications and often fatal without treatment, we believe our clinical programs will generally be eligible to proceed to registration without having to conduct one or more Phase 1 safety studies in healthy volunteers or Phase 3 randomized, double-blind and placebo-controlled clinical trials. For purposes of this prospectus, we refer to an exploratory study, which is sometimes referred to as a Phase 1 or Phase 1/2 clinical trial, as a proof of concept trial, and a confirmatory efficacy and safety study to support submission of a potential marketing application with the applicable regulatory authorities, which is sometimes referred to as a Phase 2/3 or Phase 3 clinical trial or a pivotal trial, as a registrational trial.

The diseases we target affect patients around the world, which require us to have the infrastructure to deliver gene therapies globally. We are therefore building a commercial-scale manufacturing infrastructure and leveraging technologies that will allow us to deliver our gene therapies globally and in a fully-integrated manner. In order to meet anticipated demand for our growing pipeline of product candidates and planned product offerings, we are initially utilizing our existing network of contract manufacturing organizations, or CMOs, to manufacture vectors and drug product. In addition, we have established process development capabilities in Menlo Park, California and in London, UK, and have leased a facility in Fremont, California to

accommodate our expanding technical operations and build in-house drug product and vector manufacturing capabilities.

Cryopreservation of our gene-modified HSCs is a key component of our strategy to deliver potentially transformative gene therapies to patients worldwide, facilitating both local treatment and local product reimbursement. In anticipation of commercialization, we have developed cryopreserved formulations of our three most advanced product candidates and are working to demonstrate comparability to the fresh cell formulations used in our registrational trials. The registrational trials for all of our earlier stage product candidates will be conducted using a cryopreserved formulation.

We have global commercial rights to Strimvelis and all our clinical product candidates and plan to commercialize our gene therapies in key markets worldwide, including the United States and Europe initially, subject to obtaining the necessary marketing approvals for these jurisdictions. We plan to deploy a focused commercial infrastructure to deliver our product candidates to patients, and are focused on working closely with all relevant stakeholders, including patients, caregivers, specialist physicians and payors, to ensure the widest possible post-approval access for our product candidates.

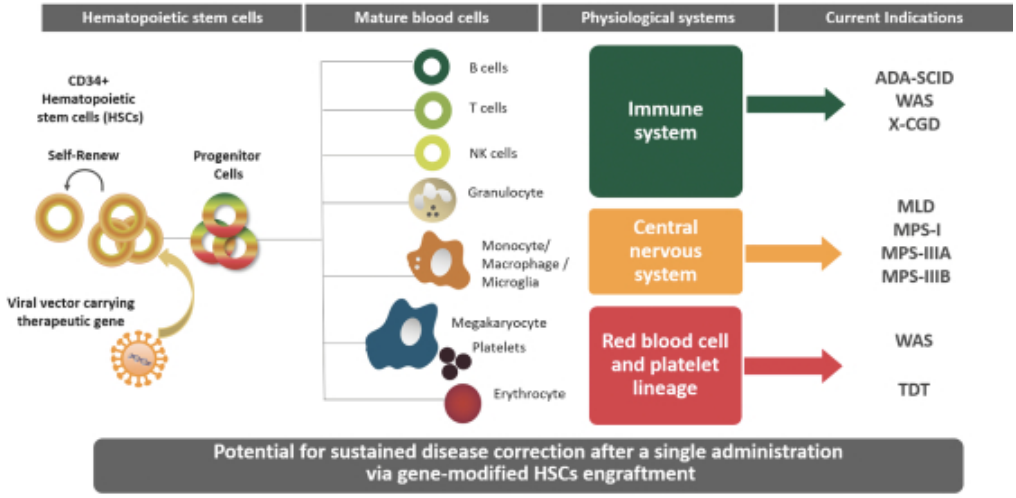
As we continue to develop and expand our portfolio, we believe that the deep experience of our management team and our extensive academic relationships are key strategic strengths. Our management team has extensive experience in rare diseases and in the manufacturing, preclinical and clinical development and commercialization of gene and cell therapies. In addition, we partner with leading academic institutions, which are pioneers in *ex vivo* autologous gene therapy. We plan to leverage our internal expertise combined with our relationships with leading academic institutions to transition our lead clinical-stage product candidates to commercialization and continue to expand our portfolio of *ex vivo* autologous HSC gene therapy products for rare diseases.

Our *ex vivo* autologous HSC gene therapy approach

Our *ex vivo* HSC gene therapy approach seeks to transform a patient's autologous HSCs into a gene-modified cellular drug product to treat the patient's disease. HSCs are self-renewing cells that are capable of differentiating into all types of blood cells, including white blood cells, red blood cells, platelets and microglia. HSCs can be obtained directly from the bone marrow, which requires administration of a general anesthetic, or from the patient's peripheral blood with the use of a mobilizing agent, which is an agent that can move HSCs from the bone marrow into the peripheral blood. By delivering gene-modified HSCs back to patients, we seek to take advantage of the self-renewing capability of HSCs to enable a durable effect following a single administration, as has been seen in our commercial and development programs. In addition, the ability of HSCs to differentiate into multiple different cell types has the potential to enable the delivery of gene-modified cells to different physiological systems and allow the correction of a broad range of different diseases.

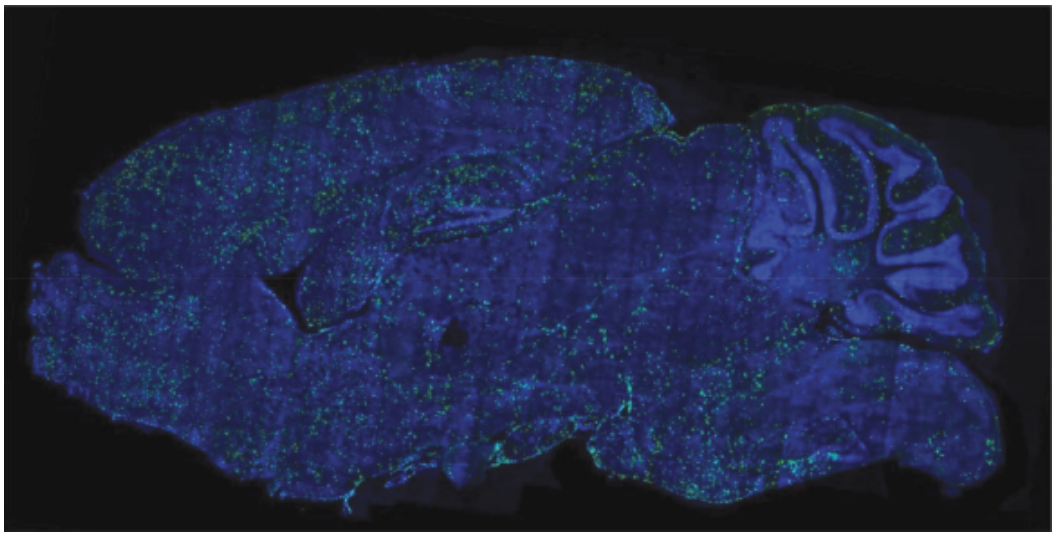
Clinical validation already exists for hematopoietic stem cell transplantation, or HSCT, an approach of treating a patient with a genetic disease with HSCs contributed by a healthy donor individual, thereby using HSCs that contain a functioning copy of the gene of interest. However, this approach has significant limitations, including difficulties in finding appropriate genetically-

matched donors and the risk of graft-versus-host disease, transplant-related rejection and mortality from these and other complications, and is therefore typically only offered on a limited basis. Our approach is intended to address the significant limitations of HSCT.



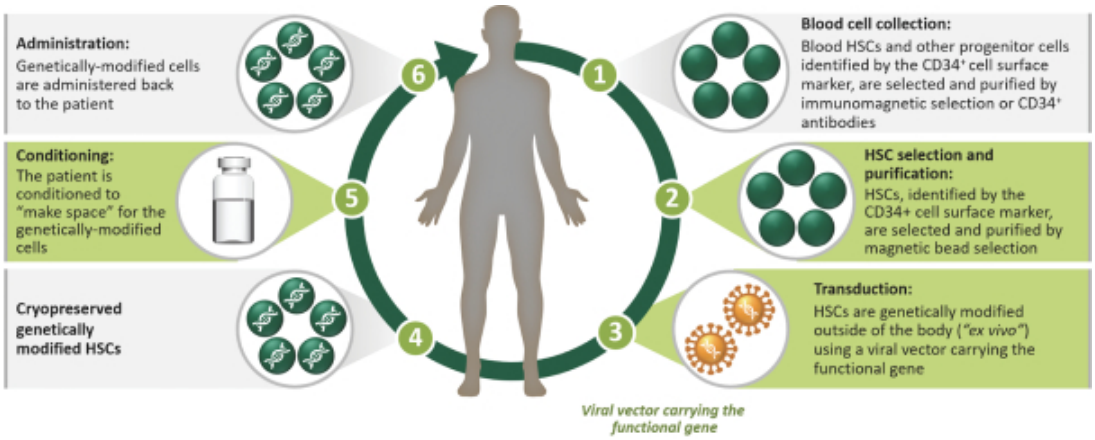
One example of the potential of our *ex vivo* autologous HSC gene therapy approach to deliver genes to different physiological systems is demonstrated below. In a preclinical study conducted by one of our scientific advisors and published in *Proceedings of the National Academy of Sciences of the United States of America,* or *PNAS*, a subpopulation of gene-modified HSCs have demonstrated the potential to cross the blood-brain barrier, engraft in the brain as microglia and express genes and proteins within the central nervous system. As published in *PNAS*, the image below shows a cross-section of the brain of a mouse that was infused intravenously with HSCs, which had been genetically modified using a lentiviral vector carrying green fluorescent protein, or GFP. The GFP expression observed throughout the brain illustrates the potential of gene-modified HSCs to cross the blood-brain barrier, engraft in the brain and express the functional protein throughout the brain, thereby potentially addressing a range of diseases that affect the central nervous system. Our OTL-200 program for MLD leverages this same mechanism of action to deliver gene-modified HSCs through the blood-brain barrier and deliver a therapeutic gene that can prevent neuronal degeneration.

Transgene distribution in brain of mouse model following administration of HSCs transduced with GFP encoding vector



With respect to each of our product candidates, our *ex vivo* autologous HSC gene therapy approach utilizes a non-replicating lentiviral vector to introduce a functional copy of the missing or faulty gene into the patient's autologous HSCs through an *ex vivo* process called transduction, resulting in a cellular drug product that can then be re-introduced into the patient. Unlike other viral vectors, such as adeno-associated viral, or AAV, vectors, lentiviral vectors integrate into the chromosomes of patients' HSCs. We believe this allows us to achieve stable integration of the modified gene into the HSCs and to achieve durable expression of the target protein by the gene-modified HSCs and their progeny after a single administration of gene therapy. Strimvelis, our commercial-stage product, utilizes an older generation non-replicating gammaretroviral vector.

The image below illustrates the steps in our approach to transform a patient's autologous HSCs *ex vivo* into therapeutic product.



Initial clinical trials conducted using our product candidates utilized a fresh product formulation, resulting in a limited drug product shelf life. We plan to market our current and future product candidates, if approved, in a cryopreserved product formulation to enable the shipment of the drug product to specialized treatment centers throughout the world, allowing patients to receive treatment closer to their home. Cryopreservation also allows us to conduct a number of quality control tests on the genetically modified HSCs prior to introducing them into the patient.

In addition, certain of our clinical-stage product candidates have been evaluated in registrational trials using drug product derived from HSCs extracted from the patients' bone marrow. To optimize our potential product label and the number of patients that we may be able to treat, as part of any BLA or MAA submission for such product candidates, we plan to demonstrate comparability between drug product manufactured using HSCs derived from the patients' peripheral blood and drug product manufactured using HSCs derived from the patients' bone marrow. In cases where clinical trials were conducted using vector and/or drug product manufactured at academic centers, we plan to demonstrate comparability between vector and/or drug product manufactured by our selected third party commercial CMOs with vector and drug product manufactured at such academic centers.

Initially, we are employing our *ex vivo* autologous HSC gene therapy approach to three franchise areas: primary immune deficiencies, neurometabolic disorders and hemoglobinopathies. Data from clinical trials suggests that *ex vivo* autologous HSC gene therapy has the potential to be well-tolerated and to provide sustainable and improved outcomes over existing standards of care for diseases in these franchise areas. We believe that we can apply our approach beyond our initial target indications to treat an even broader range of diseases.

Our strengths

We believe that the combination of our growing body of clinical data evidencing the potential of our *ex vivo* autologous HSC gene therapy approach, and our deep expertise in the development,

manufacturing and commercialization of gene and cell therapies, positions us well to provide potentially transformative therapies through a single administration to patients suffering from a broad range of rare diseases. We believe our key strengths include:

- **Durable, sustained therapeutic potential:** Durable and sustained clinical activity has been observed in patients in each of our lead programs across six different diseases following a single administration. For example, our commercial-stage gammaretroviral program, Strimvelis, has demonstrated sustained recovery of the immune system, resulting in survival and reconstitution of the immune system over approximately 18 years after a single administration. As of April 2019 overall survival has been observed in a maximum follow-up of six years in patients treated with our lentiviral gene therapy OTL-101 for ADA-SCID and eight years in patients treated with our lentiviral gene therapies OTL-200 for MLD and OTL-103 for WAS. Without treatment, these indications are almost always fatal early in life.
- **Demonstrated safety record:** Our *ex vivo* autologous HSC gene therapy approach has been well-tolerated in patients treated to date. Lentiviral vectors have a history of safety in clinical trials. In over 10 years of patient follow-up, there have been no reported instances of insertional mutagenesis or leukemogenesis. Our *ex vivo* modification of the patient's own HSCs also allows us to engineer and test the patient's cells prior to administering the therapy to the patient. Over 150 patients have been treated with our commercial product and clinical-stage product candidates, and each of these therapies have been well-tolerated overall, with no suspected unexpected serious adverse reactions, or SUSARs, related to the drug products observed to date. The most common adverse reactions observed in clinical trials across these programs have included pyrexia and infections. We believe that the long-term extensive follow-up across multiple different diseases and with viral vectors expressing different genes demonstrates the potential safety of our *ex vivo* autologous HSC gene therapy approach.

  Our *ex vivo* autologous HSC gene therapy approach offers important advantages over HSCT, which is the standard of care for several of the indications that we are targeting. HSCT carries a significant risk of complications and mortality. In order to make bone marrow space for incoming donor cells, patients undergoing HSCT need to receive conditioning which often involves two to three chemotherapy agents that are associated with significant short- and long-term organ toxicities. We employ a milder conditioning regimen for most of our *ex vivo* autologous HSC gene therapy product candidates, which is associated with reduced toxicity and length of hospitalization. HSCT also requires the identification of a well-matched third-party donor to provide the cells. A poor cell donor match can result in graft rejection or acute and chronic graft-versus-host disease, or GvHD, a serious complication of HSCT in which the third party donor's immune cells identify the cells of the patient as "foreign" and attack them. GvHD is a severe autoimmune reaction that can lead to organ failure and death. In general, a higher degree of mismatch between the donor and the recipient is associated with a greater risk of disease or graft rejection; however, a well-matched cell transplant can still result in GvHD. By using the patient's own cells, our *ex vivo* autologous HSC gene therapies eliminate the risk of GvHD or graft rejection by providing the patient with a perfect cell match.
- **Applicability to a potentially large number of patients and indications:** A core part of our mission is to bring potentially transformative therapies to the broadest number of patients suffering from rare diseases. We believe our *ex vivo* autologous HSC gene therapy approach has broad therapeutic potential across a large number of rare diseases in our target franchise

areas. The lentiviral vectors that we employ in our clinical-stage programs have large capacity payloads that have the potential to introduce a target gene of choice into the patient's HSCs. The transduction of these vectors into a patient's own HSCs allows for the potentially life-long production of gene-modified HSCs in the body and thus distribution of the target gene throughout multiple organs and tissues, including the central nervous system.

- **Our deep expertise in gene therapy and rare diseases:** Our management team has extensive collective experience in rare diseases and the manufacturing, preclinical and clinical development and commercialization of gene and cell therapies. Members of our executive leadership team have held senior positions at GSK, Amgen, Shire, BioMarin, Alexion, PTC Therapeutics, Osiris, Fate Therapeutics and other companies specializing in gene and cell therapies and rare diseases. In addition, we partner with academic institutions that are pioneers in *ex vivo* autologous HSC gene therapy and we have obtained exclusive licenses to extensive preclinical data, clinical data and know-how to build our portfolio of *ex vivo* autologous HSC gene therapies. These partnerships with leading institutions such as The University of California Los Angeles, Boston Children's Hospital and the United States National Institutes of Health in the United States, and University College London, Great Ormond Street Hospital, Telethon Institute of Gene Therapy, San Raffaele Hospital, The University of Manchester, the Manchester Foundation Trust, and Généthon in Europe, are a core part of our research engine through which we are advancing our lead clinical-stage programs and working to identify other opportunities with comparably high probabilities of success. We plan to leverage our internal expertise combined with our relationships with leading academic institutions to transition our lead clinical-stage product candidates from the academic setting to commercial-ready production and further expand our pipeline.

Our strategy

Our mission is to transform the lives of patients with rare genetic diseases using our *ex vivo* autologous HSC gene therapy approach. We are building a leading, global, fully-integrated gene therapy company focused on serious and life-threatening rare diseases. To achieve this, we are pursuing the following strategies:

- **Advance our six clinical-stage product candidates towards marketing approvals:** Our pipeline currently includes six clinical-stage programs including three in advanced registrational trials. Our programs OTL-101 for ADA-SCID, OTL-200 for MLD and OTL-103 for WAS have all achieved their primary endpoints in registrational trials. Though the primary endpoints in these registrational trials have been achieved, patient follow-up remains ongoing in accordance with the trial protocols. We plan to submit a BLA with the FDA for our product candidate OTL-101 for ADA-SCID in 2020, followed by an MAA with the EMA. We plan to submit an MAA for our product candidate OTL-200 with the EMA in the first half of 2020, followed approximately one year later by a BLA with the FDA, and we intend to submit an MAA with the EMA and a BLA with the FDA for our product candidate OTL-103 in 2021. Furthermore, our clinical proof of concept-stage programs OTL-102 for X-CGD, OTL-203 for MPS-I and OTL-300 for TDT have been observed to be generally well-tolerated and continue to generate clinical activity data in initial clinical trials, and, assuming these trials are successful, we plan to advance these programs to registrational trials and through clinical development to regulatory submission.

- **Leverage the power of our therapeutic approach to expand our product pipeline across multiple indications:** Through our clinical trials, we believe we have exhibited the potential of our *ex vivo* autologous HSC gene therapy approach to target multiple physiological systems in the human body, including the central nervous system, immune system and red blood cell lineage. We seek to leverage our academic collaborations and focus our preclinical and clinical research on rare disease indications with high unmet need and for which we believe there is a high probability of clinical success, based on the results observed in our clinical trials to date. For example, we are expanding our neurometabolic disorders franchise with the development of two preclinical programs, OTL-201 for MPS-IIIA and OTL-202 for MPS-IIIB. We anticipate the submission of a clinical trial application with the applicable regulatory authority in Europe and the initiation of a proof of concept trial for OTL-201 by the end of 2019 and plan to continue to progress preclinical development of OTL-202.
- **Establish an efficient and scalable manufacturing infrastructure:** The rare diseases we target affect patients around the world, and therefore we are building the required infrastructure to deliver our gene therapies globally. To meet our near-term supply needs for initial commercialization primarily in the United States and Europe, we have established supply agreements with an international network of CMOs for vector manufacturing and for the production of drug product. We are investing in in-house manufacturing capabilities to accommodate our expanding process development and vector and drug product manufacturing activities and to continue building our international supply chain. We are also developing and implementing cryopreservation processes for our clinical-stage product candidates, which, in combination with our international network of CMOs and our planned in-house manufacturing capabilities, will help enable the distribution and administration of our gene therapies to wherever patients are located across the globe. In addition, we are investing in several initiatives to improve the efficiency of our manufacturing processes, including evaluation of transduction enhancers and the automation of certain aspects of our production processes with the goal of reducing production costs and our cost of goods. We are also executing on our plans for development of stable cell lines for OTL-102 and OTL-300. We believe that these initiatives will ultimately position us to deliver our gene therapy products efficiently and at a global scale commensurate with patient demand as our product offerings grow.
- **Establish a patient-centered, global commercial infrastructure:** We have global commercial rights to all our clinical product candidates and plan to commercialize our gene therapies in key markets worldwide, subject to obtaining necessary marketing approvals. Leveraging the knowledge gained through our commercial product Strimvelis for ADA-SCID, and given our focus on rare genetic diseases, we plan to deploy a focused commercial infrastructure to deliver our product candidates to patients. In addition, we believe there is an urgent need to improve the early diagnosis of patients with rare genetic diseases, including those in our current focus areas, and we are implementing programs to improve patient and physician education regarding early access to transformative gene therapies for these conditions. We believe the value proposition for patients, caregivers, specialist physicians and payors is significant, given the potentially long-lasting benefits anticipated from our gene therapies. Accordingly, we are focused on working closely with all relevant stakeholders to ensure the widest possible post-approval access for our product candidates.

- **Execute a disciplined business development strategy to strengthen our portfolio of product candidates:** We have built our broad pipeline of product candidates through partnerships with leading academic institutions and through multiple successful in-licensing and acquisition deals. We will continue to evaluate new in-licensing opportunities and collaboration agreements with leading academic institutions and other biotechnology companies around programs that seek to address areas of high unmet need and for which we believe there is a high probability of clinical success, including programs beyond our target franchise areas and current technology footprint.

Recent developments

Credit facility

On May 24, 2019, we entered into a senior term facilities agreement, or the Credit Facility, agented by MidCap Financial (Ireland) Limited, or MidCap, and the additional lenders party thereto from time to time, or together with MidCap, the Lenders. The Lenders agreed to make term loans available to us of up to a $75 million comprised of separate term loans to be issued in three tranches: (1) the first tranche being a $25 million term loan funded on May 28, 2019; (2) the second tranche being a $25 million term loan available no earlier than September 30, 2019 and no later than December 31, 2020 upon submission of certain regulatory filings and evidence of $100 million in cash and cash equivalent investments; and (3) the third tranche being a $25 million term loan available no earlier than July 1, 2020 and no later than September 30, 2021 upon certain regulatory approvals and evidence of $125 million in cash and cash equivalent investments.

Upon entering into the Credit Facility, we were required to pay an arrangement fee of $0.4 million. The term loan matures on May 24, 2024. Each term loan under the Credit Facility requires interest-only payments for 24 months following the date of the Credit Facility, unless the third tranche is drawn, in which case for all payment dates prior to 36 months following the date of the Credit Facility. The term loans under the Credit Facility will be amortizing on either the 24-month or 36-month anniversary of the Credit Facility (as applicable) in equal monthly installments until the loan maturity date . Each term loan under the Credit Facility bears interest at an annual rate equal to 6% plus LIBOR.

At our option, we may prepay the outstanding principal balance of the term loan in whole or in part, subject to a prepayment fee of 3.0% of any amount prepaid if the prepayment occurs on or prior to the first anniversary of the closing date, 2.0% of the amount prepaid if the prepayment occurs after the first anniversary of the closing date but on or prior to the second anniversary of the closing date, and 1.0% of any amount prepaid after the second anniversary of the closing date but on or prior to the third anniversary of the closing date. In addition, a final payment equal to 4.5% is due on the loan maturity date. The Credit Facility includes an ongoing minimum cash financial covenant the requires we maintain not less than $20 million following utilization of the second tranche and not less than $35 million following utilization of the third tranche. In addition, we have granted English law and US law governed security over all of our personal property, including intellectual property, for the payment or discharge of all of our obligations under the Credit Facility.

Fondazione Telethon and Ospedale San Raffaele S.r.l. license agreement

On May 24, 2019, we entered into a license agreement, or the TIGET Agreement, with Fondazione Telethon and Ospedale San Raffaele S.r.l., or together, TIGET, under which TIGET granted us an exclusive worldwide license for the research, development, manufacture and commercialization of *ex vivo* autologous HSC lentiviral based gene therapy products for the treatment of MPS-I, including the Hurler variant. Under the terms of the TIGET Agreement, TIGET is entitled to receive an upfront payment and we may be required to make milestone payments if certain development, regulatory and commercial milestones are achieved. Additionally, we will be required to pay TIGET a tiered mid-single to low-double digit royalty percentage on annual net sales of licensed products.

MPS-I is a condition which is caused by mutations in the gene that produces alpha-L-iduronidase, or IDUA, an enzyme that breaks down lysosomal storage products. MPS-I is a multisystemic disease that affects the skeleton, the joints, the heart and in its most severe form, known as Hurler syndrome, it affects the brain and causes significant neurodegeneration. Current treatments include enzyme replacement therapy and transplant, each of which have multiple limitations. There is limited efficacy with enzyme replacement therapy due to its inability to cross the blood brain barrier and correct the underlying neurodegenerative phenotype, which is one of the most significant characteristics of the disease. Allogeneic transplantation also has limitations and works best when patients are treated at a young age and when IDUA enzyme activity is restored to normal levels. Transplant also comes with risks of morbidity and mortality most commonly related to alloreactivity. Our approach, similar to that which has been used in MLD, is to over-express the IDUA gene in autologous HSCs and then deliver those cells intravenously to patients with this severe disease.

As of data presented by TIGET at the American Society of Gene & Cell Therapy, or ASGCT, meeting in April 2019, four patients with the Hurler sub-type have been treated in an ongoing investigator-sponsored, proof-of-concept study at San Rafaelle Hospital in Milan, Italy. The primary objectives of the study are to evaluate the safety and biological efficacy of a cryopreserved formulation of OTL-203 in patients with the Hurler sub-type of MPS-I at one-year post-treatment. Engraftment and high IDUA expression were seen in the first two patients with sufficient follow-up to assess these parameters. In the first treated patient to achieve nine months follow-up in this study, rapid hematological engraftment was observed at 60 days post-treatment followed by supraphysiological activity of IDUA in blood and cerebrospinal fluid as well as normalization of urinary glycosaminoglycans in urine. As of the data presented at the ASGCT meeting, safety data from the four patients treated indicate that the conditioning regimen was generally well-tolerated. One patient who was known to have high anti-IDUA antibody levels prior to gene therapy experienced acute anaphylactic reaction shortly post-treatment. This was appropriately treated and the patient has since been discharged in good condition. The study is anticipated to enroll up to eight patients by the first half of 2020.

Corporate information

We were originally incorporated under the laws of England and Wales in August 2018 as Orchard Rx Limited (now known as Orchard Therapeutics plc) to become a holding company for Orchard Therapeutics Limited (now known as Orchard Therapeutics (Europe) Limited). Orchard Rx Limited subsequently re-registered as a public limited company and its name was changed from Orchard Rx Limited to Orchard Therapeutics plc in October 2018. Orchard Therapeutics Limited was

originally incorporated under the laws of England and Wales in September 2015 as Newincco 1387 Limited and subsequently changed its name to Orchard Therapeutics Limited in November 2015 and to Orchard Therapeutics (Europe) Limited in October 2018. Our registered office is located at 108 Cannon Street, London EC4N 6EU, United Kingdom, and our telephone number is +44 (0) 20 3808 8286. Our website address is www.orchard-tx.com. We do not incorporate the information on or accessible through our website into this prospectus, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus.

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. In particular, you should evaluate the specific factors set forth in the section titled “Risk factors” included in this prospectus and in our Annual Report on Form 20-F for the year ended December 31, 2018 and subsequent filings with the SEC, incorporated by reference herein before deciding whether to invest in our ADSs. Among these important risks are, but not limited to, the following:

- We have incurred net losses since inception. We expect to incur net losses for the foreseeable future and may never achieve or maintain profitability.
- The interim data and ad hoc analyses summarized in this prospectus are current as of the dates specified and are preliminary in nature. Our company-sponsored clinical trials of OTL-101 for ADA-SCID, OTL-200 for MLD and OTL-103 for WAS and the investigator-sponsored clinical trials for OTL-102 for X-CGD and OTL-300 for TDT are ongoing and not complete. Success in preclinical studies or early clinical trials may not be indicative of results obtained in later trials.
- The results from our clinical trials for OTL-101 for ADA-SCID, OTL-200 for MLD, OTL-103 for WAS and for any of our other product candidates may not be sufficiently robust to support the submission of marketing approval for our product candidates. Before we submit our product candidates for marketing approval, the FDA and/or the EMA may require us to conduct additional clinical trials, or evaluate patients for an additional follow-up period.
- Gene therapies are novel, complex and difficult to manufacture. We have limited manufacturing experience. We could experience manufacturing problems that result in delays in the development or commercialization of our product candidates or otherwise harm our business.
- We currently have limited sales and marketing capabilities. If we are unable to establish effective sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates that may be approved, we may not be successful in commercializing our product candidates if and when approved, and we may be unable to generate any product revenue.
- Third parties may claim that we are infringing, misappropriating or otherwise violating their intellectual property rights, which intellectual property infringement may prevent or delay our development and commercialization efforts and have a material adverse effect on our business.

- We are aware of third-party issued U.S. and foreign patents relating to the lentiviral vectors used in the manufacture or use of our product candidates. While we believe that we have defenses against a claim of infringement of these patents, including that such patents would not be infringed by one or more of our product candidates and/or are not valid, we cannot guarantee that a court of competent jurisdiction will agree with our assessment.
- We face significant competition in our industry and there can be no assurance that our product candidates, if approved, will achieve acceptance in the market over existing established therapies. In addition, our competitors may develop therapies that are more advanced or effective than ours, which may adversely affect our ability to successfully market or commercialize any of our product candidates.

Implications of being an emerging growth company and a foreign private issuer

We qualify as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. An emerging growth company may take advantage of specified reduced reporting and other burdens that are otherwise applicable generally to public companies. These provisions include an exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting pursuant to the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act.

We may take advantage of these exemptions for up to five years from the date of our initial public offering or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company upon the earlier to occur of: (i) the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more; (ii) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years; (iii) the date on which we are deemed to be a large accelerated filer under the rules of the SEC; or (iv) December 31, 2023. We may choose to take advantage of some but not all of these exemptions.

In addition, under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards until such time as those standards apply to private companies.

We are also considered a “foreign private issuer.” 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 continue to 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 with respect to a security registered under the Exchange Act;
- the requirement to comply with Regulation FD, which requires selective disclosure of material information;
- the sections of the Exchange Act requiring insiders to file public reports of their share 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 specified information, or current reports on Form 8-K upon the occurrence of specified significant events.

Both foreign private issuers and emerging growth companies are also 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. As a result, some investors may find our ADSs less attractive, which could result in a less active trading market for our ADSs or more volatility in the price of our ADSs.

The offering

ADSs offered by us	9,000,000 ADSs, each representing one ordinary share.
Underwriters' option to purchase additional ADSs	We have granted the underwriters an option for a period of 30 days from the date of this prospectus to purchase up to an additional 1,350,000 ADSs from us.
Ordinary shares to be outstanding immediately after this offering	94,867,028 ordinary shares (or 96,217,028 ordinary shares if the underwriters exercise in full their option to purchase an additional 1,350,000 ADSs).
American depositary shares	Each ADS represents one ordinary share, nominal value £0.10 per share. You will have the rights of an ADS holder or beneficial owner (as applicable) as provided in the deposit agreement among us, the depositary and all holders and beneficial owners of ADSs issued thereunder. 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.
ADS depositary	Citibank, N.A.
Use of proceeds	We estimate that the net proceeds to us from this offering, after deducting the estimated underwriting discounts and estimated offering expenses payable by us, to be approximately $157.6 million based on an assumed public offering price of $18.91 per ADS, the last reported sale price of our ADSs on the Nasdaq Global Select Market on May 31, 2019 . We intend to use the net proceeds from this offering to fund ongoing development of our product candidates; ongoing commercialization of Strimvelis in the European Union and the expansion of our marketing and sales infrastructure in key markets, including the United States and Europe; and the remainder for ongoing business development, general and administrative expenses, working capital and other general corporate purposes. See "Use of proceeds" for a more complete description of the intended use of proceeds from this offering.
Risk factors	See "Risk factors" and the other information included in this prospectus and incorporated by reference for a discussion of factors you should carefully consider before deciding to invest in our ADSs.
Nasdaq Global Select Market symbol	"ORTX."

The total number of ordinary shares to be outstanding after this offering is based on 85,867,028 of our ordinary shares outstanding as of March 31, 2019, and excludes:

- 12,576,677 ordinary shares issuable upon the exercise of options for ordinary shares outstanding as of March 31, 2019, with a weighted-average exercise price of $5.15 per share;
- 573,672 ordinary shares issuable upon the vesting of performance-based restricted stock units, or RSUs, outstanding as of March 31, 2019;
- 5,518,538 ordinary shares available for future issuance under our 2018 Share Option and Incentive Plan as of March 31, 2019; and
- 1,709,604 ordinary shares available for future issuance under our 2018 Employee Share Purchase Plan as of March 31, 2019.

Unless otherwise indicated, all information contained in this prospectus also reflects and assumes:

- no issuance or exercise of outstanding options after March 31, 2019; and
- no exercise by the underwriters of their option to purchase up to 1,350,000 additional shares of ADSs in this offering.

Risk factors

Investing in our ADSs involves a high degree of risk. Before you invest in our ADSs, you should carefully consider the following risks, as well as general economic and business risks, including those set forth under the heading "Risk Factors" in our Annual Report on Form 20-F for the fiscal year ended December 31, 2018 incorporated by reference herein, and all of the other information contained in this prospectus and in the documents incorporated by reference herein. Any of the following risks, including those discussed in the documents incorporated by reference herein, could have a material adverse effect on our business, operating results and financial condition and cause the trading price of our ADSs to decline, which would cause you to lose all or part of your investment. When determining whether to invest, you should also refer to the other information contained or incorporated by reference in this prospectus, including our financial statements and the related notes thereto. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us may also adversely affect our business

Risks related to this offering and ownership of our securities

The market price of our ADSs may be highly volatile, and may fluctuate due to factors beyond our control. An active public trading market for our ADSs may not be sustained.

We completed our initial public offering in November 2018. Prior to that time, there was no public trading market for our ADSs or ordinary shares. Although we have completed our initial public offering and our ADSs are listed and trading on the Nasdaq Global Select Market, an active trading market for our ADSs may not be sustained. If an active market for our ADSs is not sustained, it may be difficult for existing shareholders to sell our ADSs without depressing the market price for our securities or at all. An inactive trading market may also impair our ability to raise capital to continue to fund operations by selling ADSs and may impair our ability to acquire other companies or assets by using our ADSs as consideration.

In addition, the trading price of our ADSs has fluctuated, and is likely to continue to fluctuate significantly. The market price of our ADSs depends on a number of factors, some of which are beyond our control. In addition to the factors discussed in this "Risk factors" section and in the "Risk Factors" section of our Annual Report on Form 20-F for the year ended December 31, 2018, these factors include:

- adverse results or delays in preclinical studies or clinical trials;
- reports of adverse events in other gene therapy products or clinical trials of such products;
- an inability to obtain additional funding;
- failure by us to successfully develop and commercialize our product candidates;
- failure by us to maintain our existing strategic collaborations or enter into new collaborations;
- failure by us or our licensors and strategic partners to prosecute, maintain or enforce our intellectual property rights;
- changes in laws or regulations applicable to future products;
- an inability to obtain adequate product supply for our product candidates or the inability to do so at acceptable prices;

- adverse regulatory decisions;
- the introduction of new products, services or technologies by our competitors;
- failure by us to meet or exceed financial projections we may provide to the public;
- failure by us to meet or exceed the financial projections of the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us, our strategic partner or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent or shareholder litigation;
- changes in the market valuations of similar companies;
- sales of our ADSs by us or our shareholders in the future; and
- the trading volume of our ADSs.

In addition, companies trading in the stock market in general, and Nasdaq in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our ADSs, regardless of our actual operating performance.

If you purchase ADSs in this offering, you will suffer immediate dilution of your investment.

The public offering price of our ADSs is substantially higher than the adjusted net tangible book value per ADS. Therefore, if you purchase ADSs in this offering, you will pay a price per ADS that substantially exceeds our adjusted net tangible book value per ADS after this offering. Based on an assumed public offering price of $18.91 per ADS (which was the last reported sale price of our ADSs on the Nasdaq Global Select Market on May 31 , 2019), you will experience immediate dilution of $14.22 per ADS, representing the difference between our adjusted net tangible book value per ADS after this offering and the public offering price per ADS. After this offering, we will also have outstanding options to purchase ordinary shares with exercise prices lower than the public offering price. To the extent these outstanding options are exercised, there will be further dilution to investors in this offering. For further information regarding the dilution resulting from this offering, see the section titled “Dilution” in this prospectus.

Concentration of ownership of our ordinary shares (including ordinary shares in the form of ADSs) among our existing executive officers, directors and principal shareholders may prevent new investors from influencing significant corporate decisions.

Our executive officers, directors, greater than five percent shareholders and their affiliates beneficially own approximately 66.6% of our ordinary shares and, upon closing of this offering,

that same group will beneficially own approximately 60.5% of our outstanding ordinary shares. 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 determine 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. Among other consequences, this concentration of ownership may prevent or discourage unsolicited acquisition proposals that you may believe are in your best interest as one of our shareholders. Some of these persons or entities may have interests different than yours. For example, because many of these shareholders purchased their ordinary shares at prices substantially below the price at which ADSs are being sold in this offering and have held their ordinary shares for a longer period, they may be more interested in selling our company to an acquirer than other investors or they may want us to pursue strategies that deviate from the interests of other shareholders.

Future sales, or the possibility of future sales, of a substantial number of our securities could adversely affect the price of the shares and dilute shareholders.

If our existing shareholders sell, or indicate an intent to sell, substantial amounts of our securities in the public market, the trading price of the ADSs could decline significantly and could decline below the public offering price in this offering. Upon completion of this offering, and assuming no exercise of the underwriters' option to purchase additional ADSs, we will have 94,867,028 outstanding ordinary shares (including ordinary shares represented by the ADSs), of which approximately 625,075 are subject to a 90-day contractual lock-up. The representatives of the underwriters may permit us and the holders of the lock-up shares to sell shares or ADSs prior to the expiration of the lock-up agreements. See "Underwriting." After the lock-up agreements pertaining to this offering expire, and based on the number of ordinary shares (including ordinary shares represented by ADSs) outstanding upon completion of this offering, these approximately 625,075 additional ordinary shares will be eligible for sale in the public market, all of which shares are held by directors and certain members of our executive management and will be subject to volume limitations under Rule 144 under the Securities Act of 1933, as amended, or the Securities Act, for sales in the United States. In addition, ordinary shares subject to outstanding options under our equity incentive plans and the ordinary shares reserved for future issuance under our equity incentive plans are eligible for sale in the public market in the future, subject to volume limitations applicable to affiliates and the lock-up agreements described in the "Shares and ADSs eligible for future sale" section of this prospectus.

Holders of ADSs are not treated as holders of our ordinary shares.

By participating in this offering you will become a holder of ADSs with underlying ordinary shares in a company incorporated under English law. Holders of ADSs are not treated as holders of our ordinary shares, unless they withdraw the ordinary shares underlying their ADSs in accordance with the deposit agreement and applicable laws and regulations. The depositary is the holder of the ordinary shares underlying the ADSs. Holders of ADSs therefore do not have any rights as holders of our ordinary shares, other than the rights that they have pursuant to the deposit agreement. See "Description of American depositary shares."

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

Under current English law, a company's accumulated realized profits must exceed its accumulated realized losses (on a non-consolidated basis) before dividends can be declared and paid. Therefore, we must have distributable profits before declaring and paying 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. As a result, capital appreciation, if any, on our ADSs 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 at or above the public offering price. Investors seeking cash dividends should not purchase our ADSs in this offering.

A significant portion of our total outstanding ordinary shares are restricted from immediate resale but may be sold into the market in the near future, which could cause the market price of our ADSs to drop significantly.

Sales of a substantial number of our ADSs in the public market could occur at any time, subject to certain restrictions described below. These sales, or the perception in the market that holders of a large number of ADSs intend to sell, could reduce the market price of our ADSs. After this offering, assuming no exercise of the underwriters' option to purchase additional ADSs, we will have outstanding 94,867,028 ordinary shares based on the number of ordinary shares outstanding as of March 31, 2019, (or 96,217,028 ordinary shares if the underwriters exercise their option to purchase additional ADSs in full). This includes the 9,000,000 ADSs that we are selling in this offering (or 10,350,000 ADSs if the underwriters exercise their option to purchase additional ADSs in full), which may be resold in the public market immediately without restriction, unless purchased by our affiliates. 625,075 shares currently are restricted as a result of securities laws or lock-up agreements but will be able to be sold after the offering as described in the "Shares and ADSs eligible for future sale" and "Underwriting" sections of this prospectus. Moreover, after this offering, holders of an aggregate of approximately 32,862,902 ordinary shares will have rights, subject to certain conditions, to require us to file registration statements covering their ordinary shares or to include their ordinary shares in registration statements that we may file for ourselves or other shareholders. In addition, 12,576,677 ordinary shares reserved for issuance upon the exercise of existing options outstanding as of March 31, 2019 under our current equity incentive plans will become eligible for sale in the public market, subject to volume limitations applicable to affiliates and the lock-up agreements described in the "Underwriting" section of this prospectus.

In addition, J.P. Morgan Securities LLC, Goldman Sachs & Co. LLC, Cowen and Company, LLC and Barclays Capital Inc. may, in their sole discretion, release all or some portion of the ordinary shares subject to lock-up agreements at any time and for any reason. Sales of a substantial number of such ordinary shares upon expiration of the lock-up agreements, the perception that such sales may occur, or early release of these agreements, could cause our market price to fall or make it more difficult for you to sell your ADSs at a time and price that you deem appropriate.

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

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in the section entitled “Use of proceeds,” and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest the net proceeds from this offering in short-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our shareholders.

Special note regarding forward-looking statements

This prospectus and the documents incorporated by reference into it contain express or implied forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, that involve substantial risks and uncertainties. All statements other than statements of historical fact, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. In some cases, you can identify forward-looking statements by the words “may,” “might,” “will,” “could,” “would,” “should,” “expect,” “intend,” “plan,” “objective,” “anticipate,” “believe,” “estimate,” “predict,” “potential,” “continue,” “ongoing,” or the negative of these terms, or other comparable terminology intended to identify statements about the future. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. The forward-looking statements and opinions contained in this prospectus are based upon information available to our management as of the date of this prospectus and, while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. Forward-looking statements contained in this prospectus include, but are not limited to, statements about:

- the timing, progress and results of clinical trials and preclinical studies for our programs and product candidates, including statements regarding the timing of initiation and completion of trials or studies and related preparatory work, the period during which the results of the trials will become available and our research and development programs;
- the timing, scope or likelihood of regulatory submissions, filings, and approvals;
- our ability to develop and advance product candidates into, and successfully complete, clinical trials;
- our expectations regarding the size of the patient populations for our product candidates, if approved for commercial use;
- the implementation of our business model and our strategic plans for our business, commercial product, product candidates and technology;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the pricing and reimbursement of our commercial product and product candidates, if approved;
- the scalability and commercial viability of our manufacturing methods and processes, including our plans to develop our in-house manufacturing operations;
- the rate and degree of market acceptance and clinical utility of our commercial product and product candidates, in particular, and gene therapy, in general;
- our ability to establish or maintain collaborations or strategic relationships or obtain additional funding;

- our competitive position;
- the scope of protection we and/or our licensors are able to establish and maintain for intellectual property rights covering our commercial product and product candidates;
- developments and projections relating to our competitors and our industry;
- our expectations related to the use of proceeds from this offering;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- the impact of laws and regulations;
- our ability to contract with third party suppliers and manufacturers and their ability to perform adequately;
- our ability to attract and retain qualified employees and key personnel;
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act; and
- other risks and uncertainties, including those listed under the caption “Risk factors” in this prospectus as well as those risk factors that are incorporated by reference in this prospectus.

You should refer to the important factors in the cautionary statements included in this prospectus and in other documents incorporated herein for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements included or incorporated by reference in this prospectus will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

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.

Use of proceeds

We estimate that the net proceeds to us in this offering will be $157.6 million, after deducting the estimated underwriting discounts and estimated offering expenses payable by us, based on an assumed public offering price of $18.91 per ADS, which was the last reported sale price of our ADSs on the Nasdaq Global Select Market on May 31, 2019. If the underwriters exercise their option to purchase additional ADSs in full, we estimate that the net proceeds to us from this offering will be $181.4 million, after deducting the estimated underwriting discounts and estimated offering expenses payable by us.

Each $1.00 increase (decrease) in the assumed public offering price of $18.91 per ADS would increase (decrease) the net proceeds to us from this offering by $8.4 million, assuming that the number of ADSs offered by us, as set forth on the cover page of this prospectus, remains the same. An increase (decrease) of 1,000,000 in the number of ADSs we are offering would increase (decrease) the net proceeds to us from this offering by $17.6 million, assuming the assumed public offering price remains the same.

We expect to use the net proceeds from this offering as follows:

- approximately $70 million initiating trials to support registrations for OTL-102 for X-CGD and OTL-300 for TDT, establishing clinical proof of concept for OTL-201 for MPS-IIIA and OTL-203 for MPS-I, further progressing OTL-202 for MPS-IIIB and advancing our numerous additional preclinical programs;
- approximately $10 million to fund the ongoing commercialization of Strimvelis in the European Union and to expand our marketing and sales infrastructure in key markets, including the United States and Europe, in preparation for the potential commercial approval of OTL-101, OTL-200 and OTL-103;
- approximately $20 million to fund the ongoing development of our late-stage clinical product candidates, including completing registrational trials and submitting for regulatory approvals in the United States and Europe for OTL-101 for ADA-SCID, OTL-200 for MLD and OTL-103 for WAS; and
- the remainder to fund ongoing business development activities, general and administrative expenses, working capital and other general corporate purposes.

This expected use of net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. We may also use a portion of the net proceeds to in-license, acquire, or invest in additional businesses, technologies, products or assets. We cannot predict with certainty all of the particular uses for the net proceeds to be received upon the closing of this offering or the amounts that we will actually spend on the uses set forth above. Predicting the cost necessary to commercialize approved products and develop product candidates can be difficult and the amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development, our plans to develop our in-house drug product and vector manufacturing capabilities, the status of and results from clinical trials, any collaborations that we may enter into with third parties for our product candidates and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

Based on our planned use of the net proceeds from this offering and our existing cash, we estimate that such funds will be sufficient to fund our operations and capital expenditure requirements into the second half of 2021. We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect.

Pending our use of proceeds from this offering, we plan to invest these net proceeds in a variety of capital preservation instruments, including short-term, interest bearing obligations and investment-grade instruments.

Dividend policy

We have never declared or paid any cash dividend, and we do not anticipate declaring or paying any cash dividends in the foreseeable future. We intend to retain all available funds and any future earnings to fund the development and expansion of our business. See the section titled “Risk factors—Risks related to this offering and ownership of our securities—Because we do not anticipate paying any cash dividends on our ADSs in the foreseeable future, capital appreciation, if any, will be your sole source of gains and you may never receive a return on your investment.”

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.

Capitalization

The following table sets forth our cash and capitalization as of March 31, 2019 on:

- an actual basis; and
- an as adjusted basis giving effect to the sale of 9,000,000 ADSs in this offering.

The as adjusted calculations assume a public offering price of $18.91 per ADS, which was the last reported sale price of our ADSs on the Nasdaq Global Select Market on May 31, 2019, after deducting estimated underwriting discounts and estimated offering expenses payable by us.

You should read this information together with our audited consolidated financial statements and related notes incorporated by reference in this prospectus and the information set forth under the sections titled “Selected consolidated financial data” and “Use of proceeds” in this prospectus, “Operating and Financial Review and Prospects” included in our Annual Report on Form 20-F for the year ended December 31, 2018 incorporated herein by reference and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” included in our Report of Foreign Private issuer on Form 6-K furnished to the SEC on May 28, 2019 including the interim results for Orchard Therapeutics plc for the three months ended March 31, 2019 incorporated herein by reference.

	As of March 31, 2019 (in thousands, except share and per share data)	
	Actual	As adjusted(1)
Cash	$ 295,407	$ 453,034
Shareholders’ equity:		
Ordinary shares, £0.10 par value; authority to allot up to a maximum nominal value of £13,023,851.50, 85,865,557 issued and outstanding, actual; issued and outstanding, as adjusted	10,924	12,094
Additional paid-in capital	591,316	747,773
Accumulated other comprehensive (loss) income	6,214	6,214
Accumulated deficit	(320,978)	(320,978)
Total shareholders’ equity	287,476	445,103
Total capitalization	$ 287,476	$ 445,103

(1) The as adjusted balance sheet data give further effect to our issuance and sale of 9,000,000 shares of our ordinary shares in this offering at an assumed public offering price of $18.91 per share, which was the last reported sale price of our ADSs on the Nasdaq Global Select Market on May 31, 2019, after deducting estimated underwriting discounts and estimated offering expenses payable by us.

The as adjusted information discussed above is illustrative only and will change based on the actual public offering price and other terms of this offering determined at pricing. Each $1.00 increase (decrease) in the assumed public offering price of $18.91 per ADS, which was the last reported sale price of our ADSs on the Nasdaq Global Select Market on May 31, 2019, would increase (decrease) the as adjusted amount of each of cash, working capital, total shareholders' equity and total capitalization by $8.4 million, assuming that the number of ADSs offered by us, as set forth on the cover page of this prospectus, remains the same. An increase (decrease) of 1,000,000 in the number of ADSs offered by us, as set forth on the cover page of this prospectus, would increase (decrease) the as adjusted amount of each of cash, total shareholders' equity and total capitalization by $17.6 million, assuming no change in the public offering price per ADS.

The number of ordinary shares outstanding in the table above does not include:

- 12,576,677 ordinary shares issuable upon the exercise of options for ordinary shares outstanding as of March 31, 2019, with a weighted-average exercise price of $5.15 per share;
- 573,672 ordinary shares issuable upon the vesting of performance-based RSUs outstanding as of March 31, 2019;

- 5,518,538 ordinary shares available for future issuance under our 2018 Share Option and Incentive Plan as of March 31, 2019; and
- 1,709,604 ordinary shares available for future issuance under our 2018 Employee Share Purchase Plan as of March 31, 2019.

Dilution

If you invest in our ADSs in this offering, your interest will be immediately diluted to the extent of the difference between the public offering price per ADS in this offering and the as adjusted net tangible book value per ADS after this offering. Dilution results from the fact that the public offering price per ADS is substantially in excess of the net tangible book value per ADS. As of March 31, 2019, we had a historical net tangible book value of $287.5 million, or $3.35 per ordinary share (equivalent to $3.35 per ADS). Our net tangible book value per share represents total tangible assets less total liabilities, divided by the number of ordinary shares outstanding on March 31, 2019.

After giving effect the sale of 9,000,000 ADSs in this offering at an assumed public offering price of $18.91 per ADS, which was the last reported sale price of our ADSs on the Nasdaq Global Select Market on May 31, 2019, and after deducting the estimated underwriting discounts and estimated offering expenses payable by us, our as adjusted net tangible book value at March 31, 2019 would have been $4.69 per ordinary share, or $4.69 per ADS. This represents an immediate increase in as adjusted net tangible book value, of $1.34 per ADS to new investors and immediate dilution of $14.22 per ADS to new investors. The following table illustrates this dilution to new investors purchasing ADSs in this offering:

Assumed public offering price per ADS		$18.91
Historical net tangible book value per ADS as of March 31, 2019	$3.35	
Effect attributable to new investors purchasing ADSs in this offering(1)	1.34	
As adjusted net tangible book value per ADS as of March 31, 2019		4.69
Dilution per share to new investors purchasing ADSs in this offering		$14.22

(1) 9,000,000 outstanding ordinary shares were included in the dilution per share calculation attributable to new investors purchasing ADSs in this offering.

If the underwriters exercise their option to purchase additional ADSs in full, the as adjusted net tangible book value per ADS after the offering would be $4.87, the increase in net tangible book value per ADS to existing shareholders would be $1.52 and the immediate dilution in net tangible book value per ADS to new investors in this offering would be $14.04.

The table and discussion above does not include:

- 12,576,677 ordinary shares issuable upon the exercise of options for ordinary shares outstanding as of March 31, 2019, with a weighted-average exercise price of $5.15 per share;
- 573,672 ordinary shares issuable upon the vesting of performance-based RSUs outstanding as of March 31, 2019;
- 5,518,538 ordinary shares available for future issuance under our 2018 Share Option and Incentive Plan as of March 31, 2019; and
- 1,709,604 ordinary shares available for future issuance under our 2018 Employee Share Purchase Plan as of March 31, 2019.

To the extent that outstanding options are exercised, new options are issued under our 2018 Share Option and Incentive Plan, or we issue additional ordinary shares or ADSs in the future, there will be further dilution to investors participating in this offering.

Selected consolidated financial data

The following tables present our selected consolidated financial data as of the dates and for the periods indicated. We derived the selected consolidated statements of operations and comprehensive loss data for the years ended December 31, 2016, 2017 and 2018 and the consolidated balance sheet data as of December 31, 2017 and 2018 from our audited consolidated financial statements included in our Annual Report on Form 20-F for the year ended December 31, 2018, which is incorporated by reference in this prospectus. Consolidated balance sheet data as of December 31, 2016 comes from other financial statements not incorporated by reference in this prospectus. The financial data for the three-month periods ended March 31, 2019 and 2018 are derived from our unaudited condensed consolidated financial statements included in our report of Foreign Private Issuer on Form 6-K furnished to the SEC on May 28, 2019, which is incorporated by reference in this prospectus.

We prepare our consolidated financial statements in accordance with U.S. GAAP. Our historical results are not necessarily indicative of our future results. You should read this data together with our consolidated financial statements and related notes and information incorporated by reference herein and the information under the section titled “Capitalization.”

Our functional currency is the pound sterling. However, for financial reporting purposes, our financial statements, which are prepared using the functional currency, have been translated into U.S. Dollars. Our assets and liabilities are translated at the exchange rates at the balance sheet date, our revenue and expenses are translated at average exchange rates and shareholders’ equity is translated based on historical exchange rates. Translation adjustments are not included in determining net loss but are included in foreign exchange translation adjustment within accumulated other comprehensive (loss) income, a component of shareholders’ equity.

Foreign currency transactions in currencies different from the functional currency are translated into the functional currency using the exchange rates prevailing at the dates of the transactions. Foreign exchange differences resulting from the settlement of such transactions and from the translation at period-end exchange rates of monetary assets and liabilities denominated in foreign currencies are recorded in other expense in the statement of operations and comprehensive loss.

In August 2018, Orchard Rx Limited (now known as Orchard Therapeutics plc) was incorporated under the laws of England and Wales to become the holding company for Orchard Therapeutics Limited (now known as Orchard Therapeutics (Europe) Limited). Subsequently, Orchard Rx Limited re-registered as a public limited company and its name was changed from Orchard Rx Limited to Orchard Therapeutics plc. Prior to its incorporation, Orchard Rx Limited had only engaged in activities incidental to its formation. For more details on the corporate

reorganization, see Note 7 to our audited financial statements included in our Annual Report on Form 20-F for the year ended December 31, 2018 incorporated herein by reference.

	Year ended December 31,			Three months ended March 31,	
	2018	2017	2016	2019	2018
					(in thousands)
Consolidated Statement of Operations and Comprehensive Loss Data:					
Product Sales, net	$ 2,076	$ —	$ —	$ —	$ —
Costs and operating expenses:					
Cost of product sales	422	—	—	—	—
Research and development	205,319	32,527	16,206	17,493	9,171
Selling, general and administrative	31,366	5,985	2,997	10,790	4,527
Total operating expenses	237,107	38,512	19,203	28,283	13,698
Loss from operations	(235,031)	(38,512)	(19,203)	(28,283)	(13,698)
Other income (expense), net	5,506	(1,179)	138	(1,863)	(1,696)
Net loss before income taxes	(229,525)	(39,691)	(19,065)	(30,146)	(15,394)
Income tax expense	(970)	(53)	(20)	(593)	83
Net loss attributable to ordinary shareholders	$ (230,495)	$ (39,744)	$ (19,085)	$ (30,739)	$ (15,311)
Other comprehensive (loss) income:					
Foreign currency translation adjustment	(964)	4,398	(271)	3,051	3,432
Total comprehensive loss	$ (231,459)	$ (35,346)	$ (19,356)	$ (27,688)	$ (11,879)
Net loss per share attributable to ordinary shareholders, basic and diluted	$ (10.22)	$ (4.48)	$ (2.69)	$ (0.35)	$ (1.53)
Weighted average number of ordinary shares outstanding, basic and diluted	22,559,389	8,872,768	7,100,528	87,010,596	9,983,754

	As of December 31,			As of March 31,
	2018	2017	2016	2019
				(in thousands)
Consolidated Balance Sheet Data:				
Cash	$335,844	$89,856	$ 3,497	$ 295,407
Working capital(1)	307,612	83,466	163	283,886
Total assets	366,042	97,294	4,283	329,319
Convertible preferred shares in temporary equity	—	—	16,970	—
Total shareholders' (deficit) equity	311,338	86,405	(16,524)	287,476

(1) We define working capital as current assets less current liabilities.

Management

The following table sets forth the name, age and position our executive officers and directors as of March 31, 2019.

Name	Age	Position(s)
Executive Officers:		
Mark Rothera	56	President, Chief Executive Officer and Director
Frank E. Thomas	49	Chief Financial Officer and Chief Business Officer
Bobby Gaspar, M.D., Ph.D.	55	Chief Scientific Officer and Director
Non-Executive Directors:		
James A. Geraghty	64	Chairman of the Board of Directors
Joanne T. Beck, Ph.D.	58	Director
Marc Dunoyer	66	Director
Jon Ellis, Ph.D.	52	Director
Charles A. Rowland, Jr.	60	Director
Hong Fang Song	53	Director
Alicia Secor	56	Director

There are no family relationships among any of our executive officers or directors. The business address of each of our directors and members of senior management is c/o Orchard Therapeutics plc, 108 Cannon Street, London EC4N 6EU, United Kingdom.

Related party transactions

Since January 1, 2016, we have engaged in the following transactions with our directors, executive officers or holders of more than 5% of our outstanding share capital and their affiliates, which we refer to as our related parties.

GSK asset purchase and license agreement

On April 11, 2018, we entered the GSK Agreement pursuant to which GSK transferred to us its portfolio of approved and investigational rare disease gene therapies, including Strimvelis, the first approved gene therapy by the EMA, two late-stage clinical gene therapy programs in ongoing registrational trials: OTL-200 for MLD and OTL-103 for WAS; and OTL-300, a clinical-stage gene therapy program for TDT. In addition, under this agreement, GSK novated to us their R&D Agreement with the Telethon-OSR which includes an exclusive option to license three preclinical programs in development at San Raffaele Hospital in Italy for MPS-I, CGD and GLD.

Upon execution of the agreement, we paid GSK a one-time upfront fee of £10.0 million, and we issued GSK 12,455,252 of our Series B-2 convertible preferred shares. Under the GSK Agreement we are also obligated to pay non-refundable royalties and milestone payments in relation to the gene therapy programs acquired and OTL-101. We will pay a mid single-digit percentage royalty on the combined annual net sales of ADA-SCID products, which includes Strimvelis and our product candidate, OTL-101. We will also pay tiered royalty rates at percentages from the mid-teens to the low twenties for the MLD and WAS products, upon marketing approval, calculated as percentages of aggregate cumulative net sales of the MLD and WAS products, respectively. We will pay a tiered royalty at percentages from the high single-digits to the low teens for the TDT product, upon marketing approval, calculated as percentages of aggregate annual net sales of the TDT product. These royalties owed to GSK are in addition to any royalties owed to other third parties under various license agreements for the GSK programs. In aggregate, we may pay up to £90.0 million of milestone payments upon achievement of certain sales milestones. Our royalty obligations with respect to MLD and WAS may be deferred for a certain period in the interest of prioritizing available capital to develop each product. Our royalty obligations are subject to reduction on a product-by-product basis in the event of market control by biosimilars, and will expire in April 2048. See “Business—License agreements—GSK asset purchase and license agreement” for further information regarding the GSK Agreement.

In connection with this agreement, we also entered into (i) a transitional services agreement with GSK on April 11, 2018, pursuant to which GSK has agreed to provide us certain transitional services in connection with the transfer of the assets acquired under the GSK Agreement, and (ii) an inventory sale agreement with GSK on April 11, 2018, pursuant to GSK agreed to transfer certain inventory related to the assets acquired under the GSK Agreement.

As a result of the GSK Agreement, GSK is currently a greater than 5% beneficial owner of our outstanding ordinary shares.

Director nomination agreement

In October 2018, we entered into a director nomination agreement with Glaxo Group Limited, or GSK, pursuant to which we have agreed to nominate and appoint to our board of directors a designee of GSK until such time as we obtain marketing approval and commercially launch OTL-200 for MLD.

Subscription of our Series A convertible preferred shares

In February 2016, with subsequent closings in May 2016, July 2016, August 2016, January 2017 and February 2017, we sold an aggregate of 16,806,299 shares of our Series A convertible preferred shares at a purchase price of £1.25 per share, pursuant to agreements entered into with the investors. The following table summarizes purchases of our Series A convertible preferred shares by related persons:

Shareholder	Series A convertible preferred shares	Total purchase price
Affiliates of F-Prime Capital(1)	16,006,000	£ 20,000,001

(1) Consists of (i) 8,003,000 shares of Series A convertible preferred shares held by F-Prime Capital Partners Healthcare Fund IV LP, and (ii) 8,003,000 shares of Series A convertible preferred shares held by F-Prime Capital Partners Healthcare Fund IV-A LP. F-Prime Capital is a holder of 5% or more of our outstanding ordinary shares.

Subscription of our Series B convertible preferred shares

In March 2017, with subsequent closings in August 2017, October 2017, December 2017 and January 2018, we sold an aggregate of 16,964,875 shares of our Series B convertible preferred shares at a subscription price of £5.022 per share, pursuant to agreements entered into with the investors. The following table summarizes purchases of our Series B convertible preferred shares by related persons:

Shareholder	Series B convertible preferred shares	Total purchase price
Entities affiliated with F-Prime Capital(1)	2,400,900	£ 12,057,000
Scottish Mortgage Investment Trust plc(2)	3,201,200	£ 16,076,000
Mark Rothera(3)	39,825	£ 199,998

(1) Consists of (i) 1,200.45- shares of Series B convertible preferred shares held by F-Prime Capital Partners Healthcare Fund IV LP, and (ii) 1,200,450 shares of Series B convertible preferred shares held by F-Prime Capital Partners Healthcare Fund IV-A LP. F-Prime Capital is a holder of 5% or more of our outstanding ordinary shares.

(2) Scottish Mortgage Investment Trust plc is a holder of 5% or more of our outstanding ordinary shares.

(3) Mr. Rothera is our President, Chief Executive Officer and a member of our board of directors.

Subscription of our Series C convertible preferred shares

In August 2018, we sold an aggregate of 17,421,600 shares of our Series C convertible preferred shares at a purchase price of $8.61 per share, pursuant to agreements entered into with the investors. The following table summarizes purchases of our Series C convertible preferred shares by related persons:

Shareholder	Series C convertible preferred shares	Total purchase price
Entities affiliated with Deerfield Management Company(1)	4,647,500	$ 49,999,992
Scottish Mortgage Investment Trust plc(2)	697,125	$ 7,499,998
Mark Rothera(3)	24,979	$ 268,796
Frank E. Thomas(4)	9,294	$ 100,000
James A. Geraghty(5)	34,391	$ 370,000
Joanne T. Beck, Ph.D.(6)	9,294	$ 100,000
Marc Dunoyer(7)	37,179	$ 400,000
Charles A. Rowland, Jr.(8)	9,294	$ 100,000

(1) Consists of (i) 464,750 shares of Series C convertible preferred shares held by Deerfield Special Situations Fund, L.P.; (ii) 2,091,375 shares of Series C convertible preferred shares held by Deerfield Private Design Fund III, L.P.; and (iii) 2,091,375 shares of Series C convertible preferred shares held by Deerfield Private Design Fund IV, L.P. Deerfield Management Company is a holder of 5% or more of our outstanding ordinary shares.

(2) Scottish Mortgage Investment Trust plc is a holder of 5% or more of our outstanding ordinary shares.

(3) Mr. Rothera is our President, Chief Executive Officer and a member of our board of directors.

(4) Mr. Thomas is our Chief Financial Officer and Chief Business Officer.

(5) Mr. Geraghty is the chairman of our board of directors.

(6) Dr. Beck is a member of our board of directors.

(7) Mr. Dunoyer is a member of our board of directors.

(8) Mr. Rowland, Jr. is a member of our board of directors.

Agreements with shareholders

In connection with the subscriptions of our Series A, Series B and Series C convertible preferred shares, we entered into subscription and shareholder agreements containing registration rights and information rights, among other things, with certain holders of our convertible preferred shares. These shareholder agreements terminated upon the closing of our initial public offering, except for the registration rights granted under our investors' rights agreement, as more fully described in "Description of share capital and articles of association—Registration rights."

As part of our reorganization, we entered into a share exchange agreement with the shareholders of Orchard Therapeutics Limited (now known as Orchard Therapeutics (Europe) Limited) pursuant to which all of the interests in Orchard Therapeutics Limited were exchanged for the same number and class of newly issued shares of Orchard Rx Limited (now Orchard Therapeutics plc) and, as a result, Orchard Therapeutics Limited became a wholly-owned subsidiary of Orchard Rx Limited.

Participation in Our Initial Public Offering

In November 2018, we sold an aggregate of 16,103,572 ADSs in our initial public offering at a price of $14.00 per share. The following table summarizes purchases of ADSs in our initial public offering by related persons:

Shareholder	ADSs in initial public offering	Total purchase price
Entities affiliated with Deerfield Management Company(1)	3,376,100	$47,265,400
Entities affiliated with RA Capital Management, LLC(2)	2,000,000	$28,000,000
Entities affiliated with Temasek(3)	1,000,000	$14,000,000
Scottish Mortgage Investment Trust plc(4)	925,000	$12,950,000
Mark Rothera(5)	18,500	$ 259,000
Frank E. Thomas(6)	5,000	$ 70,000
James A. Geraghty(7)	10,000	$ 140,000
Charles A. Rowland, Jr.(8)	3,000	$ 42,000

(1) Consists of (i) 1,209,434 ADSs held by Deerfield Partners, L.P., (ii) 1,083,333 ADSs held by Deerfield Private Design Fund III, L.P., and (iii) 1,083,333 ADSs held by Deerfield Private Design Fund IV, L.P.

(2) Consists of 2,000,000 ADSs held by RA Capital Healthcare Fund.

(3) Consists of 1,000,000 ADSs held by V-Sciences Investments Pte. Ltd.

(4) Consists of 925,000 ADSs held by Scottish Mortgage Investment Trust plc.

(5) Mr. Rothera is our President, Chief Executive Officer and a member of our board of directors.

(6) Mr. Thomas is our Chief Financial Officer and Chief Business Officer.

(7) Mr. Geraghty is the chairman of our board of directors.

(8) Mr. Rowland is a member of our board of directors.

Agreements with our executive officers and directors

We have entered into employment agreements with certain of our executive officers and service agreements with our non-executive directors. These agreements contain customary provisions and representations, including confidentiality, non-competition, non-solicitation and inventions assignment undertakings by the executive officers. However, the enforceability of the non-competition provisions may be limited under applicable law.

Indemnification agreements

We have entered into a deed of indemnity with each of our directors and executive officers. These agreements and our Articles of Association require us to indemnify our directors and executive officers to the fullest extent permitted by law.

Related person transaction policy

In connection with our initial public offering, we adopted a written related party transactions policy that such transactions must be approved by our audit committee. Pursuant to this policy, the audit committee has the primary responsibility for reviewing and approving or disapproving “related person transactions,” which are transactions between us and related persons in which the related person has a direct or indirect material interest. For purposes of this policy, a related person will be defined as a director, executive officer, nominee for director, or greater than 5% beneficial owner of any class of our voting securities, and their immediate family members.

Principal shareholders

The following table sets forth information with respect to the beneficial ownership of our ordinary shares as of May 15, 2019 for:

- each beneficial owner of 5% or more of our outstanding ordinary shares;
- each of our directors and executive officers; and
- all of our directors and executive officers as a group.

Beneficial ownership is determined in accordance with the rules of the SEC. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities and include ordinary shares that can be acquired within 60 days of May 15, 2019. These ordinary shares, however, are not included in the computation of the percentage ownership of any other person. The percentage ownership information shown in the column titled “Before Offering” in the table is based on 86,168,631 ordinary shares outstanding (including ordinary shares in the form of ADSs) as of May 15, 2019. The percentage ownership information shown in the column titled “After Offering” in the table is based on 94,867,028 ordinary shares outstanding after this offering, assuming the sale of 9,000,000 ADSs by us in this offering, and no exercise of the underwriters’ option to purchase additional ADSs.

Except as otherwise indicated, all of the shares reflected in the table are ordinary shares and all persons listed below have sole voting and investment power with respect to the shares beneficially owned by them, subject to applicable community property laws. The information is not necessarily indicative of beneficial ownership for any other purpose.

As of May 15, 2019, assuming that all of our ordinary shares represented by ADSs are held by residents of the United States other than the ADSs held by Scottish Mortgage Investment Trust and Temasek Holdings (Private) Limited, we estimate that approximately 58.5% of our outstanding ordinary shares (including ordinary shares underlying ADSs) were held in the United States by 42 holders of record. The actual number of holders is greater, as the number of record holders does not include beneficial owners whose ordinary shares are held in street name by brokers and other nominees. This number of holders of record also does not include holders whose shares may be held in trust by other entities.

Except as otherwise indicated in the table below, addresses of the directors, executive officers and named beneficial owners are in care of Orchard Therapeutics plc, 108 Cannon Street, London EC4N 6EU, United Kingdom.

Name of beneficial owner	Number of shares beneficially owned	Percentage of shares beneficially owned	
		Before offering	After offering
5% or Greater Shareholders:			
Entities affiliated with F-Prime(1)	20,407,650	23.7%	21.5%
Glaxo Group Limited(2)	12,455,252	14.5%	13.1%
Entities affiliated with Deerfield Management Company(3)	8,023,600	9.3%	8.5%
Entities affiliated with RA Capital Management(4)	4,845,933	5.6%	5.1%
Scottish Mortgage Investment Trust plc(5)	4,823,325	5.6%	5.1%
Entities affiliated with Temasek Holdings (Private) Limited(6)	4,319,049	5.0%	4.6%

Name of beneficial owner	Number of shares beneficially owned	Percentage of shares beneficially owned	
		Before offering	After offering
Executive Officers and Directors:			
Mark Rothera(7)	1,095,416	1.3	1.1
Frank E. Thomas(8)	238,831	*	*
Bobby Gaspar, M.D., Ph.D.(9)	971,666	1.1	1.0
James A. Geraghty(10)	167,903	*	*
Joanne T. Beck, Ph.D.(11)	37,938	*	*
Marc Dunoyer(12)	65,823	*	*
Jon Ellis, Ph.D.	—	—	—
Charles A. Rowland, Jr.(13)	40,938	*	*
Hong Fang Song	—	—	—
Alicia Secor	—	—	—
All current directors and executive officers as a group (11 persons)(14)	2,618,515	2.9%	2.7%

* Represents beneficial ownership of less than one percent.

(1) Consists of (i) 10,203,825 of our ordinary shares held of record by F-Prime Capital Partners Healthcare Fund IV LP; and (ii) 10,203,825 of our ordinary shares held of record by F-Prime Capital Partners Healthcare Fund IV-A LP. F-Prime Capital Partners Healthcare Advisors Fund IV LP is the general partner of F-Prime Capital Partners Healthcare Fund IV LP. F-Prime Capital Partners Healthcare Advisors Fund IV-A LP is the general partner of F-Prime Capital Partners Healthcare Fund IV-A LP. Each of F-Prime Capital Partners Healthcare Advisors Fund IV LP and F-Prime Capital Partners Healthcare Advisors Fund IV-A LP is solely managed by Impresa Management LLC, the managing member of its general partner and investment manager. Each of the entities listed above expressly disclaims beneficial ownership of the securities listed above except to the extent of any pecuniary interest therein. The address of these entities is 245 Summer Street, Boston, MA 02210.

(2) Consists of 12,445,252 of our ordinary shares. The board of directors of Glaxo Group Limited, or GSK, may be deemed to share voting and investment authority over the shares held by GSK. The address of GSK is 980 Great West Road, Brentford, Middlesex, London TW8 9GS, UK.

(3) Consists of (i) 464,750 of our ordinary shares held by Deerfield Special Situations Fund, L.P.; (ii) 3,174,708 of our ordinary shares and ADSs held by Deerfield Private Design Fund III, L.P.; (iii) 3,174,708 of our ordinary shares and ADSs held by Deerfield Private Design Fund IV, L.P.; and (iv) 1,209,434 of our ordinary shares and ADSs held by Deerfield Partners, L.P. Deerfield Mgmt, L.P. is the general partner of Deerfield Special Situations Fund, L.P and Deerfield Partners, L.P. Deerfield Mgmt III, L.P. is the general partner of Deerfield Private Design Fund III, L.P. Deerfield Mgmt IV, L.P. is the general partner of Deerfield Private Design Fund IV, L.P. (collectively with Deerfield Special Situations Fund, L.P. and Deerfield Private Design Fund III, L.P., the "Deerfield Funds"). Deerfield Management Company, L.P. is the investment manager of each of the Deerfield Funds. Mr. James E. Flynn is the sole member of the general partner of each of Deerfield Mgmt, L.P., Deerfield Mgmt III, L.P., Deerfield Mgmt. IV, L.P. and Deerfield Management Company, L.P. Deerfield Mgmt, L.P. may be deemed to beneficially own the shares held by Deerfield Special Situations Fund, L.P. and Deerfield Partners, L.P. Deerfield Mgmt III, L.P. may be deemed to beneficially own the shares held by Deerfield Private Design III, L.P. Deerfield Mgmt IV, L.P. may be deemed to beneficially own the shares held by Deerfield Private Design Fund IV, L.P. Each of Deerfield Management Company, L.P. and Mr. James E. Flynn may be deemed to beneficially own the securities held by the Deerfield Funds. The address of the Deerfield Funds is 780 Third Avenue, 37th Floor, New York, NY 10017.

(4) Based solely on a Schedule 13G filed jointly filed by RA Capital Management, LLC and Dr. Peter Kolchinsky on February 14, 2019. Consists of 4,845,933 of our ADSs held by RA Capital Healthcare Fund, L.P. RA Capital Management, LLC is the general partner of RA Capital Healthcare Fund, L.P. Dr. Kolchinsky is the manager of RA Capital Management, LLC. Each of RA Capital Management, LLC and Dr. Kolchinksy may be deemed to beneficially own the ADSs owned by RA Capital Healthcare Fund, L.P., and each of RA Capital Management, LLC and Dr. Kolchinsky expressly disclaim beneficial ownership of such securities. The address of RA Capital Management, LLC is 20 Park Plaza, Suite 1200, Boston, MA 02116.

(5) Consists of (i) 4,823,325 of our ordinary shares and ADSs held by Scottish Mortgage Investment Trust plc ("SMIT"). As investment manager for SMIT, Baillie Gifford & Co. may be deemed to share voting and investment control over the shares held by SMIT. SMIT is a publicly traded company. The address for SMIT is c/o Baillie Gifford & Co., Calton Square, 1 Greenside Row, Edinburgh EH1 3AN, United Kingdom.

(6) Based solely on a Schedule 13G filed jointly filed by Temasek Holdings (Private) Limited, or Temasek, Fullerton Management Pte Ltd, or FMPL, and Temasek Life Sciences Private Limited, or TLS, on November 13, 2018. Consists of (i) 3,319,049 ordinary shares and ADSs held by TLS Beta Pte. Ltd, and (ii) 1,000,000 ADSs held by V-Sciences Investments Pte Ltd. TLS Beta Pte. Ltd and V-Sciences Investments Pte Ltd are wholly-owned subsidiaries of TLS which is a wholly owned subsidiary of FMPL, which is a wholly owned subsidiary of Temasek. Each of TLS, FMPL, and Temasek, through the ownership described herein, may be deemed to beneficially own the shares held by TLS Beta Pte. Ltd and V-Sciences Investments Pte Ltd. The address of Temasek is 60B Orchard Road, #06-18 Tower 2, The Atrium@Orchard, Singapore 238891.

(7) Consists of (i) 90,304 of our ordinary shares and ADSs and (ii) 1,005,112 of our ordinary shares issuable upon exercise of options within 60 days of May 15, 2019.
(8) Consists of (i) 14,294 of our ordinary shares and (ii) 224,537 of our ordinary shares issuable upon exercise of options within 60 days of May 15, 2019.
(9) Consists of (i) 417,319 of our ordinary shares and (ii) 554,347 of our ordinary shares issuable upon exercise of options within 60 days of May 15, 2019.
(10) Consists of 44,391 of our ordinary shares and ADSs and (ii) 123,512 of our ordinary shares issuable upon exercise of options within 60 days of May 15, 2019.
(11) Consists of 9,294 of our ordinary shares and ADSs and (ii) 28,644 of our ordinary shares issuable upon exercise of options within 60 days of May 15, 2019.
(12) Consists of 37,179 of our ordinary shares and ADSs and (ii) 28,644 of our ordinary shares issuable upon exercise of options within 60 days of May 15, 2019.
(13) Consists of 12,294 of our ordinary shares and ADSs and (ii) 28,644 of our ordinary shares issuable upon exercise of options within 60 days of May 15, 2019.
(14) Consists of (i) 625,075 of our ordinary shares and ADSs and (ii) 1,933,440 of our ordinary shares issuable upon exercise of options within 60 days of May 15, 2019.

Description of share capital and articles of association

The following describes our issued share capital, summarizes the material provisions of our articles of association and highlights certain differences in corporate law in the United Kingdom and the United States. Please note that this summary is not intended to be exhaustive. For further information, please refer to the full version of our articles of association, which are incorporated by reference herein.

We were incorporated pursuant to the laws of England and Wales as Orchard Rx Limited (now known as Orchard Therapeutics plc) in August 2018 to become a holding company for Orchard Therapeutics Limited (now known as Orchard Therapeutics (Europe) Limited). Subsequently, in October 2018, Orchard Rx Limited re-registered as a public limited company and its name changed to Orchard Therapeutics plc.

We are registered with the Registrar of Companies in England and Wales under number 11494381, and our registered office is at 108 Cannon Street, London EC4N 6EU, United Kingdom.

Certain resolutions were passed by our shareholders in connection with our initial public offering. These include resolutions for the:

- adoption of new articles of association that became effective upon the completion of our initial public offering. See "—Articles of association" below;
- general authorization of our directors for purposes of Section 551 of the Companies Act 2006 to issue shares in the company and grant rights to subscribe for or convert any securities into shares in the company up to a maximum aggregate nominal amount of £13,023,851.50 for a period of five years; and
- empowering of our directors pursuant to Section 570 of Companies Act 2006 to issue equity securities for cash pursuant to the Section 551 authority referred to above as if the statutory preemption rights under Section 561(1) of the Companies Act 2006 did not apply to such allotments.

Issued share capital

As of March 31, 2019, our issued share capital was 85,867,028 ordinary shares with a nominal value of £0.10 per share.

Ordinary shares

In accordance with our Articles of Association, 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 on all matters to be voted on by shareholders generally;
- the holders of the ordinary shares are entitled to receive notice of, attend, speak and vote at our general meetings; and
- the 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 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. Holders of our ADSs are not treated as one of our shareholders and their names are therefore not entered in our share register. The depositary, the custodian or their nominees is the holder of the shares underlying our ADSs. Holders of our ADSs have a right to receive the ordinary shares underlying their ADSs. For discussion on our ADSs and ADS holder rights, see “Description of American depositary shares” in this prospectus.

Under the Companies Act 2006, we must enter an allotment of shares in our share register as soon as practicable and in any event within two months of the allotment. We will perform all procedures necessary to update the share register to reflect the ordinary shares being sold in this offering, including updating the share register with the number of ordinary shares to be issued to the depositary upon the closing of this offering. We also are required by the Companies Act 2006 to register a transfer of shares (or give the transferee notice of and reasons for refusal as the transferee may reasonably request) 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 delay 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 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). In October 2018, our shareholders approved the exclusion of preemptive rights for a period of five years from the date of approval, 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). In October 2018, our shareholders approved the exclusion of preemptive rights for the allotment of ordinary shares in connection with this offering.

Registration rights

The holders of 32,862,902 shares of our ordinary shares are entitled to rights with respect to the registration of these securities under the Securities Act. These rights are provided under the terms of an investment and shareholders’ agreement between us and holders of our convertible preferred shares, which were subsequently converted into ordinary shares in connection with our initial public offering in November 2018. The investment and shareholders’ agreement includes demand registration rights, short-form registration rights and piggyback registration rights.

Demand registration rights

The holders of 32,862,902 shares of our ordinary shares are entitled to demand registration rights. Under the terms of the investment and shareholders' agreement, we will be required, upon the written request of holders of a majority of these securities to file a registration statement and use best efforts to effect the registration of all or a portion of these shares for public resale. We are required to effect only two registrations pursuant to this provision of the investment and shareholders' agreement.

Short-form registration rights

Pursuant to the investment and shareholders' agreement, if we are eligible to file a registration statement on Form F-3 or Form S-3, upon the written request of holders of a majority of these securities at an aggregate offer price of at least $5.0 million, we will be required to effect a registration of such shares. We are required to effect only two registrations in any twelve month period pursuant to this provision of the investment and shareholders' agreement. The right to have such shares registered on Form F-3 or Form S-3 is further subject to other specified conditions and limitations.

Piggyback registration rights

Pursuant to the investment and shareholders' agreement, if we register any of our securities either for our own account or for the account of other security holders, other than in connection with our initial public offering or a registration for any employee benefit plan, corporate reorganization, or the offer or sale of debt securities, the holders of these shares are entitled to include their shares in the registration. Subject to certain exceptions contained in the investment and shareholders' agreement, we and the underwriters may limit the number of shares included in the underwritten offering to the number of shares which we and the underwriters determine in our sole discretion will not jeopardize the success of the offering.

Indemnification

Our investors' rights agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

Expiration of registration rights

The registration rights granted under the investment and shareholders' agreement will terminate on the earliest of (i) a deemed liquidation event, as defined in our Articles of Association, and (ii) the fifth anniversary of the completion of our initial public offering.

Articles of association

Our Articles of Association, or the Articles, were approved by our shareholders prior to the completion of our initial public offering and were adopted with effect from the completion of the initial public offering. A summary of the terms of the Articles is set out below. The summary below is not a complete copy of the terms of the Articles.

The Articles contain no specific restrictions on our purpose and therefore, by virtue of section 31(1) of the Companies Act 2006, our purpose is unrestricted.

The Articles contain, among other things, provisions to the following effect:

Share capital

Our share capital currently consists of ordinary shares. We may issue shares with such rights or restrictions as may be determined by ordinary resolution, including shares which are to be redeemed, or are liable to be redeemed at our option or the holder of such shares.

Voting

The shareholders have the right to receive notice of, and to vote at, our general meetings. Each shareholder who is present in person (or, being a corporation, by representative) at a general meeting on a show of hands has one vote and, on a poll, every such holder who is present in person (or, being a corporation, by representative) or by proxy has one vote in respect of every share held by him.

Variation of rights

Whenever our share capital is divided into different classes of shares, the special rights attached to any class may be varied or abrogated either with the consent in writing of the holders of three-fourths in nominal value of the issued shares of that class or with the sanction of a special resolution passed at a general meeting of the holders of the shares of that class and may be so varied and abrogated whilst the company is a going concern.

Dividends

We may, subject to the provisions of the Companies Act 2006 and the Articles, by ordinary resolution from time to time declare dividends to be paid to shareholders not exceeding the amount recommended by our board of directors. Subject to the provisions of the Companies Act 2006, in so far as, in the board of directors' opinions, our profits justify such payments, the board of directors may pay interim dividends on any class of our shares.

Any dividend unclaimed after a period of 12 years from the date such dividend was declared or became payable shall, if the board of directors resolve, be forfeited and shall revert to us. No dividend or other moneys payable on or in respect of a share shall bear interest as against us.

Liquidation Preference

On a distribution of assets on a liquidation, the surplus assets remaining after payment of liabilities shall be distributed among the holders of ordinary shares pro rata to the number of ordinary shares held.

Transfer of ordinary shares

Each member may transfer all or any of his shares which are in certificated form by means of an instrument of transfer in any usual form or in any other form which the board of directors may approve. Each member may transfer all or any of his shares which are in uncertificated form by means of a "relevant system" (i.e., the CREST System) in such manner provided for, and subject as provided in, the CREST Regulations.

The Board may, in its absolute discretion, refuse to register a transfer of certificated shares unless:

(i) it is for a share which is fully paid up;

(ii) it is for a share upon which the company has no lien;

(iii) it is only for one class of share;

(iv) it is in favor of a single transferee or no more than four joint transferees;

(v) it is duly stamped or is duly certificated or otherwise shown to the satisfaction of the board of directors to be exempt from stamp duty; and

(vi) it is delivered for registration to the registered office of the company (or such other place as the board of directors may determine), accompanied (except in the case of a transfer by a person to whom the company is not required by law to issue a certificate and to whom a certificate has not been issued or in the case of a renunciation) by the certificate for the shares to which it relates and such other evidence as the board of directors may reasonably require to prove the title of the transferor (or person renouncing) and the due execution of the transfer or renunciation by him or, if the transfer or renunciation is executed by some other person on his behalf, the authority of that person to do so.

The board of directors may refuse to register a transfer of uncertificated shares in any circumstances that are allowed or required by the CREST Regulations and the CREST System.

Allotment of shares and preemption rights

Subject to the Companies Act 2006 and to any rights attached to existing shares, any share may be issued with or have attached to it such rights and restrictions as the company may by ordinary resolution determine, or if no ordinary resolution has been passed or so far as the resolution does not make specific provision, as the board of directors may determine (including shares which are to be redeemed, or are liable to be redeemed at the option of the company or the holder of such shares).

In accordance with section 551 of the Companies Act 2006, the board of directors may be generally and unconditionally authorized to exercise all the powers of the company to allot shares up to an aggregate nominal amount equal to the amount stated in the relevant ordinary resolution authorizing such allotment. The authorities referred to above were included in the special resolution passed in October 2018 and remain in force at the date of this prospectus.

The provisions of section 561 of the Companies Act 2006 (which confer on shareholders rights of preemption in respect of the allotment of equity securities which are paid up in cash) apply to the company except to the extent disapplied by special resolution of the company. Such preemption rights have been disapplied pursuant to the special resolution passed in October 2018.

Alteration of share capital

The company may by ordinary resolution consolidate or divide all of its share capital into shares of larger nominal value than its existing shares, or cancel any shares which, at the date of the ordinary resolution, have not been taken or agreed to be taken by any person and diminish the amount of its share capital by the nominal amount of shares so cancelled or sub-divide its shares, or any of them, into shares of smaller nominal value.

The company may, in accordance with the Companies Act 2006, reduce or cancel its share capital or any capital redemption reserve or share premium account in any manner and with and subject to any conditions, authorities and consents required by law.

Board of directors

Unless otherwise determined by the company by ordinary resolution, the number of directors (other than any alternate directors) shall not be less than two, but there shall be no maximum number of directors.

Subject to the Articles and the Companies Act 2006, the company may by ordinary resolution appoint a person who is willing to act as a director and the board of directors shall have power at any time to appoint any person who is willing to act as a director, in both cases either to fill a vacancy or as an addition to the existing board of directors.

The Articles provide that our board of directors will be divided into three classes, each of which will consist, as nearly as possible, of one-third of the total number of directors constituting our entire board and which will serve staggered three-year terms. At each annual general meeting, the successors of directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election.

At every subsequent annual general meeting any director who either (i) has been appointed by the board of directors since the last annual general meeting or (ii) was not appointed or reappointed at one of the preceding two annual general meetings, must retire from office and may offer themselves for reappointment by the shareholders by ordinary resolution.

Subject to the provisions of the Articles, the board of directors may regulate their proceedings as they deem appropriate. A director may, and the secretary at the request of a director shall, call a meeting of the directors.

The quorum for a meeting of the board of directors shall be fixed from time to time by a decision of the board of directors, but it must never be less than two and unless otherwise fixed, it is two.

Questions and matters requiring resolution arising at a meeting shall be decided by a majority of votes of the participating directors, with each director having one vote. In the case of an equality of votes, the chairman will only have a casting vote or second vote when an acquisition has been completed.

Directors shall be entitled to receive such remuneration as the board shall determine for their services to the company as directors, and for any other service which they undertake for the company provided that the aggregate fees payable to the directors must not exceed £250,000 per annum. The directors shall also be entitled to be paid all reasonable expenses properly incurred by them in connection with their attendance at meetings of shareholders or class meetings, board of director or committee meetings or otherwise in connection with the exercise of their powers and the discharge of their responsibilities in relation to the company.

The board of directors may, in accordance with the requirements in the Articles, authorize any matter proposed to them by any director which would, if not authorized, involve a director breaching his duty under the Companies Act 2006, to avoid conflicts of interests.

A director seeking authorization in respect of such conflict shall declare to the board of directors the nature and extent of his interest in a conflict as soon as is reasonably practicable. The director

shall provide the board with such details of the matter as are necessary for the board to decide how to address the conflict together with such additional information as may be requested by the board.

Any authorization by the board of directors will be effective only if:

(i) to the extent permitted by the Companies Act 2006, the matter in question shall have been proposed by any director for consideration in the same way that any other matter may be proposed to the directors under the provisions of the Articles;

(ii) any requirement as to the quorum for consideration of the relevant matter is met without counting the conflicted director and any other conflicted director; and

(iii) the matter is agreed to without the conflicted director voting or would be agreed to if the conflicted director's and any other interested director's vote is not counted.

Subject to the provisions of the Companies Act 2006, every director, secretary or other officer of the company (other than an auditor) is entitled to be indemnified against all costs, charges, losses, damages and liabilities incurred by him in the actual purported exercise or discharge of his duties or exercise of his powers or otherwise in relation to them.

General meetings

The company must convene and hold general meetings in accordance with the Companies Act. Under the Companies Act 2006, an annual general meeting must be called by notice of at least 21 days and a general meeting must be called by notice of at least 14 days.

No business shall be transacted at any general meeting unless a quorum is present when the meeting proceeds to business, but the absence of a quorum shall not preclude the choice or appointment of a chairman of the meeting which shall not be treated as part of the business of the meeting. Save as otherwise provided by the Articles, two shareholders present in person or by proxy and entitled to vote shall be a quorum for all purposes.

Borrowing Powers

Subject to the Articles and the Companies Act 2006, the board of directors may exercise all of the powers of the company to:

(a) borrow money;

(b) indemnify and guarantee;

(c) mortgage or charge;

(d) create and issue debentures and other securities; and

(e) give security either outright or as collateral security for any debt, liability or obligation of the company or of any third party.

Capitalization of profits

The directors may, if they are so authorized by an ordinary resolution of the shareholders, decide to capitalize any undivided profits of the company (whether or not they are available for

distribution), or any sum standing to the credit of the company's share premium account or capital redemption reserve. The directors may also, subject to the aforementioned ordinary resolution, appropriate any sum which they so decide to capitalize to the persons who would have been entitled to it if it were distributed by way of dividend and in the same proportions.

Uncertificated shares

Subject to the Companies Act 2006, the board of directors may permit title to shares of any class to be issued or held otherwise than by a certificate and to be transferred by means of a "relevant system" (i.e., the CREST System) without a certificate.

The board of directors may take such steps as it sees fit in relation to the evidencing of and transfer of title to uncertificated shares, any records relating to the holding of uncertificated shares and the conversion of uncertificated shares to certificated shares, or vice-versa.

The company may by notice to the holder of an uncertificated share, require that share to be converted into certificated form.

The board of directors may take such other action that the board considers appropriate to achieve the sale, transfer, disposal, forfeiture, re-allotment or surrender of an uncertified share or otherwise to enforce a lien in respect of it.

Other relevant laws and regulations

Mandatory bid

(i) The Takeover Code will apply to the company for so long as its central management and control is considered to be in the United Kingdom. Under the Takeover Code, where:

(a) any person, together with persons acting in concert with him, acquires, whether by a series of transactions over a period of time or not, an interest in shares which (taken together with shares in which he is already interested, and in which persons acting in concert with him are interested) carry 30% or more of the voting rights of a company; or

(b) any person who, together with persons acting in concert with him, is interested in shares which in the aggregate carry not less than 30% of the voting rights of a company but does not hold shares carrying more than 50% of such voting rights and such person, or any person acting in concert with him, acquires an interest in any other shares which increases the percentage of shares carrying voting rights in which he is interested;

such person shall, except in limited circumstances, be obliged to extend offers, on the basis set out in Rules 9.3, 9.4 and 9.5 of the Takeover Code, to the holders of any class of equity share capital, whether voting or non-voting, and also to the holders of any other class of transferable securities carrying voting rights. Offers for different classes of equity share capital must be comparable; the Takeover Panel should be consulted in advance in such cases.

(ii) An offer under Rule 9 of the Takeover Code must be in cash and at the highest price paid for any interest in the shares by the person required to make an offer or any person acting in concert with him during the 12 months prior to the announcement of the offer.

(iii) Under the Takeover Code, a "concert party" arises where persons acting together pursuant to an agreement or understanding (whether formal or informal and whether or not in writing) actively cooperate, through the acquisition by them of an interest in shares in a company, to

obtain or consolidate control of the company. “Control” means holding, or aggregate holdings, of an interest in shares carrying 30% or more of the voting rights of the company, irrespective of whether the holding or holdings give *de facto* control.

Squeeze-out

(i) Under sections 979 to 982 of the Companies Act 2006, if an offeror were to acquire, or unconditionally contract to acquire, not less than 90% of the ordinary shares of the company, it could then compulsorily acquire the remaining 10%. It would do so by sending a notice to outstanding shareholders telling them that it will compulsorily acquire their shares, provided that no such notice may be served after the end of: (a) the period of three months beginning with the day after the last day on which the offer can be accepted; or (b) if earlier, and the offer is not one to which section 943(1) of the Companies Act 2006 applies, the period of six months beginning with the date of the offer.

(ii) Six weeks following service of the notice, the offeror must send a copy of it to the company together with the consideration for the ordinary shares to which the notice relates, and an instrument of transfer executed on behalf of the outstanding shareholder(s) by a person appointed by the offeror.

(iii) The company will hold the consideration on trust for the outstanding shareholders.

Sell-out

(i) Sections 983 to 985 of the Companies Act 2006 also give minority shareholders in the company a right to be bought out in certain circumstances by an offeror who has made a takeover offer. If a takeover offer relating to all the ordinary shares of the company is made at any time before the end of the period within which the offer could be accepted and the offeror held or had agreed to acquire not less than 90% of the ordinary shares, any holder of shares to which the offer related who had not accepted the offer could by a written communication to the offeror require it to acquire those shares. The offeror is required to give any shareholder notice of his right to be bought out within one month of that right arising. The offeror may impose a time limit on the rights of minority shareholders to be bought out, but that period cannot end less than three months after the end of the acceptance period, or, if longer a period of three months from the date of the notice.

(ii) If a shareholder exercises his rights, the offeror is bound to acquire those shares on the terms of the offer or on such other terms as may be agreed.

Differences in corporate law

The applicable provisions of the Companies Act 2006 differ from laws applicable to U.S. corporations and their shareholders. Set forth below is a summary of certain differences between the provisions of the Companies Act 2006 applicable to us and the 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 Companies Act 2006, a public limited company must have at least two directors and the number of directors may be fixed by or in the manner provided in a company's articles of association.	Under Delaware law, a corporation must have at least one director and the number of directors shall be fixed by or in the manner provided in the bylaws.
Removal of Directors	Under the Companies Act 2006, shareholders may remove a director without cause by an ordinary resolution (which is passed by a simple majority of those voting in person or by proxy at a general meeting) irrespective of any provisions of any service contract the director has with the company, provided 28 clear days' notice of the resolution has been given to the company and its shareholders. On receipt of notice of an intended resolution to remove a director, the company must forthwith send a copy of the notice to the director concerned. Certain other procedural requirements under the Companies Act 2006 must also be followed, such as allowing the director to make representations against his or her removal either at the meeting or in writing.	Under Delaware law, any director or the entire board of directors may be removed, with or without cause, by the holders of a majority of the shares then entitled to vote at an election of directors, except (i) unless the certificate of incorporation provides otherwise, in the case of a corporation whose board of directors is classified, stockholders may effect such removal only for cause, or (ii) 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,	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 (i) otherwise provided in the certificate of incorporation or bylaws of the

	England and Wales	Delaware
	resolutions appointing each director must be voted on individually.	corporation or (ii) the certificate of incorporation directs that a particular class of stock is to elect such director, in which case a majority of the other directors elected by such class, or a sole remaining director elected by such class, will fill such vacancy.
Annual General Meeting	Under the Companies Act 2006, a public limited company must hold an annual general meeting 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 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 Companies Act 2006, at least 21 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 days' notice is required for any other general meeting of a public limited company. In addition, certain matters, such as the removal of directors or auditors, require special notice, which is 28 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	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
	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.	
Proxy	Under the Companies Act 2006, at any meeting of shareholders, a shareholder may designate another person to attend, speak and vote at the meeting on their behalf by proxy.	Under Delaware law, at any meeting of stockholders, a stockholder may designate another person to act for such stockholder by proxy, but no such proxy shall be voted or acted upon after three years from its date, unless the proxy provides for a longer period. A director of a Delaware corporation may not issue a proxy representing the director's voting rights as a director.
Preemptive Rights	Under the Companies Act 2006, "equity securities," being (i) shares in the company other than shares that, with respect to dividends and capital, carry a right to participate only up to a specified amount in a distribution, referred to as "ordinary shares," or (ii) rights to subscribe for, or to convert securities into, ordinary shares, proposed to be allotted for cash must be offered first to the existing equity shareholders in the company in proportion to the respective nominal value of their holdings, unless an exception applies or a special resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise in each case in accordance with the provisions of the Companies Act.	Under Delaware law, shareholders have no preemptive rights to subscribe to additional issues of stock or to any security convertible into such stock unless, and except to the extent that, such rights are expressly provided for in the certificate of incorporation.
Authority to Allot	Under the Companies Act 2006, the directors of a company must not allot shares or grant rights to subscribe for or convert any security into shares unless	Under Delaware law, if the corporation's charter or certificate of incorporation so provides, the board of directors has the power to

	England and Wales	Delaware
	an exception applies or an ordinary resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise, in each case in accordance with the provisions of the Companies Act.	authorize the issuance of stock. The board 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 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 otherwise attach to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company, is void. Any provision by which a company directly or indirectly provides an indemnity, to any extent, for a director of the company or of an associated company against any liability attaching to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company of which he is a director is also void except as permitted by the Companies Act, which provides exceptions for the company to company against any liability attaching to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company of which he is a director is also void except as permitted by the Companies Act 2006, which provides exceptions for the company to (i) purchase and maintain insurance against such liability; (ii) provide a "qualifying third party indemnity," or an indemnity against	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 fiduciary duty as a director. However, no provision can limit the liability of a director for: • any breach of the director's duty of loyalty to the corporation or its stockholders; • acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law; • intentional or negligent payment of unlawful dividends or stock purchases or redemptions; or • any transaction from which the director derives an improper personal benefit.

	England and Wales	Delaware
	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 (iii) provide a "qualifying pension scheme indemnity," or an indemnity against liability incurred in connection with the company's activities as trustee of an occupational pension plan.	
Voting Rights	Under English law, unless a poll is demanded by the shareholders of a company or is required by the chairman of the meeting or the company's articles of association, shareholders shall vote on all resolutions on a show of hands. Under the Companies Act, a poll may be demanded by (i) not fewer than five shareholders having the right to vote on the resolution; (ii) 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 (iii) 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 total sum paid up on all the shares conferring that right. A company's articles of association may provide more extensive rights for shareholders to call a poll. Under English law, an ordinary resolution is passed on a show of hands if it is approved by a simple majority (more than 50%) 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	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.

	England and Wales	Delaware
	present, in person or by proxy, who, being entitled to 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.	
Shareholder Vote on Certain Transactions	The Companies Act 2006 provides for schemes of arrangement, which are arrangements or compromises between a company and any class of shareholders or creditors and used in certain types of reconstructions, amalgamations, capital reorganizations or takeovers. These arrangements require: • the approval at a shareholders' or creditors' meeting convened by order of the court, of a majority in number representing 75% in value of the shareholders or creditors or class thereof present and voting, either in person or by proxy; and • the approval of the court.	Generally, under Delaware law, unless the certificate of incorporation provides for the vote of a larger portion of the stock, completion of a merger, consolidation, sale, lease or exchange of all or substantially all of a corporation's assets or dissolution requires: • the approval of the board of directors; and • the 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 the corporation entitled to vote on the matter.
Standard of Conduct for Directors	Under English law, a director owes various statutory and fiduciary duties to the company, including: • to act in the way he considers, in good faith, would be most likely to promote the success of the company for the benefit of its members as a whole; • to avoid a situation in which he has, or can have, a direct or indirect interest that conflicts, or possibly conflicts, with the interests of the company; • to act in accordance with the company's constitution and only exercise his powers for the purposes for which they are conferred;	Delaware law does not contain specific provisions setting forth the standard of conduct of a director. The scope of the fiduciary duties of directors is generally determined by the courts of the State of Delaware. In general, directors have a duty to act without self-interest, on a well-informed basis and in a manner they reasonably believe to be in the best interest of the stockholders. Directors of a Delaware corporation owe fiduciary duties of care and loyalty to the corporation and to its shareholders. The duty of care generally requires that a director act in good faith, with the care that an ordinarily prudent person would

	England and Wales	Delaware
	• 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 • to declare any interest that he has, whether directly or indirectly, in a proposed or existing transaction or arrangement with the company.	exercise under similar circumstances. Under this duty, a director must inform himself of all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director act in a manner he reasonably believes to be in the best interests of the corporation. He must not use his corporate position for personal gain or advantage. In general, but subject to certain exceptions, actions of a director are presumed to have been made on an informed basis, in good faith and in the honest belief that the action taken was in the best interests of the corporation. However, this presumption may be rebutted by evidence of a breach of one of the fiduciary duties. Delaware courts have also imposed a heightened standard of conduct upon directors of a Delaware corporation who take any action designed to defeat a threatened change in control of the corporation. In addition, under Delaware law, when the board of directors of a Delaware corporation approves the sale or break-up of a corporation, the board of directors may, in certain circumstances, have a duty to obtain the highest value reasonably available to the shareholders.
Stockholder Suits	Under English law, generally, the company, rather than its shareholders, is the proper claimant in an action in respect of a wrong done to the company or where there is an irregularity in the company's internal management. Notwithstanding this general position, the Companies Act 2006 provides that (i) a court may allow a shareholder to bring a derivative	Under Delaware law, a stockholder may initiate a derivative action to enforce a right of a corporation if the corporation fails to enforce the right itself. The complaint must: • state that the plaintiff was a stockholder at the time of the transaction of which the plaintiff complains or that the plaintiffs

	England and Wales	Delaware
	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.	shares thereafter devolved on the plaintiff by operation of law; and • allege with particularity the efforts made by the plaintiff to obtain the action the plaintiff desires from the directors and the reasons for the plaintiff's failure to obtain the action; or • state the reasons for not making the effort. Additionally, the plaintiff must remain a stockholder through the duration of the derivative suit. The action will not be dismissed or compromised without the approval of the Delaware Court of Chancery.

Stock exchange listing

Our ADSs have been listed on the Nasdaq Global Select Market under the symbol "ORTX" since October 31, 2018.

Transfer agent and registrar of shares

Our share register is maintained by Equiniti Limited. The share register reflects only record owners of our ordinary shares. Holders of our ADSs are not treated as our shareholders and their names are therefore not entered in our share register. The depositary, the custodian or their nominees is the holder of the ordinary shares underlying our ADSs. Holders of our ADSs have a right to receive the ordinary shares underlying their ADSs. For discussion on our ADSs and ADS holder rights, see "Description of American depositary shares" in this prospectus.

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 is on file with the SEC under cover of a registration statement on Form F-6. You may obtain a copy of the deposit agreement from the SEC's website (www.sec.gov). Please refer to registration number 333-227905 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. 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, one ordinary share that is 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-ordinary 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 of the United States.

In addition, applicable laws and regulations may require you to satisfy reporting requirements and obtain regulatory approvals in certain circumstances. You are solely responsible for complying with such reporting requirements and obtaining such approvals. Neither the depositary, 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.

The manner in which you own the ADSs (e.g., in a brokerage account vs. as registered holder, or as holder of certificated vs. uncertificated ADSs) may affect your rights and obligations, and the manner in which, and extent to which, the depositary's services are made available to you. As an owner of ADSs, you may hold your ADSs either by means of an ADR registered in your name, through a brokerage or safekeeping account, or through an account established by the depositary 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 received in a currency other than U.S. Dollars to be converted into U.S. Dollars and for the distribution of the U.S. Dollars to the holders, subject to the laws and regulations of England and Wales.

The conversion into U.S. Dollars will take place only if practicable and if the U.S. Dollars are transferable to the United States. The depositary 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 share 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;
- 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 ordinary shares 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 ordinary 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 our 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 ordinary 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 this 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 offering, 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);
- the ordinary shares presented for deposit have not been stripped of any rights or entitlements; and
- the deposit of shares does not violate any applicable provision of English law.

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 consideration 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 except as a result of:

- temporary delays that may arise because (i) the transfer books for the ordinary shares or ADSs are closed, or (ii) ordinary shares are immobilized on account of a shareholders' meeting or a payment of dividends;
- obligations to pay fees, taxes and similar charges;
- restrictions imposed because of laws or regulations applicable to ADSs or the withdrawal of securities on deposit; and
- other circumstances specifically contemplated by Section I.A.(I) of the General Instructions to Form F-6 (as such General Instructions may be amended from time to time)

The deposit agreement may not be modified to impair your right to withdraw the ordinary shares 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.

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 ordinary shares represented by ADSs. In lieu of distributing such materials, the depositary bank may distribute to holders of ADSs instructions on how to retrieve such materials upon request.

If the depositary timely receives voting instructions from a holder of ADSs, it will endeavor to vote (or cause the custodian 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 shares represented by ADSs 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 represented by ADSs in accordance with the voting instructions received from the holders of ADSs.

Securities for which no voting instructions have been received will not be voted (except as otherwise contemplated in the deposit agreement). Please note that the ability of the depositary 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 $0.05 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 $0.05 per ADS cancelled
Distribution of cash dividends or other cash distributions (e.g., upon a sale of rights and other entitlements)	Up to $0.05 per ADS held
Distribution of ADSs pursuant to (i) share dividends or other free share distributions, or (ii) exercise of rights to purchase additional ADSs	Up to $0.05 per ADS held
Distribution of securities other than ADSs or rights to purchase additional ADSs (e.g., upon a spin-off)	Up to $0.05 per ADS held
ADS Services	Up to $0.05 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 for whom the ADSs are issued (in the case of ADS issuances) and to the person for whom ADSs are cancelled (in the case of ADS cancellations). In the case of ADSs issued by the depositary 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 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 ADS 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 ADS 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 are not 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 ordinary 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.

Nothing in the deposit agreement gives rise to a partnership or joint venture, or establishes a fiduciary relationship, among us, the depositary bank and you as ADS holder.

Nothing in the deposit agreement precludes Citibank (or its affiliates) from engaging in transactions in which parties adverse to us or the ADS owners have interests, and nothing in the deposit agreement obligates Citibank to disclose those transactions, or any information obtained in the course of those transactions, to us or to the ADS owners, or to account for any payment received as part of those transactions.

Taxes

You will be responsible for the taxes and other governmental charges payable on the ADSs and the ordinary shares 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 depositary and the custodian may take reasonable administrative actions to obtain tax refunds and reduced tax withholding for any distributions on your behalf. However, you may be required to provide to the depositary and to the custodian proof of taxpayer status and residence and such other information as the depositary and the custodian may require to fulfill legal obligations. You are required to indemnify us, the depositary and the custodian for any claims with respect to taxes based on any tax benefit obtained for you.

Foreign currency conversion

The depositary will arrange for the conversion of all foreign currency received into U.S. Dollars if such conversion is practical, and it will distribute the U.S. Dollars in accordance with the terms of the deposit agreement. You may have to pay fees and expenses incurred in converting foreign currency, such as fees and expenses incurred in complying with currency exchange controls and other governmental requirements.

If the conversion of foreign currency is not practical or lawful, or if any required approvals are denied or not obtainable at a reasonable cost or within a reasonable period, the depositary may take the following actions in its discretion:

- Convert the foreign currency to the extent practical and lawful and distribute the U.S. Dollars to the holders for whom the conversion and distribution is lawful and practical.
- Distribute the foreign currency to holders for whom the distribution is lawful and practical.
- Hold the foreign currency (without liability for interest) for the applicable holders.

Governing Law/Waiver of Jury Trial

The deposit agreement, the ADRs and ADSs will be interpreted in accordance with the laws of the State of New York. The rights of holders of ordinary shares (including ordinary shares represented by ADSs) are governed by the laws of England and Wales.

AS A PARTY TO THE DEPOSIT AGREEMENT, YOU IRREVOCABLY WAIVE YOUR RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING ARISING OUT OF THE DEPOSIT AGREEMENT, THE ADRs AND ADSs AGAINST US AND/OR THE DEPOSITARY. If we or the depositary opposed a jury trial demand based on the waiver, the court would determine whether the waiver was enforceable in the facts and circumstances of that case in accordance with applicable case law. However, you will not be deemed by agreeing to the terms of the deposit agreement to have waived our or the depositary's compliance with U.S. federal securities laws and the rules and regulations promulgated thereunder.

Shares and ADSs eligible for future sale

Upon completion of this offering, and assuming no exercise of the underwriters' option to purchase additional ADSs, we will have 94,867,028 ADSs outstanding, representing ordinary shares. Future sales of ADSs in the public market immediately after this offering, and the availability of ADSs for future sale, could adversely affect the market price of the ADSs prevailing from time to time. Some of our ordinary shares are subject to contractual and legal restrictions on resale as described below. There may be sales of substantial amounts of our ADSs or ordinary shares in the public market after such restrictions lapse, which could adversely affect prevailing market prices of our ADSs.

We expect 9,000,000 ADSs, or 10,350,000 ADSs if the underwriters exercise in full their option to purchase additional ADSs, sold in this offering will be freely transferable without restriction, except for any shares purchased by one or more of our existing "affiliates," as that term is defined in Rule 144 under the Securities Act.

Rule 144

In general, persons who have beneficially owned restricted ordinary shares for at least six months, and any affiliate of the company who owns either restricted or unrestricted securities, are entitled to sell their securities without registration with the SEC under an exemption from registration provided by Rule 144 under the Securities Act.

Non-Affiliates

Any person who is not deemed to have been one of our affiliates at the time of, or at any time during the three months preceding, a sale may sell an unlimited number of restricted securities under Rule 144 if:

- the restricted securities have been held for at least six months, including the holding period of any prior owner other than one of our affiliates;
- we have been subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale; and
- we are current in our Exchange Act reporting at the time of sale.

Any person who is not deemed to have been an affiliate of ours at the time of, or at any time during the three months preceding, a sale and has held the restricted securities for at least one year, including the holding period of any prior owner other than one of our affiliates, will be entitled to sell an unlimited number of restricted securities without regard to the length of time we have been subject to Exchange Act periodic reporting or whether we are current in our Exchange Act reporting.

Affiliates

Persons seeking to sell restricted securities who are our affiliates at the time of, or any time during the three months preceding, a sale, would be subject to the restrictions described above. They are also subject to additional restrictions, by which such person would be required to comply with the manner of sale and notice provisions of Rule 144 and would be entitled to sell

within any three-month period only that number of securities that does not exceed the greater of either of the following:

- 1% of the number of ordinary shares then outstanding, which will equal approximately 948,670 shares immediately after the closing of this offering based on the number of ordinary shares outstanding as of March 31, 2019; or
- the average weekly trading volume of our ordinary shares in the form of ADSs on the Nasdaq Global Select Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale.

Additionally, persons who are our affiliates at the time of, or any time during the three months preceding, a sale may sell unrestricted securities under the requirements of Rule 144 described above, without regard to the six-month holding period of Rule 144, which does not apply to sales of unrestricted securities.

Rule 701

Rule 701 under the Securities Act, as in effect on the date of this prospectus, permits resales of shares in reliance upon Rule 144 but without compliance with certain restrictions of Rule 144, including the holding period requirement. Most of our employees, executive officers or directors who purchased shares under a written compensatory plan or contract may be entitled to rely on the resale provisions of Rule 701. However, substantially all Rule 701 shares held by our executive officers and directors are subject to lock-up agreements as described below and in the section of this prospectus titled “Underwriting” and will become eligible for sale upon the expiration of the restrictions set forth in those agreements.

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 directors and executive officers have agreed, subject to limited exceptions, not to offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise dispose of, directly or indirectly, or enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of our ADSs, ordinary shares or such other securities for a period of 90 days after the date of this prospectus, without the prior written consent of J.P. Morgan Securities LLC, Goldman Sachs & Co. LLC, Cowen and Company, LLC and Barclays Capital Inc.. See “Underwriting.”

Material income tax considerations

The following summary contains a description of material U.K. and U.S. federal income tax consequences of the acquisition, ownership and disposition of our ordinary shares or ADSs. This summary should not be considered a comprehensive description of all the tax considerations that may be relevant to the decision to acquire ordinary shares or ADSs in this offering.

Material U.S. federal income tax considerations for U.S. holders

The following is a description of the material U.S. federal income tax consequences to the U.S. Holders described 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 securities. This discussion applies only to a U.S. Holder that is an initial purchaser of the ordinary shares or ADSs pursuant to the offering and 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 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; 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 holding 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 holding and disposing of ordinary shares or ADSs.

The discussion is based on 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 and is:

(i) An individual who is a citizen or individual resident of the United States;

(ii) 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;

(iii) an estate the income of which is subject to U.S. federal income taxation regardless of its source; or

(iv) a trust if (1) a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or (2) the trust has a valid election to be treated as a U.S. person under applicable U.S. Treasury Regulations.

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 holding 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 creditability of foreign taxes, if any, as described below, could be affected by actions taken by intermediaries in the chain of ownership between the holders of ADSs and our company if as a result of such actions the holders of ADSs are not properly treated as beneficial owners of the underlying ordinary shares. These actions would also be inconsistent with the claiming of the reduced tax rate, described below, applicable to dividends received by certain non-corporate holders.

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

PFIC Rules

If we are classified as a PFIC in any taxable year, a U.S. Holder will be subject to special rules generally intended to reduce or eliminate any benefits from the deferral of U.S. federal income tax that a U.S. Holder could derive from investing in a non-U.S. company that does not distribute all of its earnings on a current basis.

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).

We do not believe that we were a PFIC in the 2018 taxable year, though we have not made a determination regarding our PFIC status in the current taxable year. However, 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 from year to year, and we may be classified as a PFIC currently or in the future. 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. However, if we are a “controlled foreign corporation” for any taxable year (see discussion below in “Controlled foreign corporation considerations”), the value of our assets for purposes of the asset test will be determined based on the tax basis of such assets which could increase the likelihood that we are treated as a PFIC. Because of the uncertainties involved in establishing our PFIC status, there can be no assurance regarding if we currently are treated as a PFIC, or may be treated as a PFIC in the future.

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 treated as a PFIC 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 (i) we cease to be a PFIC and the U.S. Holder has made a “deemed sale” election under the PFIC rules, or (ii) the U.S. Holder makes a Qualified Electing Fund Election, or QEF Election, with respect to all taxable years during such U.S. Holders holding period in which we are a PFIC. If the “deemed sale” election is made, a U.S. Holder will be deemed to have sold the ordinary shares or ADSs the U.S. Holder holds at their fair market value and any gain from such deemed sale would be subject to the rules described below. After the deemed sale election, so long as we do not become a PFIC in a subsequent taxable year, the U.S. Holder’s ordinary shares or ADSs with respect to which such election was made will not be treated as shares in a PFIC and the U.S. Holder will not be subject to the rules described below with respect to any “excess distribution” the U.S. Holder receives 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.

For each taxable year we are treated as a PFIC with respect to U.S. Holders, U.S. Holders will be subject to special tax rules with respect to any “excess distribution” such U.S. Holder receives and any gain such U.S. Holder recognizes from a sale or other disposition (including, under certain circumstances, a pledge) of ordinary shares or ADSs, unless (i) such U.S. Holder makes a QEF Election or (ii) our ordinary shares or ADSs constitute “marketable“ securities, and such U.S. Holder makes a mark-to-market election as discussed below. Distributions a U.S. Holder receives in a taxable year that are greater than 125% of the average annual distributions a U.S. Holder received during the shorter of the three preceding taxable years or the U.S. Holder’s 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 a U.S. Holder's 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 a U.S. Holder holds the ordinary shares or ADSs as capital assets.

If we determine that we are a PFIC for any taxable year, we currently expect that we would provide the information necessary for U.S. holders to make a QEF Election. In addition, if we are a PFIC, a U.S. Holder will generally be subject to similar rules 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. U.S. Holders should consult their tax advisors regarding the application of the PFIC rules to our subsidiaries.

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. Any trades that have as their principal purpose meeting this requirement will be disregarded. Our ADSs will be listed on Nasdaq, which is a qualified exchange for these purposes. Consequently, if our ADSs remain listed on Nasdaq and are regularly traded, and you are a holder of ADSs, we expect the mark-to-market election would be available to U.S. Holders if we are a PFIC. 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 mark-to-market election 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 at the close of the taxable year over the U.S. Holder's adjusted tax basis in the ordinary shares or ADSs. 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 over the fair market value of the ordinary shares or ADSs 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. Gains from an actual sale or other disposition of the ordinary shares or ADSs will be treated as ordinary income, and any losses incurred on a sale or other disposition of the shares will be treated as an ordinary loss to the extent of any net mark-to-market gains for prior years. Once made, the election cannot be

revoked without the consent of the Internal Revenue Service, or the IRS, unless the ordinary shares or ADSs 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." 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 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 to determine whether any of these elections would be available and if so, what the consequences of the alternative treatments would be 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.

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.

Controlled foreign corporation considerations

Each "Ten Percent Shareholder" (as defined below) in a non-U.S. corporation that is classified as a "controlled foreign corporation," or a CFC, for U.S. federal income tax purposes generally is required to include in income each year for U.S. federal tax purposes such Ten Percent Shareholder's pro rata share of certain types of income earned by the CFC, including "Subpart F income," "global intangible low-taxed income" and certain other income generated by the CFC, even if the CFC has made no distributions to its shareholders. In addition, a Ten Percent Shareholder that realizes gain from the sale or exchange of shares in the CFC may be required to classify a portion of such gain as dividend income rather than capital gain (see discussion below in "Taxation of distributions" regarding the tax treatment of dividend income). A non-U.S. corporation generally will be classified as a CFC for U.S. federal income tax purposes if Ten Percent Shareholders own, directly or indirectly, more than 50% of either the total combined voting power of all classes of stock of such corporation entitled to vote or of the total value of the stock of such corporation. A "Ten Percent Shareholder" is a United States person (as defined by the Code) who owns or is considered to own 10% or more of either the total combined voting power of all classes of stock of such corporation entitled to vote or of the total value of the stock of such corporation.

We believe that we were not a CFC in the 2018 taxable year, though we have not made a determination regarding our CFC status in the current taxable year, and we may become a CFC in a subsequent taxable year. The determination of CFC status is complex and includes attribution rules, the application of which is not entirely certain. In addition, recent changes to the attribution rules relating to the determination of CFC status may make it difficult to determine

our CFC status for any taxable year. It is possible that, following this offering, a shareholder treated as a U.S. person for U.S. federal income tax purposes will acquire, directly or indirectly, enough shares to be treated as a Ten Percent Shareholder. We also believe that immediately following this offering we may have certain shareholders that are Ten Percent Shareholders for U.S. federal income tax purposes. U.S. Holders should consult their own tax advisors with respect to the potential adverse U.S. tax consequences of becoming a Ten Percent Shareholder in a CFC. If we are classified as both a CFC and a PFIC, we generally will not be treated as a PFIC with respect to those U.S. Holders that meet the definition of a Ten Percent Shareholder during the period in which we are a CFC.

Taxation of distributions

Subject to the discussion above under "PFIC 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 may 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 and the discussions above regarding concerns expressed by the U.S. Treasury, dividends paid to certain non-corporate U.S. Holders may be taxable at preferential rates applicable to "qualified dividend income" if we are a "qualified foreign corporation" and certain other requirements are met. However, the qualified dividend income treatment may not apply if we are treated as a PFIC with respect to the U.S. Holder. 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 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.

For foreign tax credit limitation purposes, our dividends will generally be treated as passive category income. Because no U.K. income taxes will be withheld from dividends on ordinary shares or ADSs, there will be no creditable foreign taxes associated with any dividends that a U.S. Holder will receive. The rules governing foreign tax credits are complex and U.S. Holders should therefore consult their tax advisers regarding the effect of the receipt of dividends for foreign tax credit limitation purposes.

Sale or other taxable disposition of ordinary shares and ADSs

Subject to the discussion above under "PFIC 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.

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 on a duly executed Form W-9 or otherwise establishes an exemption.

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 U.S. Holder's U.S. federal income tax liability and may entitle the U.S. Holder to a refund, provided that the required information is timely furnished to the IRS.

Information with respect to foreign financial assets

Certain U.S. Holders who are individuals (and, under 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), by filing IRS Form 8938 (Statement of Specified Foreign Financial Assets) with their federal income tax return. Such U.S. Holders who fail to timely furnish the required information may be subject to a penalty. Additionally, if a U.S. Holder does not file the required information, the statute of limitations with respect to tax returns of the U.S. Holder to which the information relates may not close until three years after such information is filed. 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.

U.K. Taxation

The following is intended as a general guide to current U.K. tax law and HMRC 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 ADSs. It does not constitute legal or tax advice and does not purport to be a complete analysis of all U.K. tax considerations relating to the holding of ADSs, or all of the circumstances in which holders of ADSs may benefit from an exemption or relief from U.K. taxation. It is 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 “Material U.S. federal income tax considerations for U.S. Holders.”

Except to the extent that the position of non-U.K. resident persons is expressly referred to, this guide relates only to persons who are resident (and in the case of individuals, domiciled or deemed domiciled) for tax purposes solely in the U.K. and do not have a permanent establishment, branch or agency (or equivalent) in any other jurisdiction with which the holding of the ADSs is connected, or U.K. Holders, who are absolute beneficial owners of the ADSs (and do not hold the ADSs through an Individual Savings Account or a Self-Invested Personal Pension) and any dividends paid in respect of the ADSs or underlying ordinary shares (where the dividends are regarded for U.K. tax purposes as that person’s own income). It is assumed for the purposes of this guide that a holder of an ADS is the beneficial owner of the underlying ordinary share and any dividend income for U.K. direct tax purposes.

This guide 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 ADSs otherwise than as an investment;
- persons who have (or are deemed to have) acquired their 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 ARE A SUMMARY OF CERTAIN U.K. TAX CONSIDERATIONS AND ARE INTENDED AS A GENERAL GUIDE ONLY. IT IS RECOMMENDED THAT ALL HOLDERS OF ADSs OBTAIN ADVICE AS TO THE CONSEQUENCES OF THE ACQUISITION, OWNERSHIP AND DISPOSAL OF THE ADSs IN THEIR OWN PARTICULAR CIRCUMSTANCES FROM THEIR OWN TAX ADVISORS. IN PARTICULAR, NON-U.K. RESIDENT OR DOMICILED PERSONS ARE ADVISED TO CONSIDER THE POTENTIAL IMPACT OF ANY RELEVANT DOUBLE TAXATION 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.

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 ADSs who is not resident for tax purposes in the United Kingdom 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) a trade, profession or vocation in the U.K. through a permanent establishment, branch or agency to which the ADSs are attributable.

Dividend income is treated as the top slice of the total income chargeable to U.K. income tax. An individual U.K. Holder who receives a dividend in the 2019/2020 tax year will be entitled to a tax-free allowance of £2,000. 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.

Corporation tax

A corporate holder of ADSs who is not resident for tax purposes in the United Kingdom should not be chargeable to U.K. corporation tax on dividends received from the company unless it carries on (whether solely or in partnership) a trade in the United Kingdom through a permanent establishment to which the ADSs are attributable.

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 should be the case, although certain conditions must be met. If the conditions for the exemption are not satisfied, or such U.K. Holder elects for an otherwise exempt dividend to be taxable, U.K. corporation tax will be chargeable on the amount of any dividends (at the current rate of 19%).

Chargeable gains

A disposal or deemed disposal of ADSs by a U.K. Holder may, depending on the U.K. Holder's circumstances and subject to any available exemptions or reliefs (such as the annual exemption), 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 is liable to U.K. capital gains tax on the disposal of ADSs, the applicable rate will be 20% (2019/2020). 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 applicable rate would be 10% (2019/2020), save to the extent that any capital gains exceed the unused basic rate tax band. In that case, the rate applicable to the excess would be 20% (2019/2020).

If a corporate U.K. Holder becomes liable to U.K. corporation tax on the disposal (or deemed disposal) of ADSs, the main rate of U.K. corporation tax (currently 19%) would apply.

A holder of 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 (or deemed disposal) of ADSs, unless the person is carrying on (whether solely or in partnership) a trade, profession or vocation in the United Kingdom through a permanent establishment, branch or agency to which the ADSs are attributable. However, an individual holder of 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 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).

Stamp duty and stamp duty reserve tax

The discussion below relates to the holders of our ordinary shares or ADSs wherever resident, however it should be noted that special rules may apply to certain persons such as market makers, brokers, dealers or intermediaries.

Issue of Ordinary Shares

No U.K. stamp duty or stamp duty reserve tax, or SDRT, is payable on the issue of the underlying ordinary shares in the company.

Transfers of Ordinary Shares

An unconditional agreement to transfer ordinary shares will normally give rise to a charge to SDRT at the rate of 0.5% of the amount or value of the consideration payable for the transfer. The purchaser of the shares is liable for the SDRT. Transfers of ordinary shares in certificated form are generally also subject to stamp duty at the rate of 0.5% of the amount or value of the consideration given for the transfer (rounded up to the next £5.00). Stamp duty is normally paid by the purchaser. The charge to SDRT will be cancelled or, if already paid, repaid (generally with interest), where a transfer instrument has been duly stamped within six years of the charge arising, (either by paying the stamp duty or by claiming an appropriate relief) or if the instrument is otherwise exempt from stamp duty.

An unconditional agreement to transfer ordinary shares to, or to a nominee or agent for, a person whose business is or includes the issue of depositary receipts or the provision of clearance services will generally be subject to SDRT (and, where the transfer is effected by a written instrument, stamp duty) at a higher rate of 1.5% of the amount or value of the consideration given for the transfer unless the clearance service has made and maintained an election under section 97A of the U.K. Finance Act 1986, or a section 97A election. It is understood that HMRC regards the facilities of DTC as a clearance service for these purposes and we are not aware of any section 97A election having been made by the DTC.

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

independent professional advisers before incurring or reimbursing the costs of such a 1.5% SDRT charge. Any stamp duty or SDRT payable on a transfer of ordinary shares to a depositary receipt system or clearance service will in practice generally be paid by the participants in the clearance service or depositary receipt system.

Transfers of ADSs

No U.K. stamp duty will in practice be payable on a written instrument transferring an ADS provided that the instrument of transfer is executed and remains at all times outside the United Kingdom. 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% of the value of the consideration.

No SDRT will be payable in respect of an agreement to transfer an ADS.

Repurchase of Ordinary Shares

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

Underwriting

We are offering the ADSs described in this prospectus through a number of underwriters. J.P. Morgan Securities LLC, Goldman Sachs & Co. LLC, Cowen and Company, LLC and Barclays Capital Inc. are acting as joint book-running managers of the offering and as representatives of the underwriters. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts set forth on the cover page of this prospectus, the number of ADSs listed next to its name in the following table:

Name	Number of ADSs
J.P. Morgan Securities LLC	
Goldman Sachs & Co. LLC	
Cowen and Company, LLC	
Barclays Capital Inc.	
Guggenheim Securities, LLC	
Wedbush Securities Inc.	
Total	

The underwriters are committed to purchase all the ADSs offered by us if they purchase any ADSs. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the ADSs directly to the public at the public offering price set forth on the cover page of this prospectus and to certain dealers at that price less a concession not in excess of $ per ADS. Any such dealers may resell ADSs to certain other brokers or dealers at a discount of up to $ per ADS from the public offering price. After the offering of the ADSs to the public, if all of the ADSs are not sold at the public offering price, the underwriters may change the offering price and the other selling terms. Sales of ADSs made outside of the United States may be made by affiliates of the underwriters. The offering of the ADSs by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part.

The underwriters have an option to buy up to additional ADSs from us to cover sales of ADSs by the underwriters which exceed the number of ADSs specified in the table above. The underwriters have 30 days from the date of this prospectus to exercise this option to purchase additional ADSs. If any ADSs are purchased with this option to purchase additional ADSs, the underwriters will purchase ADSs in approximately the same proportion as shown in the table above. If any additional ADSs are purchased, the underwriters will offer the additional ADSs on the same terms as those on which the ADSs are being offered.

The underwriting fee is equal to the public offering price per ADS less the amount paid by the underwriters to us per ADS. The underwriting fee is $ per ADS. The following table

shows the per ADS and total underwriting discounts to be paid to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase additional ADSs.

	Without option to purchase additional ADSs exercise	With full option to purchase additional ADSs exercise
Per ADS	$	$
Total	$	$

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts, will be approximately $650,000. The underwriters have agreed to reimburse us for certain fees and expenses in relation to this offering.

A prospectus in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to allocate a number of ADSs to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

We have agreed that we will not (i) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise dispose of, directly or indirectly, or file with the SEC a registration statement under the Securities Act relating to, any ADSs or securities convertible into or exchangeable or exercisable for any ADSs, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, or (ii) enter into any swap or other arrangement that transfers all or a portion of the economic consequences associated with the ownership of any ADSs or any such other securities (regardless of whether any of these transactions are to be settled by the delivery of ADSs or such other securities, in cash or otherwise), in each case without the prior written consent of J.P. Morgan Securities LLC, Goldman Sachs & Co. LLC, Cowen and Company, LLC and Barclays Capital Inc. for a period of 90 days after the date of this prospectus, other than the ADSs to be sold in this offering and any ADSs issued upon the exercise of options granted under our stock plans.

Our directors and executive officers, and certain of our significant shareholders have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each of these persons or entities, with limited exceptions, for a period of 90 days after the date of this prospectus, may not, without the prior written consent of J.P. Morgan Securities LLC, Goldman Sachs & Co. LLC, Cowen and Company, LLC and Barclays Capital Inc. (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any of our ordinary shares or ADSs or any securities exchangeable or exercisable for or convertible into our ordinary shares or ADSs, or publicly disclose the intention to make any offer, sale, pledge or disposition, (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of our ordinary shares or such other securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of ordinary shares or such other securities, in cash or otherwise, or (3) make any demand for or exercise any right with respect to the

registration of any of our ordinary shares or any security convertible into or exercisable or exchangeable for our Ordinary Shares, in each case, subject to certain exceptions, including:

- the ADSs to be sold in this offering;
- the exchange of ordinary shares of Orchard Therapeutics Limited for equivalent equity interests in Orchard Therapeutics plc in connection with our corporate reorganization;
- 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;
- sales or transfers of ADSs or ordinary shares acquired in this offering or in open market transactions after the consummation of this offering;
- transfers of our ordinary shares or ADSs as a bona fide gift or gifts; by will, other testamentary document or interstate succession to the legal representative, heir, beneficiary or member of the immediate family of the transferor in a transaction not involving a disposition for value; or pursuant to a court order in respect of, or by operation of law as a result of, a divorce, in a transaction not involving a disposition for value;
- transfer of our ordinary shares or ADSs to such person or such person's immediate family members for estate planning purposes;
- transfer of our ordinary shares or ADSs to the members, limited or general partners or shareholders of such person, its direct or indirect affiliates or other entities controlled or managed by the transferor in a transaction not involving a disposition for value;
- in the case of a trust, transfer of our ordinary shares or ADSs to beneficiaries of the transferor in a transaction not involving a disposition for value;
- the receipt of our ordinary shares or ADSs by such person in connection with the conversion of outstanding convertible preferred shares upon the consummation of this offering into ordinary shares;
- the exercise of an option or other equity award to purchase our ordinary shares or ADSs, which are set to expire during the 90-day period following the date of this prospectus;
- any transfer or disposition in connection with any bona fide third-party tender offer, merger, consolidation or other similar transaction that is approved by our board of directors and made to all holders of our ordinary shares or ADSs, the result of which is that a person, or group of persons, other than the Company becomes beneficial owner of more than 50% of our voting stock; and
- the establishment of a written trading plan meeting the requirements of Rule 10b5-1 under the Exchange Act.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act.

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling ADSs in the open market for the purpose of preventing or retarding a decline in the market price of the ADSs while this offering is in progress. These stabilizing transactions may include making short sales of the ADSs, which

involves the sale by the underwriters of a greater number of ADSs than they are required to purchase in this offering, and purchasing ADSs on the open market to cover positions created by short sales. Short sales may be "covered" shorts, which are short positions in an amount not greater than the underwriters' option to purchase additional ADSs referred to above, or may be "naked" shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option to purchase additional ADSs, in whole or in part, or by purchasing ADSs in the open market. In making this determination, the underwriters will consider, among other things, the price of ADSs available for purchase in the open market compared to the price at which the underwriters may purchase ADSs through the option to purchase additional ADSs. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the ADSs in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase ADSs in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the ADSs, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase ADSs in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those ADSs as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the ADSs or preventing or retarding a decline in the market price of the ADSs, and, as a result, the price of the ADSs may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on the Nasdaq Global Select Market, in the over-the-counter market or otherwise.

Other relationships

Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. In addition, from time to time, certain of the underwriters and their affiliates may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future. Such investment and trading activities may involve or relate to assets, securities and/or instruments of the issuer (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with the issuer. The underwriters and their affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

Selling restrictions

General

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

European Economic Area

In relation to each Member State of the European Economic Area, or each, a Relevant Member State, no offer of ADSs may be made to the public in that Relevant Member State other than:

A. to any legal entity which is a qualified investor as defined in the Prospectus Directive;

B. to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 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 representatives; or

C. in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of ADSs shall require us or the representatives 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 in a Relevant Member State who initially acquires any ADSs or to whom any offer is made will be deemed to have represented, acknowledged and agreed that 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. In the case of any ADSs being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the ADSs acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any ADSs to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the representatives has been obtained to each such proposed offer or resale.

The Company, the representatives and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

This prospectus has been prepared on the basis that any offer of ADSs 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 ADSs. Accordingly any person making or

intending to make an offer in that Relevant Member State of ADSs which are the subject of the offering contemplated in this prospectus may only do so in circumstances in which no obligation arises for the Company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the Company nor the underwriters have authorized, nor do they authorize, the making of any offer of ADSs in circumstances in which an obligation arises for the Company or the underwriters to publish a prospectus for such offer.

For the purpose of the above provisions, the expression “an offer to the public” in relation to any ADSs 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 the ADSs to be offered so as to enable an investor to decide to purchase or subscribe the ADSs, as the same may be varied in the Relevant Member State by any measure implementing the Prospectus Directive in the Relevant Member State and the expression “Prospectus Directive” means Directive 2003/71/EC (including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member States) 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 (“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 have been subject to a product approval process, which has determined that such ADSs 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 (the “Target Market Assessment”). Notwithstanding the Target Market Assessment, distributors should note that: the price of the ADSs may decline and investors could lose all or part of their investment; the ADSs offer no guaranteed income and no capital protection; and an investment in the ADSs 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. 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 the ADSs. Each distributor is responsible for undertaking its own target market assessment in respect of the ADSs and determining appropriate distribution channels.

Hong Kong

The ADSs may not be offered or sold by means of any document other than (i) in circumstances that do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), or (ii) to “professional investors” within the meaning of the Securities and Futures Ordinance (Cap.571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances that do not result in the document being a “prospectus” within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), and no advertisement,

invitation or document relating to the ADSs may be issued or may be in the possession of any person for the purpose of issue (in each case 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 (except if permitted to do so under the laws of Hong Kong) other than with respect to ADSs that are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan, or the Financial Instruments and Exchange Law, and each underwriter has agreed that it will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term, as used in this prospectus means any person resident in Japan, including any corporation or other entity organized under the laws of Japan) or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Law and any other applicable laws, regulations and ministerial guidelines of Japan.

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 may not be circulated or distributed, nor may the ADSs 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 under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) to a relevant person, 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 are subscribed or purchased under Section 275 by a relevant person that is: (a) a corporation (which is not an accredited investor) the sole business of which is to hold investments and the entire ADSs 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, ADSs, debentures and units of ADSs and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for six months after that corporation or that trust has acquired the ADSs under Section 275 except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA; (2) where no consideration is given for the transfer; or (3) by operation of law.

Notification under Section 309B(1)(c) of the SFA: We have determined that the ADSs shall be (A) prescribed capital markets products (as defined in the Securities and Futures (Capital Markets Products) Regulations 2018) and (B) Excluded Investment Products (as defined in MAS Notice SFA 04-N12: Notice on the Sale of Investment Products and MAS Notice FAA-N16: Notice on Recommendations on Investment Products).

Switzerland

The ADSs may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document, nor any other offering or marketing material relating to the ADSs or this offering, may be publicly distributed or otherwise made publicly available in Switzerland. Neither this document nor any other offering or marketing material relating to this offering, the Company, the ADSs has been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of ADSs will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, or FINMA, and the offer of ADSs has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of ADSs.

United Arab Emirates

This prospectus relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority, or DFSA. This prospectus is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus nor taken steps to verify the information set forth herein and has no responsibility for this prospectus. The ADSs to which this prospectus relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the ADSs offered should conduct their own due diligence on the ADSs. If you do not understand the contents of this prospectus, you should consult an authorized financial advisor.

United Kingdom

In addition, 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 persons who are “qualified investors” (as defined in the Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19 (5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the “Order”) and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as “relevant persons”).

Any person in the United Kingdom that is not a relevant person should not act or rely on the information included in this document or use it as basis for taking any action. In the United Kingdom, any investment or investment activity that this document relates to may be made or taken exclusively by relevant persons. 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.

Canada

The ADSs 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 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 representatives are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Expenses of this offering

Set forth below is an itemization of the total expenses, excluding the underwriting discounts, which are expected to be incurred in connection with the sale of ADSs in this offering. With the exception of the registration fee payable to the SEC, all amounts are estimates.

Expense	Amount
SEC registration fee	23,471
FINRA filing fee	29,540
Printing expenses	65,000
Legal fees and expenses	350,000
Accounting fees and expenses	170,000
Miscellaneous costs	11,989
Total	$650,000

Legal matters

The validity of our ADSs and certain other matters of English law and U.S. federal law will be passed upon for us by Goodwin Procter (UK) LLP and Goodwin Procter LLP. Legal counsel to the underwriters in connection with this offering are Davis Polk & Wardwell LLP.

Experts

The financial statements incorporated in this prospectus by reference to the Annual Report on Form 20-F for the year ended December 31, 2018 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered accounting firm, given on the authority of said firm as experts in auditing and accounting.

The registered business address of PricewaterhouseCoopers LLP is 1 Embankment Place, London, WC2N 6RH, United Kingdom.

Service of process and enforcement of liabilities

We are incorporated and currently existing under the laws of England and Wales. In addition, certain of our directors and officers reside outside of the United States and most of the assets of our non-U.S. 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 Goodwin Procter 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 predicated solely upon the United States securities laws, would not be automatically enforceable in England and Wales. We have also been advised by Goodwin Procter 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;
- 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 U.K. 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 additional 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. A related registration statement on Form F-6 has been filed with the SEC to register the ADSs. This prospectus, which forms a part of the registration statement, does not contain all of the information included in the registration statement and the exhibits and schedules to the registration statement. Certain information is omitted and you should refer to the registration statement and its exhibits and schedules for that information. 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.

The SEC maintains a website (www.sec.gov) that contains reports, proxy and information statements and other information regarding issuers like us that file electronically with the SEC.

We are subject to the information reporting requirements of the Exchange Act applicable to foreign private issuers. Accordingly, we are required to file reports and other information with the SEC, including annual reports on Form 20-F and reports on Form 6-K. As a foreign private issuer, we are exempt from the rules under the Exchange Act related to the furnishing and content of proxy statements, and our officers, directors and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we are not 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 maintain a corporate website at www.orchard-tx.com. Information contained in, or that can be accessed through, our website is not a part of, and shall not be incorporated by reference into, this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

Incorporation by reference of certain documents

The SEC allows us to ‘‘incorporate by reference’’ information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus. We incorporate by reference into this prospectus and the registration statement of which this prospectus is a part the information or documents listed below that we have filed with or furnished to the SEC:

- Our Annual Report on Form 20-F for the year ended December 31, 2018, filed with the SEC on March 22, 2019, as amended on April 26, 2019;
- Our Report of Foreign Private Issuer on Form 6-K furnished to the SEC on May 28, 2019, including the interim results for Orchard Therapeutics plc for the three months ended March 31, 2019;
- Our Reports of Foreign Private Issuer on Form 6-K furnished to the SEC on March 27, 2019, April 15, 2019, April 25, 2019, April 29, 2019, May 28, 2019 and May 28, 2019 and
- The description of our ordinary shares and ADSs contained in our Registration Statement on Form 8-A, as filed with the SEC under Section 12(b) of the Exchange Act on October 29, 2018, including any amendment or report filed for the purpose of updating such description (File No. 001-001-38722).

We will provide to each person at their request, including any beneficial owner, to whom a prospectus is delivered, a copy of any or all of the reports or documents that have been incorporated by reference into this prospectus but not delivered with this prospectus. We will provide these reports upon written or oral request at no cost to the requester. Please direct your request, either in writing or by telephone, to Orchard Therapeutics plc, Attention: Investor Relations, 108 Cannon Street, London EC4N 6EU, United Kingdom, and our telephone number is +44 (0) 20 3808 8286. In addition, copies of the documents incorporated herein by reference may be accessed at our website at www.orchard-tx.com. The reference to our website address does not constitute incorporation by reference of the information contained on or accessible through our website, and you should not consider the contents of our website in making an investment decision with respect to our ADSs.

Table of Contents

9,000,000 American Depositary Shares
Representing 9,000,000 Ordinary Shares

PRELIMINARY PROSPECTUS

J.P. Morgan
Goldman Sachs & Co. LLC
Cowen
Barclays
Guggenheim Securities
Wedbush PacGrow

, 2019

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 6. Indemnification of Directors and Officers.

Subject to the Companies Act 2006, members of the registrant's board of directors and its officers (excluding auditors) 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 or officers shall be reimbursed for:

(i) all costs, charges, losses, expenses and liabilities sustained or incurred in relation to his or her actual or purported execution of his or her duties in relation to the registrant, including any liability incurred in defending any criminal or civil proceedings; and

(ii) expenses incurred or to be incurred in defending any criminal or civil proceedings, in an investigation by a regulatory authority or against a proposed action to be taken by a regulatory authority, or in connection with any application for relief under the statutes of the United Kingdom and any other statutes that concern and affect the registrant as a company, or collectively the Statutes, arising in relation to the registrant or an associated company, by virtue of the actual or purposed execution of the duties of his or her office or the exercise of his or her powers.

In the case of current or former members of the registrant's board of directors, there shall be no entitlement to reimbursement as referred to above for (i) any liability incurred to the registrant or any associated company, (ii) the payment of a fine imposed in any criminal proceeding or a penalty imposed by a regulatory authority for non-compliance with any requirement of a regulatory nature, (iii) the defense of any criminal proceeding if the member of the registrant's board of directors is convicted, (iv) the defense of any civil proceeding brought by the registrant or an associated company in which judgment is given against the director, and (v) any application for relief under the statutes of the United Kingdom and any other statutes that concern and affect the registrant as a company in which the court refuses to grant relief to the director.

In addition, members of the registrant's board of directors and its officers 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 this offering.

Item 7. Recent Sales of Unregistered Securities.

The following list sets forth information regarding all unregistered securities sold by us or Orchard Therapeutics Limited (now known as Orchard Therapeutics (Europe) Limited) since January 1, 2016, through the date of the prospectus that forms a part of this registration statement. In August 2018, Orchard Rx Limited (now known as Orchard Therapeutics plc) was

incorporated in England and Wales with nominal assets and no liabilities, contingencies, or commitments for the purpose of consummating a corporate reorganization by which it acquired the outstanding share capital of Orchard Therapeutics Limited (now known as Orchard Therapeutics (Europe) Limited), as more fully described in Note 7 to our audited financial statements included in our Annual Report on Form 20-F for the year ended December 31, 2018, which is incorporated herein by reference. Following the share exchange by which the outstanding shares of Orchard Therapeutics Limited were exchanged for the same number and class of newly issued shares of Orchard Rx Limited, our preferred shares were redenominated as ordinary shares with a nominal value of £0.10 per share:

(a) Issuances of Share Capital

In February 2016, Orchard Therapeutics Limited issued 3,441,290 shares to one investor as consideration for entering into a license agreement.

In April 2016, Orchard Therapeutics Limited issued 800,300 ordinary shares to three investors and three individuals as consideration for entering into a license agreement.

In December 2016, Orchard Therapeutics Limited issued 588,220 ordinary shares to one investor as consideration for entering into a license agreement.

In February 2017, Orchard Therapeutics Limited issued 256.096 ordinary shares to one investor for aggregate consideration of £3.20.

In March 2017, Orchard Therapeutics Limited issued 660,247 ordinary shares to one investor as consideration for satisfying a milestone under a license agreement.

In each of November 2017 and August 2018, Orchard Therapeutics Limited issued 150,826 ordinary shares to one investor as consideration for satisfying a milestone under a license agreement.

In December 2017, Orchard Therapeutics Limited issued 563,847 ordinary shares to one investor as consideration for satisfying a milestone under a license agreement.

In February 2018, Orchard Therapeutics Limited issued 349,770 ordinary shares to one investor as consideration for entering into a license agreement.

In February 2016, with subsequent closings in May 2016, July 2016, August 2016, January 2017 and February 2017, Orchard Therapeutics Limited issued an aggregate of 16,806,297 Series A convertible preferred shares to two investors for aggregate consideration of £21.0 million.

In March 2017, with subsequent closings in August 2017, October 2017, December 2017 and January 2018, Orchard Therapeutics Limited issued an aggregate of 16,964,875 Series B convertible preferred shares to 17 investors for aggregate consideration of £85.2 million.

In April 2018, Orchard Therapeutics Limited issued an aggregate of 12,455,252 Series B-2 convertible preferred shares to GSK pursuant to the terms of an asset purchase and license agreement.

In August 2018, Orchard Therapeutics Limited issued an aggregate of 13,942,474 Series C convertible preferred shares to 60 investors for aggregate consideration of approximately $150.0 million.

In October 2018, Orchard Rx limited issued 9,592,585 ordinary shares, 16,806,299 Series A preferred shares, 16,964,875 Series B preferred shares, 12,455,252 Series B-2 preferred shares and 13,942,474 Series C preferred shares in connection with the share exchange further described above.

No underwriters were involved in the foregoing sales of securities. The sales of securities described above were deemed to be exempt from registration pursuant to Section 4(a)(2) of the Securities Act, including Regulation D and Rule 506 promulgated thereunder, as transactions by an issuer not involving a public offering. All of the purchasers in these transactions represented to us in connection with their purchase that they were acquiring the securities for investment and not distribution, that they could bear the risks of the investment and could hold the securities for an indefinite period of time. Such purchasers received written disclosures that the securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration or an available exemption from such registration. All of the foregoing securities are deemed restricted securities for the purposes of the Securities Act.

(b) Grants and Exercises of Options and Restricted Share Awards

We have granted share options to purchase an aggregate of 10,449,095 ordinary shares, with exercise prices ranging from £0.00002 to $10.30 per share, to employees and directors pursuant to the 2016 Plan. In May 2018, Orchard Therapeutics Limited issued 14,045 ordinary shares to two individuals upon exercise of options for an aggregate purchase price of $27,276.

The issuances of the securities described above were deemed to be exempt from registration pursuant to Section 4(a)(2) of the Securities Act or Rule 701 promulgated under the Securities Act as transactions pursuant to compensatory benefit plans. The ordinary shares issued upon the exercise of options are deemed to be restricted securities for purposes of the Securities Act.

Item 8. Exhibits and Financial Statement Schedules.

(a) Exhibits

Exhibit Number	Description	Incorporation by Reference			
		Schedule/ Form	File Number	Exhibit	File Date
1.1	Form of Underwriting Agreement				
2.1†	Asset Purchase and License Agreement, by and among the registrant, Glaxo Group Limited and GlaxoSmithKline Intellectual Property Development Ltd., dated April 11, 2018 (schedules, exhibits, and similar supporting attachments are omitted pursuant to Item 601(b)(2) of Regulation S-K. The registrant agrees to furnish a supplemental copy of any omitted schedule or similar attachment to the Securities and Exchange Commission upon request).	Form F-1	333-227698	2.1	10/4/18

Exhibit Number	Description	Incorporation by Reference			
		Schedule/ Form	File Number	Exhibit	File Date
3.1	Articles of Association of Orchard Therapeutics plc	Form 20-F	001-38722	1.1	3/22/19
4.1	Deposit Agreement	Form 20-F	001-38722	2.1	3/22/19
4.2	Form of American Depositary Receipt (included in Exhibit 4.1)	Form 20-F	001-38722	2.2	3/22/19
5.1	Opinion of Goodwin Procter (UK) LLP				
10.1	Investment and shareholders' agreement by and between the registrant and the shareholders named therein, dated August 2, 2018, as amended.				
10.2#	2016 Employee Share Option Plan with Non-Employee Sub-Plan and U.S. Sub-Plan, as amended.	Form F-1	333-227698	10.2	10/4/18
10.3#	2018 Share Option and Incentive Plan.	Form 20-F	001-38722	4.3	3/22/19
10.4†	Deed of Novation, by and among the registrant, Glaxo Group Limited, GlaxoSmithKline Intellectual Property Development Limited, GlaxoSmithKline S.p.A., Fondazione Telethon and Ospedale San Raffaele (in its own capacity and as successor in interest to Fondazione Centro San Raffaele Del Monte Tabor), dated April 5, 2018.	Form F-1	333-227698	10.4	10/4/18
10.5†	Research and Development Collaboration and License Agreement, by and among Glaxo Group Limited, Fondazione Telethon and Fondazione Centro San Raffaele del Monte Tabor, dated October 15, 2010, as amended.	Form F-1	333-227698	10.5	10/4/18
10.6#	Form of Deed of Indemnity between the registrant and each of its directors and executive officers.	Form F-1	333-227698	10.6	10/4/18
10.7	Lease Agreement, dated as of January 19, 2018, by and between the Registrant and New Connect Investments Limited.	Form F-1	333-227698	10.7	10/4/18
10.8†	License and Development Agreement, by and between the registrant and Oxford BioMedica (UK) Limited, dated November 28, 2016, as amended.	Form F-1	333-227698	10.8	10/4/18

Exhibit Number	Description	Incorporation by Reference			
		Schedule/ Form	File Number	Exhibit	File Date
10.9†	License Agreement between UCL Business Plc, The Regents of the University of California and the registrant, dated February 6, 2016, as amended.	Form F-1	333-227698	10.9	10/4/18
10.10#	2018 Employee Share Purchase Plan.	Form F-1/A	333-227698	10.10	10/23/18
10.11	Director Nomination Agreement, dated as of October 18, 2018, by and between the registrant and Glaxo Group Limited.	Form F-1/A	333-227698	10.11	10/23/18
10.12*	Lease Agreement, dated as of December 11, 2018, by and between BPP Pacific Industrial CA Non-REIT Owner 2 LLC and Orchard Therapeutics North America.	Form 20-F/A	001-38722	4.12	4/26/19
10.13*	Senior Term Facilities Agreement by and among the registrant, as borrower and guarantor, the other guarantors from time to time party thereto and MidCap Financial (Ireland) Limited, as agent, arranger and as a lender, and the additional lenders from time to time party thereto, dated May 24, 2019.	Form 6-K	001-38722	99.1	5/28/19
21.1	Subsidiaries of the registrant.	Form 20-F	001-38722	8.1	3/22/19
23.1	Consent of independent registered public accounting firm.				
23.2	Consent of Goodwin Procter (UK) LLP (included in exhibit 5.1).				
24.1	Power of Attorney (included on signature page to this registration statement).				

† Confidential treatment has been granted for portions of this exhibit. These portions have been omitted from the registration statement and filed separately with the United States Securities and Exchange Commission.

# Indicates a management contract or any compensatory plan, contract or arrangement.

* Portions of this exhibit have been omitted because they are both (i) not material and (ii) would likely cause competitive harm to the registrant if publicly disclosed.

(b) Financial Statement Schedules

None. All schedules have been omitted because the information required to be set forth therein is not applicable or has been included in the consolidated financial statements and notes thereto incorporated herein by reference.

Item 9. Undertakings.

The undersigned registrant hereby undertakes to provide to the underwriters at the closing specified in the underwriting agreements, certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

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 provisions described in Item 6 hereof, or otherwise, the registrant has been advised that in the opinion of the SEC 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.

The undersigned registrant hereby undertakes that:

(i) 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.

(ii) 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.

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 the City of London, United Kingdom, on June 3, 2019.

ORCHARD THERAPEUTICS PLC

By: /s/ Mark Rothera

Mark Rothera

President and Chief Executive Officer

KNOW ALL BY THESE PRESENT, that each person whose signature appears below hereby constitutes and appoints Mark Rothera and Frank E. Thomas, and each of them, his or her true and lawful agent, proxy and attorney-in-fact, with full power of substitution and resubstitution, for and in his or her name, place and stead, in any and all capacities, to (i) act on, sign and file with the Securities and Exchange Commission any and all amendments (including post-effective amendments) to this Registration Statement together with all schedules and exhibits thereto and any subsequent registration statement filed pursuant to Rule 462(b) under the Securities Act of 1933, as amended, together with all schedules and exhibits thereto, (ii) act on, sign and file such certificates, instruments, agreements and other documents as may be necessary or appropriate in connection therewith, (iii) act on and file any supplement to any prospectus included in this Registration Statement or any such amendment or any subsequent registration statement filed pursuant to Rule 462(b) under the Securities Act of 1933, as amended, and (iv) take any and all actions which may be necessary or appropriate to be done, as fully for all intents and purposes as he or she might or could do in person, hereby approving, ratifying and confirming all that such agent, proxy and attorney-in-fact or any of his or her substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Act, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Mark Rothera Mark Rothera	President, Chief Executive Officer and Director *(Principal Executive Officer)*	June 3, 2019
/s/ Frank E. Thomas Frank E. Thomas	Chief Financial Officer and Chief Business Officer *(Principal Financial Officer and Principal Accounting Officer)*	June 3, 2019
/s/ James A. Geraghty James A. Geraghty	Chairman of the Board of Directors	June 3, 2019
/s/ Joanne T. Beck Joanne T. Beck, Ph.D.	Director	June 3, 2019
/s/ Marc Dunoyer Marc Dunoyer	Director	June 3, 2019
/s/ Jon Ellis Jon Ellis, Ph.D.	Director	June 3, 2019
/s/ Bobby Gaspar Bobby Gaspar, M.D., Ph.D.	Director	June 3, 2019
/s/ Charles A. Rowland, Jr. Charles A. Rowland, Jr.	Director	June 3, 2019
/s/ Hong Fang Song Hong Fang Song	Director	June 3, 2019
/s/ Alicia Secor Alicia Secor	Director	June 3, 2019

Cogency Global Inc.

By:	/s/ Richard Arthur Name: Richard Arthur Title: Assistant Secretary on behalf of Cogency Global Inc.	Authorized Representative in the United States	June 3, 2019

Exhibit 1.1

ORCHARD THERAPEUTICS PLC

[●] American Depositary Shares,
representing [●] Ordinary Shares

Underwriting Agreement

[●], 2019

J.P. Morgan Securities LLC
Goldman Sachs & Co. LLC
Cowen and Company, LLC
Barclays Capital Inc.

As Representatives of the
several Underwriters listed
in Schedule 1 hereto

c/o J.P. Morgan Securities LLC
383 Madison Avenue
New York, New York 10179

c/o Goldman Sachs & Co. LLC
200 West Street
New York, New York 10282-2198

c/o Cowen and Company, LLC
599 Lexington Avenue
New York, New York 10022

c/o Barclays Capital Inc.
745 Seventh Avenue
New York, New York 10019

Ladies and Gentlemen:

Orchard Therapeutics plc, a public limited company incorporated under the laws of England and Wales (the "Company"), proposes to issue and sell to the several underwriters listed in Schedule 1 hereto (the "Underwriters"), for whom you are acting as representatives (the "Representatives"), an aggregate of [●] American Depositary Shares ("ADSs"), representing [●] ordinary shares, nominal value £0.10 per share (the "Ordinary Shares"), of the Company (the "Underwritten ADSs") and, at the option of the Underwriters, up to an additional [●] ADSs, representing [●] Ordinary Shares (the "Option ADSs"). The Underwritten ADSs and the Option ADSs are herein referred to as the "Offered ADSs." The Ordinary Shares represented by the

Underwritten ADSs are herein referred to as the "Underwritten Shares," the Ordinary Shares represented by the Option ADSs are herein referred to as the "Option Shares" and the Underwritten Shares and Option Shares are herein together referred to as the "Shares."

The Offered ADSs are to be issued pursuant to that certain deposit agreement (the "Deposit Agreement"), dated as of November 2, 2019, among the Company, Citibank, N.A. as depositary (the "Depositary"), and the owners and beneficial owners from time to time of the ADSs. Each Offered ADS will represent the right to receive one Ordinary Share deposited pursuant to the Deposit Agreement.

The Company hereby confirms its agreement with the several Underwriters concerning the purchase and sale of the Offered ADSs, as follows:

1. Registration Statement. The Company has prepared and filed with the Securities and Exchange Commission (the "Commission") under the Securities Act of 1933, as amended, and the rules and regulations of the Commission thereunder (collectively, the "Securities Act"), a registration statement on Form F-1 (File No. 333-[●]), including a prospectus, relating to the Offered ADSs. Such registration statement, as amended at the time it became effective, including the information, if any, deemed pursuant to Rule 430A, 430B or 430C under the Securities Act to be part of the registration statement at the time of its effectiveness ("Rule 430 Information"), is referred to herein as the "Registration Statement"; and as used herein, the term "Preliminary Prospectus" means each prospectus included in such registration statement (and any amendments thereto) before effectiveness, any prospectus filed with the Commission pursuant to Rule 424(a) under the Securities Act and the prospectus included in the Registration Statement at the time of its effectiveness that omits Rule 430 Information, and the term "Prospectus" means the prospectus in the form first used (or made available upon request of purchasers pursuant to Rule 173 under the Securities Act) in connection with confirmation of sales of the Offered ADSs. If the Company has filed an abbreviated registration statement pursuant to Rule 462(b) under the Securities Act (the "Rule 462 Registration Statement"), then any reference herein to the term "Registration Statement" shall be deemed to include such Rule 462 Registration Statement. Any reference in this underwriting agreement (this "Agreement") to the Registration Statement, any Preliminary Prospectus or the Prospectus shall be deemed to refer to and include the documents incorporated by reference therein under the Securities Act, as of the effective date of the Registration Statement or the date of such Preliminary Prospectus or the Prospectus, as the case may be, and any reference to "amend", "amendment" or "supplement" with respect to the Registration Statement, any Preliminary Prospectus or the Prospectus shall be deemed to refer to and include any documents filed after such date under the Securities Exchange Act of 1934, as amended, and the rules and regulations of the Commission thereunder (collectively, the "Exchange Act") that are deemed to be incorporated by reference therein. Capitalized terms used but not defined herein shall have the meanings given to such terms in the Registration Statement and the Prospectus.

At or prior to the Applicable Time (as defined below), the Company had prepared the following information (collectively with the pricing information set forth on Annex A, the "Pricing Disclosure Package"): a Preliminary Prospectus dated [●], 2019 and each "free-writing prospectus" (as defined pursuant to Rule 405 under the Securities Act) listed on Annex A hereto.

"Applicable Time" means [●] P.M., New York City time, on [●], 2019.

2. Purchase of the ADSs.

(a) The Company agrees to issue and sell the Underwritten ADSs to the several Underwriters as provided in this Agreement, and each Underwriter, on the basis of the representations, warranties and agreements set forth herein and subject to the conditions set forth herein, agrees, severally and not jointly, to purchase at a price per ADS of $[●] (the "Purchase Price") from the Company the respective number of Underwritten ADSs set forth opposite such Underwriter's name in Schedule 1 hereto.

In addition, the Company agrees to issue and sell the Option ADSs to the several Underwriters as provided in this Agreement, and the Underwriters, on the basis of the representations, warranties and agreements set forth herein and subject to the conditions set forth herein, shall have the option to purchase, severally and not jointly, from the Company the Option ADSs at the Purchase Price less an amount per ADS equal to any dividends or distributions declared by the Company and payable on the Underwritten ADSs but not payable on the Option ADSs.

If any Option ADSs are to be purchased, the number of Option ADSs to be purchased by each Underwriter shall be the number of Option ADSs which bears the same ratio to the aggregate number of Option ADSs being purchased as the number of Underwritten ADSs set forth opposite the name of such Underwriter in Schedule 1 hereto (or such number increased as set forth in Section 10 hereof) bears to the aggregate number of Underwritten ADSs being purchased from the Company by the several Underwriters, subject, however, to such adjustments to eliminate any fractional ADSs as the Representatives in their sole discretion shall make.

The Underwriters may exercise the option to purchase Option ADSs at any time in whole, or from time to time in part, on or before the thirtieth day following the date of the Prospectus, by written notice from the Representatives to the Company. Such notice shall set forth the aggregate number of Option ADSs as to which the option is being exercised and the date and time when the Option ADSs are to be delivered and paid for, which may be the same date and time as the Closing Date (as hereinafter defined) but shall not be earlier than the Closing Date nor later than the tenth full business day (as hereinafter defined) after the date of such notice (unless such time and date are postponed in accordance with the provisions of Section 10 hereof). Any such notice shall be given at least two business days prior to the date and time of delivery specified therein.

(b) The Company understands that the Underwriters intend to make a public offering of the ADSs, and initially to offer the Offered ADSs on the terms set forth in the Pricing Disclosure Package. The Company acknowledges and agrees that the Underwriters may offer and sell Offered ADSs to or through any affiliate of an Underwriter.

(c) Payment for the Offered ADSs shall be made by wire transfer in immediately available funds to the account specified by the Company to the

Representatives, in the case of the Underwritten ADSs, at the offices of Davis Polk & Wardwell LLP, 450 Lexington Avenue, New York, NY 10017 at 10:00 A.M. New York City time on [●], 2019, or at such other time or place on the same or such other date, not later than the fifth business day thereafter, as the Representatives and the Company may agree upon in writing or, in the case of the Option ADSs, on the date and at the time and place specified by the Representatives in the written notice of the Underwriters' election to purchase such Option ADSs. The time and date of such payment for the Underwritten ADSs is referred to herein as the "Closing Date," and the time and date for such payment for the Option ADSs, if other than the Closing Date, is herein referred to as the "Additional Closing Date."

Payment for the Offered ADSs to be purchased on the Closing Date or the Additional Closing Date, as the case may be, shall be made against delivery to the Representatives for the respective accounts of the several Underwriters of the Offered ADSs to be purchased on such date or the Additional Closing Date, as the case may be, with any stamp duties, stamp duty reserve tax or other issuance or transfer taxes payable in connection with the sale of such Offered ADSs duly paid by the Company. Delivery of the Offered ADSs shall be made through the facilities of The Depository Trust Company ("DTC") unless the Representatives shall otherwise instruct. The certificates for the Offered ADSs will be made available for inspection and packaging by the Representatives at the office of DTC or its designated custodian not later than 1:00 P.M., New York City time, on the business day prior to the Closing Date or the Additional Closing Date, as the case may be.

(d) The Company acknowledges and agrees that the Representatives and the other Underwriters are acting solely in the capacity of an arm's length contractual counterparty to the Company with respect to the offering of the Offered ADSs contemplated hereby (including in connection with determining the terms of the offering) and not as a financial advisor or a fiduciary to, or an agent of, the Company or any other person. Additionally, neither the Representatives nor any other Underwriter is advising the Company or any other person as to any legal, tax, investment, accounting or regulatory matters in any jurisdiction. The Company shall consult with its own advisors concerning such matters and shall be responsible for making its own independent investigation and appraisal of the transactions contemplated hereby, and neither the Representatives nor the other Underwriters shall have any responsibility or liability to the Company with respect thereto. Any review by the Representatives and the other Underwriters of the Company, the transactions contemplated hereby or other matters relating to such transactions will be performed solely for the benefit of the Underwriters and shall not be on behalf of the Company.

3. Representations and Warranties of the Company. The Company represents and warrants to each Underwriter that:

(a) *Preliminary Prospectus.* No order preventing or suspending the use of any Preliminary Prospectus has been issued by the Commission, and each Preliminary Prospectus included in the Pricing Disclosure Package, at the time of filing thereof, complied in all material respects with the Securities Act, and no Preliminary Prospectus,

at the time of filing thereof, contained any untrue statement of a material fact or omitted 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 that the Company makes no representation or warranty with respect to any statements or omissions made in reliance upon and in conformity with information relating to any Underwriter furnished to the Company in writing by such Underwriter through the Representatives expressly for use in any Preliminary Prospectus, it being understood and agreed that the only such information furnished by any Underwriter consists of the information described as such in Section 7(b) hereof.

(b) *Pricing Disclosure Package*. The Pricing Disclosure Package as of the Applicable Time did not, and as of the Closing Date and as of the Additional Closing Date, as the case may be, will not, contain any untrue statement of a material fact or 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 that the Company makes no representation or warranty with respect to any statements or omissions made in reliance upon and in conformity with information relating to any Underwriter furnished to the Company in writing by such Underwriter through the Representatives expressly for use in such Pricing Disclosure Package, it being understood and agreed that the only such information furnished by any Underwriter consists of the information described as such in Section 7(b) hereof. No statement of material fact included in the Prospectus has been omitted from the Pricing Disclosure Package and no statement of material fact included in the Pricing Disclosure Package that is required to be included in the Prospectus has been omitted therefrom.

(c) *Issuer Free Writing Prospectus.* Other than the Registration Statement, the Preliminary Prospectus and the Prospectus, the Company (including its agents and representatives, other than the Underwriters in their capacity as such) has not prepared, made, used, authorized, approved or referred to and will not prepare, make, use, authorize, approve or refer to any "written communication" (as defined in Rule 405 under the Securities Act) that constitutes an offer to sell or solicitation of an offer to buy the Offered ADSs (each such communication by the Company or its agents and representatives (other than a communication referred to in clause (i) below) an "Issuer Free Writing Prospectus") other than (i) any document not constituting a prospectus pursuant to Section 2(a)(10)(a) of the Securities Act or Rule 134 under the Securities Act or (ii) the documents listed on Annex A hereto, each electronic road show and any other written communications approved in writing in advance by the Representatives. Each such Issuer Free Writing Prospectus complies in all material respects with the Securities Act, has been or will be (within the time period specified in Rule 433) filed in accordance with the Securities Act (to the extent required thereby) and does not conflict with the information contained in the Registration Statement or the Pricing Disclosure Package, and, when taken together with the Preliminary Prospectus accompanying, or delivered prior to delivery of, such Issuer Free Writing Prospectus, did not, and as of the Closing Date and as of the Additional Closing Date, as the case may be, will not, contain any untrue statement of a material fact or 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 that the Company makes no representation or warranty with respect to any statements or omissions made in each such Issuer Free Writing Prospectus or Preliminary Prospectus in reliance upon and in conformity with information relating to any Underwriter furnished to the Company in writing by such Underwriter through the Representatives expressly for use in such Issuer Free Writing Prospectus or Preliminary Prospectus, it being understood and agreed that the only such information furnished by any Underwriter consists of the information described as such in Section 7(b) hereof.

(d) *Emerging Growth Company*. From the time of initial confidential submission of the Registration Statement to the Commission 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").

(e) *Registration Statement and Prospectus.* The Registration Statement has been declared effective by the Commission. No order suspending the effectiveness of the Registration Statement has been issued by the Commission, and no proceeding for that purpose or pursuant to Section 8A of the Securities Act against the Company or related to the offering of the Offered ADSs has been initiated or, to the knowledge of the Company, threatened by the Commission; as of the applicable effective date of the Registration Statement and any post-effective amendment thereto, the Registration Statement and any such post-effective amendment complied and will comply in all material respects with the applicable requirements of the Securities Act, and did not and will not contain any untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary in order to make the statements therein not misleading; and as of the date of the Prospectus and any amendment or supplement thereto and as of the Closing Date and as of the Additional Closing Date, as the case may be, the Prospectus will comply in all material respects with the applicable requirements of the Securities Act and will not contain any untrue statement of a material fact or 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 that the Company makes no representation or warranty with respect to any statements or omissions made in reliance upon and in conformity with information relating to any Underwriter furnished to the Company in writing by such Underwriter through the Representatives expressly for use in the Registration Statement and the Prospectus and any amendment or supplement thereto, it being understood and agreed that the only such information furnished by any Underwriter consists of the information described as such in Section 7(b) hereof.

(f) *Form F-6.* A registration statement on Form F-6 (File No. 333-227905), and any amendments thereto, in respect of the Offered ADSs has been filed with the Commission; such registration statement in the form heretofore delivered to the Representatives and has been declared effective by the Commission; no stop order suspending the effectiveness of such registration statement has been issued and, to the knowledge of the Company, no proceeding for that purpose has been initiated or threatened by the Commission (the various parts of such registration statement, including all exhibits thereto, each as amended at the time such part of the registration statement became effective, being hereinafter called the "ADS Registration Statement"); as of the

applicable effective date of the ADS Registration Statement and any post-effective amendment thereto, the ADS Registration Statement and any such post-effective amendment complied and will comply in all material respects with the applicable requirements of the Securities Act, and did not and will not contain any untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary in order to make the statements therein not misleading.

(g) *Incorporated Documents*. The documents incorporated by reference in the Registration Statement, the Prospectus and the Pricing Disclosure Package, when they were filed with the Commission, conformed in all material respects to the requirements of the Securities Exchange Act of 1934, as amended, and the rules and regulations of the Commission thereunder (collectively, the "Exchange Act"), and none of such documents contained any untrue statement of a material fact or omitted to state a material fact necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading; and any further documents so filed and incorporated by reference in the Registration Statement, the Prospectus or the Pricing Disclosure Package, when such documents are filed with the Commission, will conform in all material respects to the requirements of the Exchange Act and will not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading.

(h) *Financial Statements.* The financial statements (including the related notes thereto) of the Company and its consolidated subsidiaries included or incorporated by reference in the Registration Statement, the Pricing Disclosure Package and the Prospectus comply in all material respects with the applicable requirements of the Securities Act and the Exchange Act, as applicable, and present fairly the financial position of the Company and its consolidated subsidiaries as of the dates indicated and the results of their operations and the changes in their cash flows for the periods specified; such financial statements have been prepared in conformity with generally accepted accounting principles ("GAAP") in the United States applied on a consistent basis throughout the periods covered thereby, except in the case of unaudited financial statements, which are subject to normal year-end adjustments and do not contain footnotes as permitted by the applicable rules of the Commission, and any supporting schedules included or incorporated by reference in the Registration Statement present fairly in all material respects the information required to be stated therein; and the other financial information included or incorporated by reference in the Registration Statement, the Pricing Disclosure Package and the Prospectus has been derived from the accounting records of the Company and its consolidated subsidiaries and presents fairly in all material respects the information shown thereby; all disclosures included in the Registration Statement, the Pricing Disclosure Package and the Prospectus regarding "non-GAAP financial measures" (as such term is defined by the rules and regulations of Commission) comply with Regulation G of the Exchange Act and Item 10 of Regulation S-K of the Securities Act, to the extent applicable.

(i) *No Material Adverse Change.* Since the date of the most recent financial statements of the Company included or incorporated by reference in the Registration

Statement, the Pricing Disclosure Package and the Prospectus, (i) there has not been any change in the capital stock (other than the issuance of Ordinary Shares upon exercise of stock options and warrants described as outstanding in, and the grant of options and awards under existing equity incentive plans described in, or as incorporated by reference in, the Registration Statement, the Pricing Disclosure Package and the Prospectus), short-term debt 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 change, or any development involving a prospective material adverse change, in or affecting the business, properties, management, financial position, stockholders' equity, results of operations or prospects of the Company and its subsidiaries taken as a whole; (ii) neither the Company nor any of its subsidiaries has entered into any transaction or agreement (whether or not in the ordinary course of business) that is material to the Company and its subsidiaries taken as a whole or incurred any liability or obligation, direct or contingent, that is material to the Company and its subsidiaries taken as a whole; and (iii) neither the Company nor any of its subsidiaries has sustained any loss or interference with its business that is material to the Company and its subsidiaries taken as a whole and that is either from fire, explosion, flood or other calamity, whether or not covered by insurance, or from any labor disturbance or dispute or any action, order or decree of any court or arbitrator or governmental or regulatory authority, except in each case as otherwise disclosed in the Registration Statement, the Pricing Disclosure Package and the Prospectus.

(j) *Organization and Good Standing.* The Company and each of its subsidiaries have been duly incorporated and are validly existing and in good standing under the laws of their respective jurisdictions of incorporated, are duly qualified to do business and are in good standing 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 necessary to own or hold their respective properties and to conduct the businesses in which they are engaged, except where the failure to be so qualified or in good standing or have such power or authority would not, individually or in the aggregate, reasonably be expected to have a material adverse effect on the business, properties, management, financial position, stockholders' equity, results of operations or prospects of the Company and its subsidiaries taken as a whole or on the performance by the Company of its obligations under this Agreement (a "Material Adverse Effect"). The Company does not own or control, directly or indirectly, any corporation, association or other entity other than the subsidiaries listed in Exhibit 21.1 to the Registration Statement.

(k) *Capitalization.* The Company has an authorized share capital as set forth in the Registration Statement, the Pricing Disclosure Package and the Prospectus under the heading "Capitalization"; all the outstanding shares of capital stock of the Company have been duly and validly authorized and issued and are fully paid and non-assessable and are not subject to any pre-emptive or similar rights (save for those granted under applicable law); except as described in or expressly contemplated by the Registration Statement, the Pricing Disclosure Package and the Prospectus, there are no outstanding rights (including, without limitation, pre-emptive rights (save for those granted under

applicable law)), warrants or options to acquire, or instruments convertible into or exchangeable for, any shares of capital stock or other equity interest in the Company or any of its subsidiaries, or any contract, commitment, agreement, understanding or arrangement of any kind relating to the issuance of any capital stock of the Company or any such subsidiary, any such convertible or exchangeable securities or any such rights, warrants or options; the capital stock of the Company conforms in all material respects to the description thereof contained in the Registration Statement, the Pricing Disclosure Package and the Prospectus; and all the outstanding shares of capital stock or other equity interests of each subsidiary owned, directly or indirectly, by the Company have been duly and validly authorized and issued, are fully paid and non-assessable and are owned directly or indirectly by the Company, free and clear of any lien, charge, encumbrance, security interest, restriction on voting or transfer or any other claim of any third party.

(l) *Stock Options.* With respect to the stock options (the "Stock Options") granted pursuant to the stock-based compensation plans of the Company and its subsidiaries (the "Company Stock Plans"), (i) each Stock Option intended to qualify as an "incentive stock option" under Section 422 of the Code so qualifies, (ii) each grant of a Stock Option was duly authorized no later than the date on which the grant of such Stock Option was by its terms to be effective by all necessary corporate action, including, as applicable, approval by the board of directors of the Company (or a duly constituted and authorized committee thereof) and any required stockholder approval by the necessary number of votes or written consents, and the award agreement governing such grant (if any) was duly executed and delivered by each party thereto, (iii) each such grant was made in all material respects in accordance with the terms of the Company Stock Plans, the Exchange Act and all other applicable laws, and regulatory rules or requirements, including the rules of the Nasdaq Global Select Market and (iv) each such grant or issuance was properly accounted for in accordance with GAAP in the financial statements (including the related notes) of the Company and disclosed in the Company's filings with the Commission in accordance with the Exchange Act and all other applicable laws. The Company has not knowingly granted, and there is not currently and has been no policy or practice of the Company of coordinating the grant of Stock Options with, the release or other public announcement of material information regarding the Company or its subsidiaries or their results of operations or prospects.

(m) *Due Authorization.* The Company has full right, power and authority to execute and deliver this Agreement and the Deposit Agreement (collectively, the "Transaction Documents") and to perform its obligations hereunder and thereunder; and all action required to be taken for the due and proper authorization, execution and delivery by it of this Agreement and each of the Transaction Documents and the consummation by it of the transactions contemplated hereby and thereby has been duly and validly taken.

(n) *Underwriting Agreement.* This Agreement has been duly authorized, executed and delivered by the Company.

(o) *The Shares.* The Shares to be issued and sold by the Company hereunder have been duly authorized by the Company and, when issued and delivered and paid for

as provided herein, will be duly and validly issued, will be fully paid and nonassessable and will conform in all material respects to the descriptions thereof in the Registration Statement, the Pricing Disclosure Package and the Prospectus; and the issuance of the Shares is not subject to any preemptive or similar rights (save for those granted under applicable law). The Shares may be freely deposited by the Company with the Depositary against issuance of the Offered ADSs; the Offered ADSs to be sold by the Company, when issued and delivered against payment thereof, will be freely transferable by the Company to or for the account of the several Underwriters and (to the extent described in the Prospectus) the initial purchasers thereof; and there are no restrictions on subsequent transfers of the Offered ADSs under the laws of England and Wales or the United States except as disclosed or incorporated by reference in the Registration Statement, the Pricing Disclosure Package and the Prospectus under "Description of Share Capital and Articles of Association," "Description of American Depositary Shares" and "Shares and ADSs Eligible for Future Sale."

(p) *Deposit Agreement*. The Deposit Agreement has been duly authorized by the Company and delivered in accordance with its terms by each of the parties thereto, and constitutes a valid and legally binding agreement of the Company enforceable against the Company in accordance with its terms, except as enforceability may be limited by applicable bankruptcy, insolvency, reorganization or similar laws affecting the enforcement of creditors' rights generally or by equitable principles relating to enforceability.

(q) *Description of the Transaction Documents.* Each Transaction Document conforms in all material respects to the description thereof contained in the Registration Statement, the Pricing Disclosure Package and the Prospectus.

(r) *No Violation or Default.* Neither the Company nor any of its subsidiaries is (i) in violation of its charter or by-laws or similar organizational documents; (ii) in default, and no event has occurred that, 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 or other agreement or instrument to which the Company or any of its subsidiaries is a party or by which the Company or any of its subsidiaries is bound or to which any property or asset of the Company or any of its subsidiaries is subject; or (iii) in violation of any law or statute or any judgment, order, rule or regulation of any court or arbitrator or governmental or regulatory authority, except, in the case of clauses (ii) and (iii) above, for any such default or violation that would not, individually or in the aggregate, have a Material Adverse Effect.

(s) *No Conflicts.* The execution, delivery and performance by the Company of each of the Transaction Documents, the issuance and sale of the Offered ADSs and the consummation of the transactions contemplated by the Transaction Documents or the Pricing Disclosure Package and the Prospectus will not (i) conflict with or result in a breach or violation of any of the terms or provisions of, or constitute a default under, result in the termination, modification or acceleration of, or result in the creation or imposition of any lien, charge or encumbrance upon any property, right or asset 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 or any of its subsidiaries is a party or by which the Company or any of its subsidiaries is bound or to which any property, right or asset of the Company or any of its subsidiaries is subject, (ii) result in any violation of the provisions of the charter or by-laws or similar organizational documents of the Company or any of its subsidiaries or (iii) result in the violation of any law or statute or any judgment, order, rule or regulation of any court or arbitrator or governmental or regulatory authority, except, in the case of clauses (i) and (iii) above, for any such conflict, breach, violation, default, lien, charge or encumbrance that would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect.

(t) *No Consents Required.* No consent, approval, authorization, order, registration or qualification of or with any court or arbitrator or governmental or regulatory authority is required for the execution, delivery and performance by the Company of each of the Transaction Documents, the issuance and sale of the Offered ADSs and the consummation of the transactions contemplated by the Transaction Documents, except for the registration of the ADSs under the Securities Act 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 Select Market or under applicable state securities laws in connection with the purchase and distribution of the Offered ADSs by the Underwriters.

(u) *Legal Proceedings.* Except as described in the Registration Statement, the Pricing Disclosure Package and the Prospectus, there are no legal, governmental or regulatory investigations, actions, demands, claims, suits, arbitrations, inquiries or proceedings ("Actions") current or pending or, to the knowledge of the Company, threatened Actions to which the Company or any of its subsidiaries is or may be a party or to which any property of the Company or any of its subsidiaries is or may be the subject that, individually or in the aggregate, if determined adversely to the Company or any of its subsidiaries, could reasonably be expected to have a Material Adverse Effect; no such Actions are threatened or, to the knowledge of the Company, contemplated by any governmental or regulatory authority or threatened by others; and (i) there are no current or pending Actions that are required under the Securities Act to be described in the Registration Statement, the Pricing Disclosure Package or the Prospectus that are not so described in the Registration Statement, the Pricing Disclosure Package and the Prospectus and (ii) there are no statutes, regulations or contracts or other documents that are required under the Securities Act to be filed as exhibits to the Registration Statement or described in the Registration Statement, the Pricing Disclosure Package or the Prospectus that are not so filed as exhibits to the Registration Statement or described in the Registration Statement, the Pricing Disclosure Package and the Prospectus.

(v) *Independent Accountants*. PricewaterhouseCoopers LLP, who have certified certain financial statements of the Company and its subsidiaries, is an independent registered public accounting firm with respect to the Company and its subsidiaries within the applicable rules and regulations adopted by the Commission and the Public Company Accounting Oversight Board (United States) and as required by the Securities Act.

(w) *Title to Real and Personal Property*. The Company and its subsidiaries have good and marketable title in fee simple to, or have valid rights to lease or otherwise use, all items of real and personal property that are material to the respective businesses of the Company and its subsidiaries, in each case free and clear of all liens, encumbrances, claims and defects and imperfections of title except those that (i) do not materially interfere with the use made and proposed to be made of such property by the Company and its subsidiaries or (ii) could not reasonably be expected, individually or in the aggregate, to have a Material Adverse Effect.

(x) *Intellectual Property.* Except as described in the Registration Statement, the Pricing Disclosure Package and the Prospectus or as could not reasonably be expected, individually or in the aggregate, to have a Material Adverse Effect, (i) the Company and its subsidiaries own or possess adequate rights to use all patents, trademarks, service marks, trade names, domain names and other source indicators, copyrights and copyrightable works, licenses and know-how, trade secrets and other unpatented and/or unpatentable proprietary or confidential information, systems or procedures, and all other worldwide intellectual property, industrial property and proprietary rights (including all registrations and applications for registration of, and all goodwill associated with, any of the foregoing) (collectively, "Intellectual Property") used or held for use in, or otherwise necessary for, the conduct of their respective businesses as currently conducted and as proposed to be conducted in the Registration Statement, the Pricing Disclosure Package and the Prospectus; provided that this clause (i) shall not be construed as a representation or warranty of non-infringement of Intellectual Property; (ii) the Company and its subsidiaries' conduct of their respective businesses has not conflicted with, infringed, misappropriated or otherwise violated any Intellectual Property rights other than patent rights of any third party and, to knowledge of the Company, the Company and its subsidiaries' conduct of their respective business has not infringed or otherwise violated any patent of any third party (it being understood that the foregoing representation and warranty is made without giving effect to any exemption under applicable law to which the Company may be entitled (e.g., 35 U.S.C. Section 271(e)(1)); (iii) the Company and its subsidiaries have not received any written notice of any claim of infringement, misappropriation or other violation of, or conflict with, any Intellectual Property of any third party, or any written notice challenging the ownership, validity, enforceability or scope of any Intellectual Property of the Company or any of its subsidiaries; (iv) to the knowledge of the Company, the Intellectual Property of the Company and its subsidiaries has not been in conflict with, infringed, misappropriated or otherwise violated by any third party; (v) to the knowledge of the Company, all Intellectual Property of the Company and its subsidiaries is valid and enforceable; and (vi) the Company and its subsidiaries have taken reasonable steps in accordance with normal industry practice to maintain the confidentiality of all Intellectual Property of the Company and its subsidiaries the value of which to the Company or any of its subsidiaries is contingent upon maintaining the confidentiality thereof and no such Intellectual Property has been disclosed other than to employees, representatives and agents of the Company or any of its subsidiaries, all of whom are bound by written confidentiality agreements.

(y) *No Undisclosed Relationships*. No relationship, direct or indirect, exists between or among the Company or any of its subsidiaries, on the one hand, and the directors, officers, stockholders, customers, suppliers or other affiliates of the Company or any of its subsidiaries, on the other, that is required by the Securities Act to be described in each of the Registration Statement and the Prospectus and that is not so described in such documents and in the Pricing Disclosure Package.

(z) *Investment Company Act*. The Company is not and, after giving effect to the offering and sale of the Offered ADSs and the application of the proceeds thereof as described in the Registration Statement, the Pricing 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 Investment Company Act of 1940, as amended, and the rules and regulations of the Commission thereunder (collectively, the "Investment Company Act").

(aa) *Taxes.* The Company and its subsidiaries have paid all federal, state, local and foreign taxes and filed all tax returns required to be paid or filed through the date hereof; and except as otherwise disclosed in each of the Registration Statement, the Pricing Disclosure Package and the Prospectus, there is no tax deficiency that has been, or could reasonably be expected to be, asserted against the Company or any of its subsidiaries or any of their respective properties or assets that could reasonably be expected to have a Material Adverse Effect.

(bb) *Licenses and Permits.* The Company and its subsidiaries possess all licenses, sub-licenses, certificates, permits and other authorizations issued by, and have made all declarations and filings with, the appropriate federal, state, local or foreign governmental or regulatory authorities that are necessary for the ownership or lease of their respective properties or the conduct of their respective businesses as described in each of the Registration Statement, the Pricing Disclosure Package and the Prospectus, except where the failure to possess or make the same would not, individually or in the aggregate, have a Material Adverse Effect; and except as described in each of the Registration Statement, the Pricing Disclosure Package and the Prospectus, neither the Company nor any of its subsidiaries has received notice of any revocation or modification of any such license, sub-license, certificate, permit or authorization or has any reason to believe that any such license, sub-license, certificate, permit or authorization will not be renewed in the ordinary course, except where the failure to pay or file or where such revocation, modification or nonrenewal could not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect.

(cc) *No Labor Disputes.* No labor disturbance by or dispute with employees of the Company or any of its subsidiaries exists or, to the knowledge of the Company, is contemplated or threatened, and the Company is not aware of any existing or imminent labor disturbance by, or dispute with, the employees of any of its or its subsidiaries' principal suppliers, contractors or customers, except as would not have a Material Adverse Effect. Neither the Company nor any of its subsidiaries has received any notice of cancellation or termination with respect to any collective bargaining agreement to which it is a party.

(dd) *Certain Environmental Matters*. (i) The Company and its subsidiaries (x) are in compliance with all, and have not violated any, applicable federal, state, local and foreign laws (including common law), rules, regulations, requirements, decisions, judgments, decrees, orders and other legally enforceable requirements relating to pollution or the protection of human health or safety, the environment, natural resources, hazardous or toxic substances or wastes, pollutants or contaminants (collectively, "Environmental Laws"); (y) have received and are in compliance with all, and have not violated any, permits, licenses, certificates or other authorizations or approvals required of them under any Environmental Laws to conduct their respective businesses; and (z) have not received notice of any actual or potential liability or obligation under or relating to, or any actual or potential violation of, any Environmental Laws, including for the investigation or remediation of any disposal or release of hazardous or toxic substances or wastes, pollutants or contaminants, and have no knowledge of any event or condition that would reasonably be expected to result in any such notice, and (ii) there are no costs or liabilities associated with Environmental Laws of or relating to the Company or its subsidiaries, except in the case of each of (i) and (ii) above, for any such matter as would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect; and (iii) except as described in each of the Pricing Disclosure Package and the Prospectus, (x) there is no proceeding that is pending, or that is known to be contemplated, against the Company or any of its subsidiaries under any Environmental Laws in which a governmental entity is also a party, other than such proceeding regarding which it is reasonably believed no monetary sanctions of $100,000 or more will be imposed, (y) the Company and its subsidiaries are not aware of any facts or issues regarding compliance with Environmental Laws, or liabilities or other obligations under Environmental Laws or concerning hazardous or toxic substances or wastes, pollutants or contaminants, that could reasonably be expected to have a material effect on the capital expenditures, earnings or competitive position of the Company and its subsidiaries, and (z) none of the Company or its subsidiaries anticipates material capital expenditures relating to any Environmental Laws.

(ee) *Compliance with ERISA*. (i) Each employee benefit plan, within the meaning of Section 3(3) of the Employee Retirement Income Security Act of 1974, as amended ("ERISA"), for which the Company or any member of its "Controlled Group" (defined as any entity, whether or not incorporated, that is under common control with the Company within the meaning of Section 4001(a)(14) of ERISA or any entity that would be regarded as a single employer with the Company under Section 414(b),(c),(m) or (o) of the Internal Revenue Code of 1986, as amended (the "Code")) would have any liability (each, a "Plan") has been maintained in compliance with its terms and the requirements of any applicable statutes, orders, rules and regulations, including but not limited to ERISA and the Code; (ii) no prohibited transaction, within the meaning of Section 406 of ERISA or Section 4975 of the Code, has occurred with respect to any Plan, excluding transactions effected pursuant to a statutory or administrative exemption; (iii) for each Plan that is subject to the funding rules of Section 412 of the Code or Section 302 of ERISA, no Plan has failed (whether or not waived), or is reasonably expected to fail, to satisfy the minimum funding standards (within the meaning of Section 302 of ERISA or Section 412 of the Code) applicable to such Plan; (iv) no Plan is, or is

reasonably expected to be, in "at risk status" (within the meaning of Section 303(i) of ERISA) and no Plan that is a "multiemployer plan" within the meaning of Section 4001(a)(3) of ERISA is in "endangered status" or "critical status" (within the meaning of Sections 304 and 305 of ERISA) (v) the fair market value of the assets of each Plan exceeds the present value of all benefits accrued under such Plan (determined based on those assumptions used to fund such Plan); (vi) no "reportable event" (within the meaning of Section 4043(c) of ERISA and the regulations promulgated thereunder) has occurred or is reasonably expected to occur; (vii) each Plan that is intended to be qualified under Section 401(a) of the Code is so qualified, and nothing has occurred, whether by action or by failure to act, which would cause the loss of such qualification; (viii) neither the Company nor any member of the Controlled Group has incurred, nor reasonably expects to incur, any liability under Title IV of ERISA (other than contributions to the Plan or premiums to the Pension Benefit Guarantee Corporation, in the ordinary course and without default) in respect of a Plan (including a "multiemployer plan" within the meaning of Section 4001(a)(3) of ERISA); and (ix) none of the following events has occurred or is reasonably likely to occur: (A) a material increase in the aggregate amount of contributions required to be made to all Plans by the Company or its Controlled Group affiliates in the current fiscal year of the Company and its Controlled Group affiliates compared to the amount of such contributions made in the Company's and its Controlled Group affiliates' most recently completed fiscal year; or (B) a material increase in the Company and its subsidiaries' "accumulated post-retirement benefit obligations" (within the meaning of Accounting Standards Codification Topic 715-60) compared to the amount of such obligations in the Company and its subsidiaries' most recently completed fiscal year, except in each case with respect to the events or conditions set forth in (i) through (ix) hereof, as would not, individually or in the aggregate, have a Material Adverse Effect.

(ff) *Disclosure Controls*. The Company and its subsidiaries maintain an effective system of "disclosure controls and procedures" (as defined in Rule 13a-15(e) of the Exchange Act) that complies with the requirements of the Exchange Act and that has been designed to ensure that information required to be disclosed by the Company in reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the Commission's rules and forms, including controls and procedures designed to ensure that such information is accumulated and communicated to the Company's management as appropriate to allow timely decisions regarding required disclosure. The Company and its subsidiaries have carried out evaluations of the effectiveness of their disclosure controls and procedures as required by Rule 13a-15 of the Exchange Act.

(gg) *Accounting Controls.* The Company and its subsidiaries maintain systems of "internal control over financial reporting" (as defined in Rule 13a-15(f) of the Exchange Act) that comply with the requirements of the Exchange Act and have been designed by, or under the supervision of, their respective principal executive and principal financial officers, or persons performing similar functions, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with GAAP. The Company and

its subsidiaries maintain internal accounting controls sufficient to provide reasonable assurance 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 GAAP and to maintain asset accountability; (iii) access to assets is permitted only in accordance with management's general or specific authorization; (iv) the recorded accountability for assets is compared with the existing assets at reasonable intervals and appropriate action is taken with respect to any differences; and (v) the interactive data in eXtensible Business Reporting Language included or incorporated by reference in the Registration Statement, the Prospectus and the Pricing Disclosure Package fairly presents the information called for in all material respects and is prepared in accordance with the Commission's rules and guidelines applicable thereto. Based on the Company's most recent evaluation of its internal controls over financial reporting pursuant to Rule 13a-15(c) of the Exchange Act, except as disclosed in the Registration Statement, the Pricing Disclosure Package and the Prospectus, there are no material weaknesses in the Company's internal controls. The Company's auditors and the Audit Committee of the Board of Directors of the Company have been advised of: (i) all significant deficiencies and material weaknesses in the design or operation of internal controls over financial reporting which have adversely affected or are reasonably likely to adversely affect the Company's ability to record, process, summarize and report financial information; and (ii) any fraud, whether or not material, that involves management or other employees who have a significant role in the Company's internal controls over financial reporting.

(hh) *Insurance.* The Company and its subsidiaries have insurance covering their respective properties, operations, personnel and businesses, including business interruption insurance, which insurance is in amounts and insures against such losses and risks which the Company believes are adequate to protect the Company and its subsidiaries and their respective businesses; and neither the Company nor any of its subsidiaries has (i) received notice from any insurer or agent of such insurer that capital improvements or other expenditures are required or necessary to be made in order to continue such insurance or (ii) any 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 at reasonable cost from similar insurers as may be necessary to continue its business.

(ii) *Cybersecurity.* (i)(x) Except as disclosed in the Registration Statement, the Pricing Disclosure Package and the Prospectus, to the Company's knowledge, there has been no security breach or other compromise of or relating to any of the Company's or any of its subsidiaries' information technology and computer systems, networks, hardware, software, data (including the data of their respective customers, employees, suppliers, vendors and any third party data maintained by or on behalf of them), equipment or technology (collectively, "IT Systems and Data") which could have a Material Adverse Effect and (y) the Company and its subsidiaries have not been notified of, and have no knowledge of any event or condition that would reasonably be expected to result in, any security breach or other compromise to their IT Systems and Data; (ii) the Company and its subsidiaries are presently in compliance with all applicable laws or statutes and all

judgments, orders, rules and regulations of any court or arbitrator or governmental or regulatory authority, internal policies and contractual obligations relating to the privacy and security of IT Systems and Data and to the protection of such IT Systems and Data from unauthorized use, access, misappropriation or modification, except as would not, in the case of this clause (ii), individually or in the aggregate, have a Material Adverse Effect; and (iii) the Company and its subsidiaries have implemented backup and disaster recovery technology consistent with industry standards and practices. Except as would not reasonably be expected to have a Material Adverse Effect, the Company and its subsidiaries are presently in compliance with all applicable laws or statutes and all judgments, orders, rules and regulations of any court or arbitrator or governmental or regulatory authority, including Regulation (EU) 2016/679 (the General Data Protection Regulation), and all internal policies and contractual obligations of the Company relating to the privacy and security of IT Systems and Personal Data and to the protection of such IT Systems and Personal Data from unauthorized use, access, misappropriation or modification.

(jj) *No Unlawful Payments.* Neither the Company nor any of its subsidiaries nor any director, officer or employee of the Company or any of its subsidiaries nor, to the knowledge of the Company, any agent, affiliate or other person associated with or acting on behalf of the Company or any of its subsidiaries has (i) used any corporate funds for any unlawful contribution, gift, entertainment or other unlawful expense relating to political activity; (ii) made or taken an act in furtherance of an offer, promise or authorization of any direct or indirect unlawful payment or benefit to any foreign or domestic government official or employee, including of any government-owned or controlled entity or of a public international organization, or any person acting in an official capacity for or on behalf of any of the foregoing, or any political party or party official or candidate for political office; (iii) violated or is in violation of any provision of the Foreign Corrupt Practices Act of 1977, as amended, or any applicable law or regulation implementing the OECD Convention on Combating Bribery of Foreign Public Officials in International Business Transactions, or committed an offence under the Bribery Act 2010 of the United Kingdom or any other applicable anti-bribery or anti-corruption law; or (iv) made, offered, agreed, requested or taken an act in furtherance of any unlawful bribe or other unlawful benefit, including, without limitation, any rebate, payoff, influence payment, kickback or other unlawful or improper payment or benefit. The Company and its subsidiaries have instituted, maintain and enforce, and will continue to maintain and enforce policies and procedures designed to promote and ensure compliance with all applicable anti-bribery and anti-corruption laws.

(kk) *Compliance with Anti-Money Laundering Laws*. 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, where applicable, those of the Currency and Foreign Transactions Reporting Act of 1970, as amended, the applicable money laundering statutes of all jurisdictions where the Company or any of its subsidiaries conducts 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 “Anti-Money Laundering Laws”) and no action, suit or proceeding by or before any court or governmental agency,

authority or body or any arbitrator involving the Company or any of its subsidiaries with respect to the Anti-Money Laundering Laws is pending or, to the knowledge of the Company, threatened.

(ll) *No Conflicts with Sanctions Laws.* Neither the Company nor any of its subsidiaries, directors, officers, or employees, nor, to the knowledge of the Company, any agent, affiliate or other person associated with or acting on behalf of the Company or any of its subsidiaries is currently the subject or the target of any sanctions administered or enforced by the U.S. government, (including, without limitation, the Office of Foreign Assets Control of the U.S. Department of the Treasury ("OFAC") or the U.S. Department of State and including, without limitation, the designation as a "specially designated national" or "blocked person"), the United Nations Security Council ("UNSC"), the European Union, Her Majesty's Treasury ("HMT") or other relevant sanctions authority (collectively, "Sanctions"), nor is the Company or any of its subsidiaries located, organized or resident in a country or territory that is the subject or target of Sanctions, including, without limitation, Crimea, Cuba, Iran, North Korea, Sudan and Syria (each, a "Sanctioned Country"); and the Company will not directly or indirectly use the proceeds of the offering of the Offered ADSs hereunder, or lend, contribute or otherwise make available such proceeds to any subsidiary, joint venture partner or other person or entity (i) to fund or facilitate any activities of or business with any person that, at the time of such funding or facilitation, is the subject or target of Sanctions, (ii) to fund or facilitate any activities of or business in any Sanctioned Country or (iii) in any other manner that will result in a violation by any person (including any person participating in the transaction, whether as underwriter, advisor, investor or otherwise) of Sanctions. Since the Company's inception, the Company and its subsidiaries have not knowingly engaged in and are not now knowingly engaged in any dealings or transactions with any person that at the time of the dealing or transaction is or was the subject or the target of Sanctions or with any Sanctioned Country.

(mm) *No Restrictions on Subsidiaries*. 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 capital stock or similar ownership interest, 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.

(nn) *No Broker's Fees.* Neither the Company nor any of its subsidiaries is a party to any contract, agreement or understanding with any person (other than this Agreement) that would give rise to a valid claim against any of them or any Underwriter for a brokerage commission, finder's fee or like payment in connection with the offering and sale of the ADSs.

(oo) *No Registration Rights*. No person has the right to require the Company or any of its subsidiaries to register any securities for sale under the Securities Act by reason of the filing of the Registration Statement with the Commission or the issuance and sale of the Offered ADSs, other than rights that have been validly waived.

(pp) *No Stabilization.* Neither the Company nor any of its subsidiaries has taken, directly or indirectly, any action designed to or that could reasonably be expected to cause or result in any stabilization or manipulation of the price of the Offered ADSs.

(qq) *Margin Rules*. Neither the issuance, sale and delivery of the Offered ADSs nor the application of the proceeds thereof by the Company as described in each of the Registration Statement, the Pricing Disclosure Package and the Prospectus will violate Regulation T, U or X of the Board of Governors of the Federal Reserve System or any other regulation of such Board of Governors.

(rr) *Forward-Looking Statements*. No forward-looking statement (within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act) included or incorporated by reference in any of the Registration Statement, the Pricing Disclosure Package or the Prospectus has been made or reaffirmed without a reasonable basis or has been disclosed other than in good faith.

(ss) *Statistical and Market Data.* Nothing has come to the attention of the Company that has caused the Company to believe that the statistical and market-related data included or incorporated by reference in each of the Registration Statement, the Pricing Disclosure Package and the Prospectus is not based on or derived from sources that are reliable and accurate in all material respects.

(tt) *Sarbanes-Oxley Act*. There is and has been no failure on the part of the Company or any of the Company's directors or officers, in their capacities as such, to comply with any applicable provision of the Sarbanes-Oxley Act of 2002, as amended and the rules and regulations promulgated in connection therewith (the "Sarbanes-Oxley Act"), including Section 402 related to loans and Sections 302 and 906 related to certifications.

(uu) *Status under the Securities Act.* At the time of filing the Registration Statement and any post-effective amendment thereto, at the earliest time thereafter that the Company or any offering participant made a *bona fide* offer (within the meaning of Rule 164(h)(2) under the Securities Act) of the Offered ADSs and at the date hereof, the Company was not and is not an "ineligible issuer," as defined in Rule 405 under the Securities Act.

(vv) *No Ratings*. There are (and prior to the Closing Date, will be) no debt securities or preferred stock issued or guaranteed by the Company or any of its subsidiaries that are rated by a "nationally recognized statistical rating organization", as such term is defined in Section 3(a)(62) under the Exchange Act.

(ww) *Preclinical Studies and Clinical Trials*. (i) Except as described in the Registration Statement, the Pricing Disclosure Package and the Prospectus, the preclinical studies and clinical trials conducted by or, to the knowledge of the Company, on behalf of or sponsored by the Company or its subsidiaries, or in which the Company or its subsidiaries have participated, that are described in the Registration Statement, the Pricing Disclosure Package and the Prospectus, or the results of which are referred to in

the Registration Statement, the Pricing Disclosure Package and the Prospectus, as applicable, were, and if still pending are, being conducted in all material respects in accordance with all applicable statutes and all applicable rules and regulations of the applicable regulatory agencies to which they are subject, including the U.S. Food and Drug Administration and the European Medicines Agency (collectively, the "Regulatory Authorities") and Good Clinical Practice and Good Laboratory Practice requirements; (ii) the descriptions in the Registration Statement, the Pricing Disclosure Package and the Prospectus of the results of such studies and trials are accurate and complete descriptions in all material respects and fairly present the data derived therefrom as of the dates given for such data in the Registration Statement; (iii) the Company has no knowledge of any other studies or trials conducted by or on behalf of the Company not described in the Registration Statement, the Pricing Disclosure Package and the Prospectus, the results of which are inconsistent with or call into question the results described or referred to in the Registration Statement, the Pricing Disclosure Package and the Prospectus; (iv) the Company and its subsidiaries have operated at all times and are currently in compliance in all respects with all applicable statutes, rules and regulations of the Regulatory Authorities, except that where such non-compliance would not, individually or in the aggregate, have a Material Adverse Effect; (v) the Company has provided the Underwriters with all substantive written notices, correspondence and summaries of all other communications from the Regulatory Authorities; and (vi) neither the Company nor any of its subsidiaries have received any written notices, correspondence or other communications from the Regulatory Authorities or any other governmental agency requiring or threatening the termination, material modification or suspension of any preclinical studies or clinical trials that are described in the Registration Statement, the Pricing Disclosure Package and the Prospectus or the results of which are referred to in the Registration Statement, the Pricing Disclosure Package and the Prospectus, other than ordinary course communications with respect to modifications in connection with the design and implementation of such studies or trials, and, to the Company's knowledge, there are no reasonable grounds for the same.

(xx) *Regulatory Filings*. The Company has not failed to file with the Regulatory Authorities any required filing, declaration, listing, registration, report or submission with respect to the Company's product candidates that are described or referred to in the Registration Statement, the Pricing Disclosure Package and the Prospectus; all such filings, declarations, listings, registrations, reports or submissions, as applicable, were in material compliance with applicable laws when filed; and no material deficiencies regarding compliance with applicable law have been asserted by any applicable regulatory authority with respect to any such filings, declarations, listings, registrations, reports or submissions.

(yy) *Stamp Taxes*. Except as described in the Registration Statement or the Prospectus and except for any net income, or franchise taxes imposed on the Underwriters by the United Kingdom or 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 the jurisdiction imposing such tax, no stamp duty, stamp duty reserve

tax, documentary, issuance, transfer, capital, registration or other similar taxes or duties are payable by or on behalf of the Underwriters in the United Kingdom or the United States (including taxes or duties imposed by any political subdivision or taxing authority thereof) in connection with (A) the execution and delivery, performance or enforcement of this Agreement, (B) the issuance, allotment and delivery of the Shares and the Offered ADSs in the manner contemplated by this Agreement and the Prospectus, or (C) the sale and delivery by the Underwriters of the Offered ADSs as contemplated herein and in the Prospectus.

(zz) *No Immunity*. Neither the Company nor any of its subsidiaries or their properties or assets has immunity under English, U.S. federal or New York state 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 English, U.S. federal or New York state court, from service of process, attachment upon or prior to 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 their respective obligations, liabilities or any other matter under or arising out of or in connection herewith; and, to the extent that the Company or any of its subsidiaries or any of its properties, assets or revenues may have or may hereafter become entitled to any such right of immunity in any such court in which proceedings arising out of, or relating to the transactions contemplated by the Transaction Documents, may at any time be commenced, the Company has, pursuant to Section 16(e) of this Agreement, waived, and it will waive, or will cause its subsidiaries to waive, such right to the extent permitted by law.

(aaa) *Enforcement of Foreign Judgments*. Any final judgment for a fixed or determined sum of money rendered by any U.S. federal or New York state court located in the State of New York having jurisdiction under its own laws in respect of any suit, action or proceeding against the Company based upon this Agreement would be declared enforceable against the Company by the courts of England and Wales, without reconsideration or reexamination of the merits.

(bbb) *Valid Choice of Law*. The choice of laws of the State of New York as the governing law of the Transaction Documents is a valid choice of law under the laws of England and Wales and will be honored by the courts of England and Wales, subject to the restrictions described under the caption “Service of process and enforcement of liabilities” in the Registration Statement, the Pricing Disclosure Package and the Prospectus. The Company has the power to submit, and pursuant to Section 16(b) 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 and has validly and irrevocably waived any objection to the laying of venue of any suit, action or proceeding brought in such court.

(ccc) *Indemnification and Contribution*. The indemnification and contribution provisions set forth in Section 7 hereof do not contravene English law or public policy.

(ddd) *Passive Foreign Investment Company*. Subject to the qualifications, limitations, exceptions and assumptions set forth in the Registration Statement, the Pricing Disclosure Package and the Prospectus, the Company does not expect it was treated as, for the taxable year ending December 31, 2018, a passive foreign investment company as defined in Section 1297 of the Code.

(eee) *Dividends*. Except as disclosed in the Registration Statement, the Pricing Disclosure Package and the Prospectus, no approvals are currently required in the United Kingdom in order for the Company to pay dividends or other distributions declared by the Company to the holders of Shares. Under current laws and regulations of the United Kingdom and any political subdivision thereof, any amount payable with respect to the Shares upon liquidation of the Company or upon redemption thereof and dividends and other distributions declared and payable on the share capital of the Company may be paid by the Company in United States dollars or euros and freely transferred out of the United Kingdom, and no such payments made to the holders thereof or therein who are non-residents of the United Kingdom will be subject to income, withholding or other taxes under laws and regulations of the United Kingdom or any political subdivision or taxing authority thereof or therein and without the necessity of obtaining any governmental authorization in the United Kingdom or any political subdivision or taxing authority thereof or therein.

(fff) *Legality*. Other than filings required to be made with the Commission, the legality, validity, enforceability or admissibility into evidence of any of the Registration Statement, the Pricing Disclosure Package, the Prospectus, this Agreement or the Offered ADSs in any jurisdiction in which the Company is organized or does business is not dependent upon such document being submitted into, filed or recorded with any court or other authority in any such jurisdiction on or before the date hereof or that any tax, imposition or charge be paid in any such jurisdiction on or in respect of any such document.

(ggg) *Legal Action*. A holder of the Shares and each Underwriter are each entitled to sue as plaintiff in the court of the jurisdiction of formation and domicile of the Company for the enforcement of their respective rights under this Agreement and the Shares and such access to such courts will not be subject to any conditions which are not applicable to residents of such jurisdiction or a company incorporated in such jurisdiction except that plaintiffs not residing in England and Wales may be required to guarantee payment of a possible order for payment of costs or damages at the request of the defendant.

(hhh) *Foreign Issuer*. The Company is a “foreign private issuer” as defined in Rule 405 under the Securities Act.

(iii) *eXtensible Business Reporting Language*. The interactive data in eXtensible Business Reporting Language included or incorporated by reference in the Registration Statement fairly presents the information called for in all material respects and has been prepared in accordance with the Commission’s rules and guidelines applicable thereto.

4. Further Agreements of the Company. The Company covenants and agrees with each Underwriter that:

(a) *Required Filings.* The Company will file the final Prospectus with the Commission within the time periods specified by Rule 424(b) and Rule 430A, 430B or 430C under the Securities Act, will file any Issuer Free Writing Prospectus to the extent required by Rule 433 under the Securities Act; and the Company will furnish copies of the Prospectus and each Issuer Free Writing Prospectus (to the extent not previously delivered) to the Underwriters in New York City prior to 10:00 A.M., New York City time, on the business day next succeeding the date of this Agreement in such quantities as the Representatives may reasonably request.

(b) *Delivery of Copies.* The Company will deliver, without charge, (i) to the Representatives, four signed copies of the Registration Statement as originally filed and each amendment thereto, in each case including all exhibits and consents filed therewith; and (ii) to each Underwriter (A) a conformed copy of the Registration Statement as originally filed and each amendment thereto (without exhibits) and (B) during the Prospectus Delivery Period (as defined below), as many copies of the Prospectus (including all amendments and supplements thereto and each Issuer Free Writing Prospectus) as the Representatives may reasonably request. As used herein, the term "Prospectus Delivery Period" means such period of time after the first date of the public offering of the Offered ADSs as in the opinion of counsel for the Underwriters a prospectus relating to the Offered ADSs is required by law to be delivered (or required to be delivered but for Rule 172 under the Securities Act) in connection with sales of the Offered ADSs by any Underwriter or dealer.

(c) *Amendments or Supplements, Issuer Free Writing Prospectuses.* Before making, preparing, using, authorizing, approving, referring to or filing any Issuer Free Writing Prospectus, and before filing any amendment or supplement to the Registration Statement, the Pricing Disclosure Package or the Prospectus, the Company will furnish to the Representatives and counsel for the Underwriters a copy of the proposed Issuer Free Writing Prospectus, amendment or supplement for review and will not make, prepare, use, authorize, approve, refer to or file any such Issuer Free Writing Prospectus or file any such proposed amendment or supplement to which the Representatives reasonably object.

(d) *Notice to the Representatives.* The Company will advise the Representatives promptly, and confirm such advice in writing, (i) when the Registration Statement has become effective; (ii) when any amendment to the Registration Statement has been filed or becomes effective; (iii) when any supplement to the Pricing Disclosure Package, the Prospectus, any Issuer Free Writing Prospectus or any amendment to the Prospectus has been filed or distributed; (iv) of any request by the Commission for any amendment to the Registration Statement or any amendment or supplement to the Prospectus or the receipt of any comments from the Commission relating to the Registration Statement or any other request by the Commission for any additional information; (v) of the issuance by the Commission or any other governmental or regulatory authority of any order suspending the effectiveness of the Registration

Statement or preventing or suspending the use of any Preliminary Prospectus, any of the Pricing Disclosure Package, the Prospectus or the initiation or threatening of any proceeding for that purpose or pursuant to Section 8A of the Securities Act; (vi) of the occurrence of any event or development within the Prospectus Delivery Period as a result of which the Prospectus, any of the Pricing Disclosure Package or any Issuer Free Writing Prospectus as then amended or supplemented would include any untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances existing when the Prospectus, the Pricing Disclosure Package or any such Issuer Free Writing Prospectus; and (vii) of the receipt by the Company of any notice with respect to any suspension of the qualification of the Offered ADSs for offer and sale in any jurisdiction or the initiation or threatening of any proceeding for such purpose; and the Company will use its reasonable best efforts to prevent the issuance of any such order suspending the effectiveness of the Registration Statement, preventing or suspending the use of any Preliminary Prospectus or any of the Pricing Disclosure Package or the Prospectus or suspending any such qualification of the Offered ADSs and, if any such order is issued, will obtain as soon as possible the withdrawal thereof.

(e) *Ongoing Compliance.* (1) If during the Prospectus Delivery Period (i) any event or development shall occur or condition shall exist 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 in order to make the statements therein, in the light of the circumstances existing when the Prospectus is delivered to a purchaser, not misleading or (ii) it is necessary to amend or supplement the Prospectus to comply with applicable law, the Company will promptly notify the Underwriters thereof and forthwith prepare and, subject to paragraph (c) above, file with the Commission and furnish to the Underwriters and to such dealers as the Representatives may designate such amendments or supplements to the Prospectus as may be necessary so that the statements in the Prospectus as so amended or supplemented will not, in the light of the circumstances existing when the Prospectus is delivered to a purchaser, be misleading or so that the Prospectus will comply with applicable law and (2) if at any time prior to the Closing Date (i) any event or development shall occur or condition shall exist as a result of which the Pricing Disclosure Package as then amended or supplemented would include any untrue statement of a material fact or omit to state any material fact necessary in order to make the statements therein, in the light of the circumstances existing when the Pricing Disclosure Package is delivered to a purchaser, not misleading or (ii) it is necessary to amend or supplement the Pricing Disclosure Package to comply with applicable law, the Company will promptly notify the Underwriters thereof and forthwith prepare and, subject to paragraph (c) above, file with the Commission (to the extent required) and furnish to the Underwriters and to such dealers as the Representatives may designate such amendments or supplements to the Pricing Disclosure Package as may be necessary so that the statements in the Pricing Disclosure Package as so amended or supplemented will not, in the light of the circumstances existing when the Pricing Disclosure Package is delivered to a purchaser, be misleading or so that the Pricing Disclosure Package will comply with applicable law.

(f) *Blue Sky Compliance.* The Company will qualify the Offered ADSs for offer and sale under the securities or Blue Sky laws of such jurisdictions as the Representatives shall reasonably request and will continue such qualifications in effect so long as required for distribution of the ADSs; provided that the Company shall not be required to (i) qualify as a foreign corporation or other entity or as a dealer in securities in any such jurisdiction where it would not otherwise be required to so qualify, (ii) file any general consent to service of process in any such jurisdiction or (iii) subject itself to taxation in any such jurisdiction if it is not otherwise so subject.

(g) *Earning Statement.* The Company will make generally available to its security holders and the Representatives as soon as practicable an earning statement that satisfies the provisions of Section 11(a) of the Securities Act and Rule 158 of the Commission promulgated thereunder covering a period of at least twelve months beginning with the first fiscal quarter of the Company occurring after the "effective date" (as defined in Rule 158) of the Registration Statement; provided that the Company will be deemed to have furnished such statements to its security holders and the Representatives to the extent they are filed on the Commission's Electronic Data Gathering, Analysis, and Retrieval system ("EDGAR") or any successor system.

(h) *Clear Market.* For a period commencing on the date hereof and ending 90 days after the date of the Prospectus (the "Restricted Period"), the Company will not (i) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, or file with, or submit to, the Commission a registration statement under the Securities Act relating to, any Ordinary Shares or ADSs or any securities convertible into or exercisable or exchangeable for Ordinary Shares or ADSs, or publicly disclose the intention to make any offer, sale, pledge, disposition, submission or filing (other than filings on Form S-8 relating to the Company Stock Plans that are disclosed in the Pricing Disclosure Package), or (ii) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the Ordinary Shares or ADSs or any such other securities, whether any such transaction described in clause (i) or (ii) above is to be settled by delivery of Shares or such other securities, in cash or otherwise, without the prior written consent of the Representatives, other than (A) the ADSs to be sold hereunder, (B) any Ordinary Shares or ADSs of the Company issued upon the exercise of options granted under Company Stock Plans, (C) any options and other awards granted under a Company Stock Plan, or (D) up to 5% of the Company's outstanding securities issued by the Company in connection with mergers, acquisitions or commercial or strategic transactions; provided that in the case of clauses (B), (C) and (D), the recipient of such securities shall execute and deliver (if a lock-up agreement has not previously been delivered by such recipient) a lock-up agreement for the remainder of the Restricted Period in substantially the form attached as Exhibit A hereto.

(i) *Use of Proceeds.* The Company will apply the net proceeds from the sale of the ADSs in all material respects as described in each of the Registration Statement, the Pricing Disclosure Package and the Prospectus under the heading "Use of proceeds".

(j) *No Stabilization.* The Company will not take, directly or indirectly, any action designed to or that could reasonably be expected to cause or result in any stabilization or manipulation of the price of the Offered ADSs.

(k) *Exchange Listing.* The Company will use its reasonable best efforts to maintain the listing of the ADSs for quotation on the Nasdaq Global Select Market (the "Nasdaq Market").

(l) *Reports.* For a period of two years following the date of this Agreement, the Company will furnish to the Representatives, as soon as they are available, copies of all reports or other communications (financial or other) furnished to holders of the Shares or ADSs, and copies of any reports and financial statements furnished to or filed with the Commission or any national securities exchange or automatic quotation system; provided the Company will be deemed to have furnished such reports and financial statements to the Representatives to the extent they are filed on EDGAR.

(m) *Record Retention*. The Company will, pursuant to reasonable procedures developed in good faith, retain copies of each Issuer Free Writing Prospectus that is not filed with the Commission in accordance with Rule 433 under the Securities Act.

(n) *Filings.* The Company will file with the Commission such reports as may be required by Rule 463 under the Securities Act.

(o) *Emerging Growth Company; Foreign Private Issuer*. The Company will promptly notify the Representatives if the Company ceases to be an Emerging Growth Company or a Foreign Private Issuer at any time prior to the later of (i) completion of the distribution of Offered ADSs within the meaning of the Securities Act and (ii) completion of the 90-day restricted period referred to in Section 4(h) hereof.

(p) *Tax Indemnity*. The Company will bear, and indemnify and hold harmless the Underwriters against, any stamp duty, stamp duty reserve tax, documentary, issuance, transfer, capital, registration or other similar taxes or duties (including any interest and penalties imposed thereon) payable, in the United Kingdom, the United States or any other jurisdiction (including taxes or duties imposed by any political subdivision or taxing authority thereof), on (A) the execution, delivery, performance or enforcement of this Agreement, (B) the issuance, allotment and delivery of the Shares and the Offered ADSs in the manner contemplated by this Agreement and the Prospectus, or (C) the sale and delivery by the Underwriters of the Offered ADSs as contemplated herein and in the Prospectus.

(q) *Gross-up*. All payments to be made by the Company hereunder shall be made without withholding or deduction for or on account of any present or future taxes, duties or governmental charges whatsoever unless the Company is compelled by law to deduct or withhold such taxes, duties or charges. In that event, the Company shall pay such additional amounts as may be necessary in order to ensure that the net amounts received after such withholding or deductions shall equal the amounts that would have been received if no withholding or deduction had been made.

(r) *Value Added Tax*. All sums payable to the Underwriters shall be considered exclusive of any value added tax chargeable pursuant to the Value Added Tax Act 1994 ("VAT"). Where the Company is obliged to pay VAT on any amount payable hereunder to the Underwriters, the Company shall in addition to the sum payable hereunder pay an amount equal to any applicable VAT to the extent not recoverable by the Underwriters and subject to receipt of a valid VAT invoice from the Underwriters.

5. Certain Agreements of the Underwriters. Each Underwriter hereby represents and agrees that:

(a) It has not and will not use, authorize use of, refer to or participate in the planning for use of, any "free writing prospectus", as defined in Rule 405 under the Securities Act (which term includes use of any written information furnished to the Commission by the Company and not incorporated by reference into the Registration Statement and any press release issued by the Company) other than (i) a free writing prospectus that contains no "issuer information" (as defined in Rule 433(h)(2) under the Securities Act) that was not included (including through incorporation by reference) in the Preliminary Prospectus or a previously filed Issuer Free Writing Prospectus, (ii) any Issuer Free Writing Prospectus listed on Annex A or prepared pursuant to Section 3(c) or Section 4(c) above (including any electronic road show), or (iii) any free writing prospectus prepared by such Underwriter and approved by the Company in advance in writing (each such free writing prospectus referred to in clauses (i) or (iii), an "Underwriter Free Writing Prospectus").

(b) It has not and will not, without the prior written consent of the Company, use any free writing prospectus that contains the final terms of the Offered ADSs unless such terms have previously been included in a free writing prospectus filed with the Commission; *provided* that Underwriters may use a term sheet substantially in the form of Annex B hereto without the consent of the Company; *provided further* that any Underwriter using such term sheet shall notify the Company, and provide a copy of such term sheet to the Company, prior to, or substantially concurrently with, the first use of such term sheet.

(c) It is not subject to any pending proceeding under Section 8A of the Securities Act with respect to the offering (and will promptly notify the Company if any such proceeding against it is initiated during the Prospectus Delivery Period).

6. Conditions of Underwriters' Obligations. The obligation of each Underwriter to purchase the Underwritten ADSs on the Closing Date or the Option ADSs on the Additional Closing Date, as the case may be, as provided herein is subject to the performance by the Company of its covenants and other obligations hereunder and to the following additional conditions:

(a) *Registration Compliance; No Stop Order.* No order suspending the effectiveness of the Registration Statement shall be in effect, and no proceeding for such purpose or pursuant to Section 8A under the Securities Act shall be pending before or threatened by the Commission; the Prospectus and each Issuer Free Writing Prospectus

shall have been timely filed with the Commission under the Securities Act (in the case of an Issuer Free Writing Prospectus, to the extent required by Rule 433 under the Securities Act) and in accordance with Section 4(a) hereof; and all requests by the Commission for additional information shall have been complied with to the reasonable satisfaction of the Representatives.

(b) *Representations and Warranties.* The representations and warranties of the Company contained herein shall be true and correct on the date hereof and on and as of the Closing Date or the Additional Closing Date, as the case may be; and the statements of the Company and its officers made in any certificates delivered pursuant to this Agreement shall be true and correct on and as of the Closing Date or the Additional Closing Date, as the case may be.

(c) *No Material Adverse Change.* No event or condition of a type described in Section 3(i) hereof shall have occurred or shall exist, which event or condition is not described in the Pricing Disclosure Package (excluding any amendment or supplement thereto) and the Prospectus (excluding any amendment or supplement thereto) and the effect of which in the judgment of the Representatives makes it impracticable or inadvisable to proceed with the offering, sale or delivery of the Offered ADSs on the Closing Date or the Additional Closing Date, as the case may be, on the terms and in the manner contemplated by this Agreement, the Pricing Disclosure Package and the Prospectus.

(d) *Officer's Certificate.* The Representatives shall have received on and as of the Closing Date or the Additional Closing Date, as the case may be, a certificate of the chief financial officer or chief accounting officer of the Company and one additional senior executive officer of the Company who is satisfactory to the Representatives (i) confirming that such officers have carefully reviewed the Registration Statement, the Pricing Disclosure Package and the Prospectus and, to the knowledge of such officers, the representations set forth in Sections 3(b) and 3(d) hereof are true and correct, (ii) confirming that the other representations and warranties of the Company in this Agreement are true and correct and that the Company has complied with all agreements and satisfied all conditions on its part to be performed or satisfied hereunder at or prior to the Closing Date or the Additional Closing Date, as the case may be, and (iii) to the effect set forth in paragraphs (a), (b) and (c) above.

(e) *Comfort Letters.* On the date of this Agreement and on the Closing Date or the Additional Closing Date, as the case may be, PricewaterhouseCoopers LLP shall have furnished to the Representatives, at the request of the Company, letters, dated the respective dates of delivery thereof and addressed to the Underwriters, in form and substance reasonably satisfactory to the Representatives, containing statements and information of the type customarily included in accountants' "comfort letters" to underwriters with respect to the financial statements and certain financial information contained in each of the Registration Statement, the Pricing Disclosure Package and the Prospectus; provided, that the letter delivered on the Closing Date or the Additional Closing Date, as the case may be, shall use a "cut-off" date no more than two business days prior to such Closing Date or such Additional Closing Date, as the case may be.

(f) *Opinion and 10b-5 Statement of U.S. Counsel for the Company.* Goodwin Procter LLP, as U.S. counsel for the Company, shall have furnished to the Representatives, at the request of the Company, their written opinion and 10b-5 statement, dated the Closing Date or the Additional Closing Date, as the case may be, and addressed to the Underwriters, in form and substance reasonably satisfactory to the Representatives.

(g) *Opinion of UK Counsel for the Company.* Goodwin Procter (UK) LLP, as UK counsel for the Company, shall have furnished to the Representatives, at the request of the Company, their written opinion, dated the Closing Date or the Additional Closing Date, as the case may be, and addressed to the Underwriters, in form and substance reasonably satisfactory to the Representatives.

(h) *Opinion of IP Counsel for the Company.* Clark+Elbing LLP, IP counsel for the Company, shall have furnished to the Representatives, at the request of the Company, their written opinion, dated the Closing Date or the Additional Closing Date, as the case may be, and addressed to the Underwriters, in form and substance reasonably satisfactory to the Representatives.

(i) *Opinion and 10b-5 Statement of Counsel for the Underwriters.* The Representatives shall have received on and as of the Closing Date or the Additional Closing Date, as the case may be, an opinion and 10b-5 statement, addressed to the Underwriters, of Davis Polk & Wardwell LLP, counsel for the Underwriters, with respect to such matters as the Representatives may reasonably request, and such counsel shall have received such documents and information as they may reasonably request to enable them to pass upon such matters.

(j) *Opinion of Counsel for the Depositary.* The Representatives shall have received on and as of the Closing Date or the Additional Closing Date, as the case may be, an opinion of Patterson Belknap Webb & Tyler LLP, counsel for the Depositary, with respect to such matters as the Representatives may reasonably request and in form and substance reasonably satisfactory to the Representatives.

(k) *No Legal Impediment to Issuance and Sale.* No action shall have been taken and no statute, rule, regulation or order shall have been enacted, adopted or issued by any federal, state or foreign governmental or regulatory authority that would, as of the Closing Date or the Additional Closing Date, as the case may be, prevent the issuance or sale of the Offered ADSs; and no injunction or order of any federal, state or foreign court shall have been issued that would, as of the Closing Date or the Additional Closing Date, as the case may be, prevent the issuance or sale of the Offered ADSs.

(l) *Good Standing*. The Representatives shall have received on and as of the Closing Date or the Additional Closing Date, as the case may be, reasonably satisfactory evidence of the good standing of the Company and its subsidiaries in their respective jurisdictions of organization and their good standing 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.

(m) *Exchange Listing*. The ADSs to be delivered on the Closing Date or the Additional Closing Date, as the case may be, have been or shall have been duly listed on the Nasdaq Global Select Market.

(n) *Lock-up Agreements*. The "lock-up" agreements, each substantially in the form of Exhibit A hereto, between you and the individuals listed on Exhibit A-2 hereto relating to sales and certain other dispositions of Ordinary Shares, ADSs or certain other securities, delivered to you on or before the date hereof, shall be full force and effect on the Closing Date or the Additional Closing Date, as the case may be.

(o) *Certificates at Closing Date.* The Depositary shall have furnished or caused to be furnished to the Representatives at the Closing Date or Additional Closing Date, as the case may be, certificates reasonably satisfactory to the Representatives evidencing the deposit with it or its nominee of the Shares being so deposited against issuance of the Offered ADSs to be delivered by the Company at the Closing Date or Additional Closing Date, as the case may be, and the execution, countersignature (if applicable), issuance and delivery of such Offered ADSs pursuant to the Deposit Agreement.

(p) *Additional Documents.* On or prior to the Closing Date or the Additional Closing Date, as the case may be, the Company shall have furnished to the Representatives such further certificates and documents as the Representatives may reasonably request.

All opinions, letters, certificates and evidence 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) *Indemnification of the Underwriters.* The Company agrees to indemnify and hold harmless each Underwriter, its affiliates, directors and officers and each person, if any, who controls such Underwriter within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act, from and against any and all losses, claims, damages and liabilities (including, without limitation, documented legal fees and other documented expenses incurred in connection with any suit, action or proceeding or any claim asserted, as such fees and expenses are incurred), joint or several, that arise out of, or are based upon, (i) any untrue statement or alleged untrue statement of a material fact contained in the Registration Statement or caused by any omission or alleged omission to state therein a material fact required to be stated therein or necessary in order to make the statements therein, not misleading, or (ii) any untrue statement or alleged untrue statement of a material fact contained in the Prospectus (or any amendment or supplement thereto), any Preliminary Prospectus, any Issuer Free Writing Prospectus, any "issuer information" filed or required to be filed pursuant to Rule 433(d) under the Securities Act, any road show as defined in Rule 433(h) under the Securities Act (a "road show") or any Pricing Disclosure Package (including any Pricing Disclosure Package that has subsequently been amended), or caused by any omission or alleged omission to state

therein a material fact necessary in order to make the statements therein, in light of the circumstances under which they were made, not misleading, in each case except insofar as such losses, claims, damages or liabilities arise out of, or are based upon, any untrue statement or omission or alleged untrue statement or omission made in reliance upon and in conformity with any information relating to any Underwriter furnished to the Company in writing by such Underwriter through the Representatives expressly for use therein, it being understood and agreed that the only such information furnished by any Underwriter consists of the information described as such in subsection (b) below.

(b) *Indemnification of the Company.* Each Underwriter agrees, severally and not jointly, to indemnify and hold harmless the Company, its directors, its officers who signed the 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 to the same extent as the indemnity set forth in paragraph (a) above, but only with respect to any losses, claims, damages or liabilities that arise out of, or are based upon, any untrue statement or omission or alleged untrue statement or omission made in reliance upon and in conformity with any information relating to such Underwriter furnished to the Company in writing by such Underwriter through the Representatives expressly for use in the Registration Statement, the Prospectus (or any amendment or supplement thereto), any Preliminary Prospectus, any Issuer Free Writing Prospectus, any road show or any Pricing Disclosure Package (including any Pricing Disclosure Package that has subsequently been amended), it being understood and agreed upon that the only such information furnished by any Underwriter consists of the following information in the Prospectus furnished on behalf of each Underwriter: [the third paragraph, the first sentence of the twelfth paragraph and the thirteenth, fourteenth and fifteenth paragraphs describing passive market making activities and stabilization under the caption "Underwriting."][1]

(c) *Notice and Procedures.* If any suit, action, proceeding (including any governmental or regulatory investigation), claim or demand shall be brought or asserted against any person in respect of which indemnification may be sought pursuant to the preceding paragraphs of this Section 7, such person (the "Indemnified Person") shall promptly notify the person against whom such indemnification may be sought (the "Indemnifying Person") in writing; provided that the failure to notify the Indemnifying Person shall not relieve it from any liability that it may have under the preceding paragraphs of this Section 7 except to the extent that it has been materially prejudiced (through the forfeiture of substantive rights or defenses) by such failure; and provided, further, that the failure to notify the Indemnifying Person shall not relieve it from any liability that it may have to an Indemnified Person otherwise than under the preceding paragraphs of this Section 9. If any such proceeding shall be brought or asserted against an Indemnified Person and it shall have notified the Indemnifying Person thereof, the Indemnifying Person shall retain counsel reasonably satisfactory to the Indemnified Person (who shall not,

[1] NTD: To be confirmed.

without the consent of the Indemnified Person, be counsel to the Indemnifying Person) to represent the Indemnified Person and any others entitled to indemnification pursuant to this Section that the Indemnifying Person may designate in such proceeding and shall pay the documented fees and expenses in such proceeding and shall pay the fees and expenses of such counsel related to such proceeding, as incurred. In any such proceeding, any Indemnified Person shall have the right to retain its own counsel, but the fees and expenses of such counsel shall be at the expense of such Indemnified Person unless (i) the Indemnifying Person and the Indemnified Person shall have mutually agreed to the contrary; (ii) the Indemnifying Person has failed within a reasonable time to retain counsel reasonably satisfactory to the Indemnified Person; (iii) the Indemnified Person shall have reasonably concluded that there may be legal defenses available to it that are different from or in addition to those available to the Indemnifying Person; or (iv) the named parties in any such proceeding (including any impleaded parties) include both the Indemnifying Person and the Indemnified Person and representation of both parties by the same counsel would be inappropriate due to actual or potential differing interests between them. It is understood and agreed that the Indemnifying Person shall not, in connection with any proceeding or related proceeding in the same jurisdiction, be liable for the fees and expenses of more than one separate firm (in addition to any local counsel) for all Indemnified Persons, and that all such fees and expenses shall be paid or reimbursed as they are incurred. Any such separate firm for any Underwriter, its affiliates, directors and officers and any control persons of such Underwriter shall be designated in writing by the Representatives and any such separate firm for the Company, its directors, its officers who signed the Registration Statement and any control persons of the Company shall be designated in writing by the Company. The Indemnifying Person shall not be liable for any settlement of any proceeding effected without its written consent, but if settled with such consent, the Indemnifying Person agrees to indemnify each Indemnified Person from and against any loss or liability by reason of such settlement. Notwithstanding the foregoing sentence, if at any time an Indemnified Person shall have requested that an Indemnifying Person reimburse the Indemnified Person for fees and expenses of counsel as contemplated by this paragraph, the Indemnifying Person shall be liable for any settlement of any proceeding effected without its written consent if (i) such settlement is entered into more than 30 days after receipt by the Indemnifying Person of such request and (ii) the Indemnifying Person shall not have reimbursed the Indemnified Person in accordance with such request prior to the date of such settlement. No Indemnifying Person shall, without the written consent of the Indemnified Person, effect any settlement of any pending or threatened proceeding in respect of which any Indemnified Person is or could have been a party and indemnification could have been sought hereunder by such Indemnified Person, unless such settlement (x) includes an unconditional release of such Indemnified Person, in form and substance reasonably satisfactory to such Indemnified Person, from all liability on claims that are the subject matter of such proceeding and (y) does not include any statement as to or any admission of fault, culpability or a failure to act by or on behalf of any Indemnified Person.

(d) *Contribution.* If the indemnification provided for in paragraphs (a) and (b) above is unavailable to an Indemnified Person or insufficient in respect of any losses, claims, damages or liabilities referred to therein, then each Indemnifying Person under

such paragraph, in lieu of indemnifying such Indemnified Person thereunder, shall contribute to the amount paid or payable by such Indemnified Person as a result of such losses, claims, damages or liabilities (i) in such proportion as is 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 ADSs or (ii) if the allocation provided by clause (i) is not permitted by applicable law, in such proportion as is appropriate to reflect not only the relative benefits referred to in clause (i) but also the relative fault of the Company, on the one hand, and the Underwriters on the other, in connection with the statements or omissions that resulted in such losses, claims, damages or liabilities, 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, shall be deemed to be in the same respective proportions as the net proceeds (before deducting expenses) received by the Company from the sale of the Offered ADSs and the total underwriting discounts and commissions received by the Underwriters in connection therewith, in each case as set forth in the table on the cover of the Prospectus, bear to the aggregate offering price of the Offered ADSs. 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 or by the Underwriters and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such statement or omission.

(e) *Limitation on Liability.* The Company and the Underwriters agree that it would not be just and equitable if contribution pursuant to paragraph (d) above were determined by pro rata allocation (even if the Underwriters were treated as one entity for such purpose) or by any other method of allocation that does not take account of the equitable considerations referred to in paragraph (d) above. The amount paid or payable by an Indemnified Person as a result of the losses, claims, damages and liabilities referred to in paragraph (d) above shall be deemed to include, subject to the limitations set forth above, any reasonable documented legal or other expenses incurred by such Indemnified Person in connection with any such action or claim. Notwithstanding the provisions of paragraphs (d) and (e), in no event shall an Underwriter 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 ADSs exceeds the amount of any damages that such Underwriter has otherwise been required to pay by reason of such untrue or alleged untrue statement or omission or alleged omission. 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 pursuant to paragraphs (d) and (e) are several in proportion to their respective purchase obligations hereunder and not joint.

(f) *Non-Exclusive Remedies.* The remedies provided for in this Section 7 paragraphs (a) through (e) are not exclusive and shall not limit any rights or remedies which may otherwise be available to any Indemnified Person at law or in equity.

8. Effectiveness of Agreement. This Agreement shall become effective as of the date first written above.

9. Termination. This Agreement may be terminated in the absolute discretion of the Representatives, by notice to the Company, if after the execution and delivery of this Agreement and on or prior to the Closing Date or, in the case of the Option ADSs, prior to the Additional Closing Date (i) trading generally shall have been suspended or materially limited on or by either the New York Stock Exchange or The Nasdaq Stock Market; (ii) trading of any securities issued or guaranteed by the Company shall have been suspended on any exchange or in any over-the-counter market; (iii) a general moratorium on commercial banking activities shall have been declared by federal or New York State authorities; or (iv) there shall have occurred any outbreak or escalation of hostilities or any change in financial markets or any calamity or crisis, either within or outside the United States, that, in the judgment of the Representatives, is material and adverse and makes it impracticable or inadvisable to proceed with the offering, sale or delivery of the Offered ADSs on the Closing Date or the Additional Closing Date, as the case may be, on the terms and in the manner contemplated by this Agreement, the Pricing Disclosure Package and the Prospectus.

10. Defaulting Underwriter.

(a) If, on the Closing Date or the Additional Closing Date, as the case may be, any Underwriter defaults on its obligation to purchase the Offered ADSs that it has agreed to purchase hereunder on such date, the non-defaulting Underwriters may in their discretion arrange for the purchase of such Offered ADSs by other persons satisfactory to the Company on the terms contained in this Agreement. If, within 36 hours after any such default by any Underwriter, the non-defaulting Underwriters do not arrange for the purchase of such Offered ADSs, then the Company shall be entitled to a further period of 36 hours within which to procure other persons satisfactory to the non-defaulting Underwriters to purchase such Offered ADSs on such terms. If other persons become obligated or agree to purchase the Offered ADSs of a defaulting Underwriter, either the non-defaulting Underwriters or the Company may postpone the Closing Date or the Additional Closing Date, as the case may be, for up to five full business days in order to effect any changes that in the opinion of counsel for the Company or counsel for the Underwriters may be necessary in the Registration Statement and the Prospectus or in any other document or arrangement, and the Company agrees to promptly prepare any amendment or supplement to the Registration Statement and the Prospectus that effects any such changes. As used in this Agreement, the term "Underwriter" includes, for all purposes of this Agreement unless the context otherwise requires, any person not listed in Schedule 1 hereto that, pursuant to this Section 10, purchases Offered ADSs that a defaulting Underwriter agreed but failed to purchase.

(b) If, after giving effect to any arrangements for the purchase of the Offered ADSs of a defaulting Underwriter or Underwriters by the non-defaulting Underwriters and the Company as provided in paragraph (a) above, the aggregate number of Offered ADSs that remain unpurchased on the Closing Date or the Additional Closing Date, as the case may be, does not exceed one-eleventh of the aggregate number of Offered ADSs to be purchased on such date, then the Company shall have the right to require each non-

defaulting Underwriter to purchase the number of Offered ADSs that such Underwriter agreed to purchase hereunder on such date plus such Underwriter's pro rata share (based on the number of Offered ADSs that such Underwriter agreed to purchase on such date) of the Offered ADSs of such defaulting Underwriter or Underwriters for which such arrangements have not been made.

(c) If, after giving effect to any arrangements for the purchase of the Offered ADSs of a defaulting Underwriter or Underwriters by the non-defaulting Underwriters and the Company as provided in paragraph (a) above, the aggregate number of Offered ADSs that remain unpurchased on the Closing Date or the Additional Closing Date, as the case may be, exceeds one-eleventh of the aggregate amount of Offered ADSs to be purchased on such date, or if the Company shall not exercise the right described in paragraph (b) above, then this Agreement or, with respect to any Additional Closing Date, the obligation of the Underwriters to purchase Offered ADSs on the Additional Closing Date, as the case may be, shall terminate without liability on the part of the non-defaulting Underwriters. Any termination of this Agreement pursuant to this Section 10 shall be without liability on the part of the Company, except that the Company will continue to be liable for the payment of expenses as set forth in Section 11 hereof and except that the provisions of Section 7 hereof shall not terminate and shall remain in effect.

(d) Nothing contained herein shall relieve a defaulting Underwriter of any liability it may have to the Company or any non-defaulting Underwriter for damages caused by its default.

11. Payment of Expenses.

(a) Whether or not the transactions contemplated by this Agreement are consummated or this Agreement is terminated, the Company will pay or cause to be paid all costs and expenses incident to the performance of its obligations hereunder, including without limitation, (i) the costs incident to the authorization, issuance, sale, preparation and delivery of the Shares and the Offered ADSs and any taxes payable in that connection; (ii) the costs incident to the preparation, printing and filing under the Securities Act of the Registration Statement, the Preliminary Prospectus, any Issuer Free Writing Prospectus, any Pricing Disclosure Package and the Prospectus (including all exhibits, amendments and supplements thereto) and the distribution thereof; (iii) the costs of reproducing and distributing each of the Transaction documents; (iv) the fees and expenses of the Company's counsel and independent accountants; (v) the fees and expenses incurred in connection with the registration or qualification and determination of eligibility for investment of the Offered ADSs under the state or foreign securities or blue sky laws of such jurisdictions as the Representatives may designate and the preparation, printing and distribution of a Blue Sky Memorandum (including the related fees and expenses of counsel for the Underwriters); (vi) the cost of preparing stock certificates; (vii) the costs and charges of any transfer agent and any registrar; (viii) all expenses and application fees incurred in connection with any filing with, and clearance of the offering by, FINRA; provided that the aggregate amount payable by the Company pursuant to clauses (v) and (viii) shall not exceed $15,000; (ix) all expenses incurred by the Company in connection

with any “road show” presentation to potential investors; provided, however, that the Underwriters shall pay all of the travel, lodging and other expenses of the Underwriters or any of their employees incurred by them in connection with the “road show”, and provided further, that the Company and the Underwriters shall each pay 50% of the cost of any aircraft chartered in connection with such “road show”; and (x) all expenses and application fees related to the listing of the Offered ADSs on the Nasdaq Market.

(b) If (i) this Agreement is terminated pursuant to Section 9, (ii) the Company for any reason fails to tender the Offered ADSs for delivery to the Underwriters (other than by reason of a default by any Underwriter) or (iii) the Underwriters decline to purchase the Offered ADSs for any reason permitted under this Agreement, the Company agrees to reimburse the Underwriters for all out-of-pocket costs and expenses (including the fees and expenses of their counsel) reasonably incurred by the Underwriters in connection with this Agreement and the offering contemplated hereby.

12. Persons Entitled to Benefit of Agreement. This Agreement shall inure to the benefit of and be binding upon the parties hereto and their respective successors and the officers and directors and any controlling persons referred to herein, and the affiliates of each Underwriter referred to in Section 7 hereof. Nothing in this Agreement is intended or shall be construed to give any other person any legal or equitable right, remedy or claim under or in respect of this Agreement or any provision contained herein. No purchaser of Offered ADSs from any Underwriter shall be deemed to be a successor merely by reason of such purchase.

13. Survival. The respective indemnities, rights of contribution, representations, warranties and agreements of the Company and the Underwriters contained in this Agreement or made by or on behalf of the Company or the Underwriters pursuant to this Agreement or any certificate delivered pursuant hereto shall survive the delivery of and payment for the Offered ADSs and shall remain in full force and effect, regardless of any termination of this Agreement or any investigation made by or on behalf of the Company or the Underwriters or the directors, officers, controlling persons or affiliates referred to in Section 7 hereof.

14. Certain Defined Terms. For purposes of this Agreement, (a) except where otherwise expressly provided, the term “affiliate” has the meaning set forth in Rule 405 under the Securities Act; (b) the term “business day” means any day other than a day on which banks are permitted or required to be closed in New York City; and (c) the term “subsidiary” has the meaning set forth in Rule 405 under the Securities Act.

15. Compliance with USA Patriot Act. In accordance with the requirements of the USA Patriot Act (Title III of Pub. L. 107-56 (signed into law October 26, 2001)), the Underwriters are required to obtain, verify and record information that identifies their respective clients, including the Company, which information may include the name and address of their respective clients, as well as other information that will allow the Underwriters to properly identify their respective clients.

16. Miscellaneous.

(a) *Notices.* All notices and other communications hereunder shall be in writing and shall be deemed to have been duly given if mailed or transmitted and confirmed by any standard form of telecommunication. Notices to the Underwriters shall be given to the Representatives c/o J.P. Morgan Securities LLC, 383 Madison Avenue, New York, New York 10179 (fax: (212) 622-8358), Attention: Equity Syndicate Desk, c/o Goldman Sachs & Co. LLC, 200 West Street, New York, New York 10282, Attention: Control Room, c/o Cowen and Company, LLC, 599 Lexington Avenue, 27th Floor, New York, NY 10022 (fax: (646) 562-1124), Attention: General Counsel and Barclays Capital Inc., 745 Seventh Avenue, New York, New York 10019, Attention: Syndicate Registration (fax: (646) 834-8133). Notices to the Company shall be given to it at Orchard Therapeutics plc, 108 Cannon Street, London EC4N 6EU, United Kingdom; Attention: John Ilett, General Counsel & Company Secretary.

(b) *Governing Law.* This Agreement and any claim, controversy or dispute arising under or related to this Agreement shall be governed by and construed in accordance with the laws of the State of New York.

(c) *Submission to Jurisdiction*. The Company hereby submits to the exclusive jurisdiction of the U.S. federal and New York state courts in the Borough of Manhattan in The City of New York in any suit or proceeding arising out of or relating to this Agreement or the transactions contemplated hereby. The Company waives any objection which it may now or hereafter have to the laying of venue of any such suit or proceeding in such courts. The Company agrees that final judgment in any such suit, action or proceeding brought in such court shall be conclusive and binding upon the Company and may be enforced in any court to the jurisdiction of which Company is subject by a suit upon such judgment. The Company irrevocably appoints Cogency Global Inc., located 10 E. 40th Street, 10th Floor, New York, New York 10016, as its authorized agent in the Borough of Manhattan in The City of New York upon which process may be served in any such suit or proceeding, and agrees that service of process upon such authorized agent, and written notice of such service to the Company by the person serving the same to the address provided in this Section 16, shall be deemed in every respect effective service of process upon the Company in any such suit or proceeding. The Company hereby represents and warrants that such authorized agent has accepted such appointment and has agreed to act as such authorized agent for service of process. The Company further agrees to take any and all action as may be necessary to maintain such designation and appointment of such authorized agent in full force and effect for a period of seven years from the date of this Agreement.

(d) *MIFID Product Governance*. Solely for the purposes of the requirements of Article 9(8) of the MIFID Product Governance rules under EU Delegated Directive 2017/593 (the "Product Governance Rules") regarding the mutual responsibilities of manufacturers under the Product Governance Rules (i) each manufacturer acknowledges to each other manufacturer that it understands the responsibilities conferred upon it under the Product Governance Rules relating to each of the product approval process, the target market and the proposed distribution channels as applying to the ADSs and the related information set out in the Prospectus in connection with the ADSs; and (ii) the Underwriters and the Company note the application of the Product Governance Rules and acknowledge the target market and distribution channels identified as applying to the ADSs by the manufacturers and the related information set out in the Prospectus in connection with the ADSs.

(e) *Judgment Currency*. The Company agrees to indemnify each Underwriter, its directors, officers, affiliates and each person, if any, who controls such Underwriter within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act, against any loss incurred by such Underwriter as a result of any judgment or order being given or made for any amount due hereunder and such judgment or order being expressed and paid in a currency (the "judgment currency") other than U.S. dollars and as a result of any variation as between (i) the rate of exchange at which the U.S. dollar amount is converted into the judgment currency for the purpose of such judgment or order, and (ii) the rate of exchange at which such indemnified person is able to purchase U.S. dollars with the amount of the judgment currency actually received by the indemnified person. The foregoing indemnity shall constitute a separate and independent obligation of the Company and shall continue in full force and effect notwithstanding any such judgment or order as aforesaid. The term "rate of exchange" shall include any premiums and costs of exchange payable in connection with the purchase of, or conversion into, the relevant currency.

(f) *Waiver of Immunity*. To the extent that the Company has or hereafter may acquire any immunity (sovereign or otherwise) from jurisdiction of any court of (i) England and Wales, (ii) the United States or the State of New York, (iii) any jurisdiction in which it owns or leases property or assets or from any legal process (whether through service of notice, attachment prior to judgment, attachment in aid of execution, execution, set-off or otherwise) with respect to themselves or their respective property and assets or this Agreement, the Company hereby irrevocably waives such immunity in respect of its obligations under this Agreement to the fullest extent permitted by applicable law.

(g) *Waiver of Jury Trial.* Each of the parties hereto hereby waives any right to trial by jury in any suit or proceeding arising out of or relating to this Agreement.

(h) *Counterparts.* This Agreement may be signed in counterparts (which may include counterparts delivered by any standard form of telecommunication), each of which shall be an original and all of which together shall constitute one and the same instrument.

(i) *Amendments or Waivers.* No amendment or waiver of any provision of this Agreement, nor any consent or approval to any departure therefrom, shall in any event be effective unless the same shall be in writing and signed by the parties hereto.

(j) *Headings.* The headings herein are included for convenience of reference only and are not intended to be part of, or to affect the meaning or interpretation of, this Agreement.

(k) *Recognition of the U.S. Special Resolution Regimes*. In the event that any Underwriter that is a Covered Entity becomes subject to a proceeding under a U.S. Special Resolution Regime, the transfer from such party of this Agreement and any interest and obligation in or under this Agreement will be effective to the same extent as the transfer would be effective under the U.S. Special Resolution Regime if this Agreement, and any such interest and obligation, were governed by the laws of the United States or a state of the United States.

In the event that any Underwriter that is a Covered Entity or any BHC Act Affiliate of such Underwriter becomes subject to a proceeding under a U.S. Special Resolution Regime, Default Rights under this Agreement that may be exercised against such Underwriter are permitted to be exercised to no greater extent than such Default Rights could be exercised under the U.S. Special Resolution Regime if this Agreement were governed by the laws of the United States or a state of the United States.

As used in Section (k):

"*BHC Act Affiliate*" has the meaning assigned to the term "affiliate" in, and shall be interpreted in accordance with, 12 U.S.C. 1841(k);

"*Covered Entity*" means any of the following:

(i) a "covered entity" as that term is defined in, and interpreted in accordance with, 12 C.F.R. § 252.82(b);

(ii) a "covered bank" as that term is defined in, and interpreted in accordance with, 12 C.F.R. § 47.3(b); or

(iii) a "covered FSI" as that term is defined in, and interpreted in accordance with, 12 C.F.R. § 382.2(b);

"*Default Right*" has the meaning assigned to that term in, and shall be interpreted in accordance with, 12 C.F.R. §§ 252.81, 47.2 or 382.1 as applicable;

"*U.S. Special Resolution Regime*" means each of (i) the Federal Deposit Insurance Act and the regulations promulgated thereunder and (ii) Title II of the Dodd-Frank Wall Street Reform and Consumer Protection Act and the regulations promulgated thereunder.

If the foregoing is in accordance with your understanding, please indicate your acceptance of this Agreement by signing in the space provided below.

Very truly yours,

ORCHARD THERAPEUTICS plc

By: _____
Name:
Title:

Accepted: As of the date first written above
J.P. MORGAN SECURITIES LLC
GOLDMAN SACHS & CO. LLC
COWEN AND COMPANY, LLC
BARCLAYS CAPITAL INC.

For itself and on behalf of the
several Underwriters listed
in Schedule 1 hereto.

J.P. MORGAN SECURITIES LLC

By: _____
Authorized Signatory

GOLDMAN SACHS & CO. LLC

By: _____
Authorized Signatory

COWEN AND COMPANY, LLC

By: _____
Authorized Signatory

BARCLAYS CAPITAL INC.

By: _____
Authorized Signatory

Underwriter	Number of Underwritten ADSs
J.P. Morgan Securities LLC	[●]
Goldman Sachs & Co. LLC	[●]
Cowen and Company, LLC	[●]
Barclays Capital Inc.	[●]
Total	[●]

a. **Pricing Disclosure Package**

None.

b. **Pricing Information Provided Orally by Underwriters**

Public Offering Price:	$[●]
Number of Underwritten ADSs:	[●]
Number of Option ADSs:	[●]

Orchard Therapeutics plc

Pricing Term Sheet

None.

FORM OF LOCK-UP AGREEMENT

, 2019

J.P. MORGAN SECURITIES LLC
GOLDMAN SACHS & CO. LLC
COWEN AND COMPANY, LLC
BARCLAYS CAPITAL INC.

As Representatives of the several Underwriters listed
in Schedule 1 to the Underwriting Agreement defined below

c/o J.P. Morgan Securities LLC
383 Madison Avenue
New York, New York 10179

c/o Goldman Sachs & Co. LLC
200 West Street
New York, New York 10282-2198

c/o Cowen and Company, LLC
599 Lexington Avenue
New York, New York 10022

c/o Barclays Capital Inc.
745 Seventh Avenue
New York, New York 10019

Re: Orchard Therapeutics plc — Public Offering

Ladies and Gentlemen:

The undersigned is a director, officer or record or beneficial owner of ordinary shares, nominal value £0.10 per share (the "Ordinary Shares"), of Orchard Therapeutics plc (the "Company"). The undersigned understands that you, as Representatives (the "Representatives") of the several Underwriters named in Schedule 1 to the Underwriting Agreement (the "Underwriters"), propose to enter into an underwriting agreement (the "Underwriting Agreement") with the Company, providing for the public offering (the "Public Offering") by the several Underwriters, of American Depository Shares ("ADSs") of the Company representing ordinary shares nominal value £0.10 per share (the "Securities"). Capitalized terms used herein and not otherwise defined shall have the meanings set forth in the Underwriting Agreement.

In consideration of the Underwriters' agreement to purchase and make the Public Offering of the Securities, and for other good and valuable consideration receipt of which is hereby acknowledged, the undersigned hereby agrees that, without the prior written consent of the Representatives on behalf of the

Underwriters, the undersigned will not, during the period beginning on the date of this letter agreement (this "Letter Agreement") and ending 90 days after the date of the final prospectus relating to the Public Offering (the "Prospectus") (such period, the "Restricted Period"), (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any Ordinary Shares or Related Securities, or publicly disclose the intention to make any offer, sale, pledge or disposition, (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the Ordinary Shares or such other securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of Ordinary Shares or such other securities, in cash or otherwise or (3) make any demand for or exercise any right with respect to the registration of any Ordinary Shares or any security convertible into or exercisable or exchangeable for Ordinary Shares, in each case other than:

(A) the Securities to be sold by the undersigned pursuant to the Underwriting Agreement;

(B) 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 (B) held by the undersigned shall remain subject to the terms of this Agreement;

(C) sales or transfers of ADSs or Ordinary Shares acquired in the Public Offering or in open market transactions on or after the consummation of the Public Offering;

(D) transfers of Ordinary Shares or Related Securities (i) as a bona fide gift or gifts, (ii) by will, other testamentary document or intestate succession to the legal representative, heir, beneficiary or a member of the immediate family of the undersigned in a transaction not involving a disposition for value or (iii) pursuant to a court order in respect of, or by operation of law as a result of, a divorce, in a transaction not involving disposition for value;

(E) if the undersigned is (i) an individual, transfers of Ordinary Shares or Related Securities in a transaction not involving a disposition for value to any trust for the direct or indirect benefit of the undersigned or the immediate family of the undersigned, or limited partnerships the partners of which are the undersigned and/or the immediate family members of the undersigned, in each case for estate planning purposes, (ii) a corporation, limited liability company, partnership (whether general, limited or otherwise) or other entity, distributions of Ordinary Shares or Related Securities to current or former members, stockholders, limited partners, general partners, subsidiaries or affiliates (as defined in Rule 405 promulgated under the Securities Act of 1933, as amended) of the undersigned, or to any investment fund or other entity that controls or manages the undersigned (including, for the avoidance of doubt, a fund managed by the same manager or managing member or general partner or management company or by an entity controlling, controlled by, or under common control with such manager or managing member or general partner or management company as the undersigned or who shares a common investment advisor with the undersigned) not involving a disposition for value, or (iii) a trust, distributions of Ordinary Shares or Related Securities to its beneficiaries in a transaction not involving a disposition for value;

(F) the exercise of an option or other equity award to purchase Ordinary Shares or ADSs, as applicable, which are set to expire during the Restricted Period and have been granted under any of the Company's or Orchard's current or future equity incentive plans or equity purchase plans described in the Prospectus and any transfers or dispositions of ADSs, Ordinary Shares or other securities to the Company in connection with the exercise of any such option or equity award; provided that any such ADSs or Ordinary Shares received by the undersigned shall be subject to the terms of this Letter Agreement;

(G) any transfer or disposition in connection with a change of control (it being further understood that this Letter Agreement shall not restrict the undersigned from entering into any agreement or arrangement in connection therewith, including an agreement to vote in favor of, or tender ADSs, Ordinary Shares or other securities of the Company in, any such transaction or taking or not taking any other action in connection with any such transaction); provided that in the event that the acquisition, merger, consolidation or other transaction in connection with such change of control is not completed, the ADSs or Ordinary Shares owned by the undersigned shall remain subject to the restrictions contained in this Letter Agreement;

(H) the entering into by the undersigned of a written trading plan ("Rule 10b5-1 Plan") pursuant to Rule 10b5-1 of the Securities Exchange Act of 1934, as amended (the "Exchange Act") during the Restricted Period, provided that no sales or transfers of shares of the undersigned's ADSs or Ordinary Shares shall be made pursuant to such Rule 10b5-1 Plan prior to the expiration of the Restricted Period and no filing under the Exchange Act or other public announcement shall be required or voluntarily made by the undersigned or any other person in connection therewith without the permission of the Representatives, prior to the expiration of the Restricted Period; and

(I) the sale or transfer of the undersigned's ADSs or Ordinary Shares pursuant to a 10b5-1 Plan adopted prior to the date hereof under which shares of ADSs or Ordinary Shares may be sold or transferred during the Restricted Period, which trading plan shall not be amended during the Restricted Period but may be terminated during the Restricted Period, provided that no filing under the Exchange Act or other public announcement shall be required or voluntarily made by the undersigned or any other person in connection therewith without the permission of the Representatives, prior to the expiration of the Restricted Period;

provided that in the case of any transfer or distribution pursuant to clauses (D), (E) or (G), each donee or distributee shall execute and deliver to the Representative a lock-up letter in the form of this paragraph; and provided, further, that in the case of any transfer or distribution pursuant to clauses (D), (E), or (G), no filing by any party (donor, donee, transferor or transferee) under the Securities Exchange Act of 1934, as amended, or other public announcement shall be required or shall be made voluntarily in connection with such transfer or distribution.

For purposes of this Letter Agreement, (i) "immediate family" shall mean any relationship by blood, marriage or adoption, not more remote than first cousin, (ii) "Related Securities" shall mean any ADSs, options or warrants or other rights to acquire ADSs or Ordinary Shares or any securities exchangeable or exercisable for or convertible into ADSs or Ordinary Shares, or to acquire other securities or rights ultimately exchangeable or exercisable for or convertible into ADSs or Ordinary Shares, including ordinary shares of Orchard, or securities convertible into or exchangeable or exercisable for ordinary shares of Orchard, and (iii) "change of control" shall mean any bona fide third-party tender offer, merger, consolidation or other similar transaction that is approved by the Board of Directors of the Company and made to all holders of the Company's Ordinary Shares or ADSs, as applicable, in each case, the result of which is that any "person" (as defined in Section 13(d)(3) of the Exchange Act), or group of persons, other than the Company, becomes the beneficial owner (as defined in Rules 13d-3 and 13d-5 of the Exchange Act) of a majority of total voting power of the voting stock of the Company.

If the undersigned is an officer or director of the Company, the Representatives on behalf of the Underwriters agree that, at least three business days before the effective date of any release or waiver of the foregoing restrictions in connection with a transfer of Ordinary Shares or Related Securities, the Representatives on behalf of the Underwriters will notify the Company of the impending release or waiver. 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 Letter Agreement to the extent and for the duration that such terms remain in effect at the time of the transfer.

The undersigned hereby waives any and all notice and consent requirements and any other rights of the undersigned with regard to the Company's intention to file the Registration Statement and to the Public Offering of the Securities.

In furtherance of the foregoing, the Company, and any duly appointed transfer agent for the registration or transfer of the securities described herein, are hereby authorized to decline to make any transfer of securities if such transfer would constitute a violation or breach of this Letter Agreement.

The undersigned hereby represents and warrants that the undersigned has full power and authority to enter into this Letter Agreement. All authority herein conferred or agreed to be conferred and any obligations of the undersigned shall be binding upon the successors, assigns, heirs or personal representatives of the undersigned.

The undersigned understands that, if the Underwriting Agreement does not become effective by August 31, 2019, or if the Underwriting Agreement (other than the provisions thereof which survive termination) shall terminate or be terminated prior to payment for and delivery of the Securities to be sold thereunder, the undersigned shall be released from all obligations under this Letter Agreement. The undersigned understands that the Underwriters are entering into the Underwriting Agreement and proceeding with the Public Offering in reliance upon this Letter Agreement.

This Letter Agreement and any claim, controversy or dispute arising under or related to this Letter Agreement shall be governed by and construed in accordance with the laws of the State of New York.

Very truly yours,

[*NAME OF STOCKHOLDER*]

By: _____
Name:
Title:

Exhibit A-2

Individuals Executing Lockup

Directors

James A. Geraghty
Joanne T. Beck, Ph.D.
Marc Dunoyer
Jon Ellis, Ph.D.
Charles A. Rowland, Jr.
Hong Fang Song
Alicia Secor

Officers

Mark Rothera
Frank E. Thomas
Bobby Gaspar, M.D., Ph.D.

Exhibit 5.1

Goodwin Procter (UK) LLP
100 Cheapside
London EC2V 6DY

goodwinlaw.com
+44 (0) 20 7447 4200

3 June 2019

Orchard Therapeutics plc
108 Cannon Street
London, EC4N 6EU

Ladies and Gentlemen:

Orchard Therapeutics plc – Registration Statement on Form F-1 – Exhibit 5.1

We have acted as English legal advisers to Orchard Therapeutics plc, a public limited company incorporated in England and Wales (the "**Company**") in connection with the proposed offering of American Depositary Shares (the "**ADSs**") representing ordinary shares of nominal value £0.10 each in the capital of the Company (the "**Ordinary Shares**") (the "**Offering**" and the Ordinary Shares allotted and issued in connection therewith to Citibank N.A. as the custodian and represented by ADSs, being the "**Shares**"). Each ADS represents one Ordinary Share of the Company.

1. INTRODUCTION

1.1 Purpose

In connection with the preparation and filing of a registration statement on Form F-1 (such registration statement, as amended through the date hereof, the "**Registration Statement**"), to which this letter is attached as an exhibit, with the U.S. Securities and Exchange Commission (the "**SEC**") pursuant to the U.S. Securities Act of 1933, as amended (the "**Securities Act**"), we have been asked to provide opinions on certain matters, as set out below. We have taken instruction in this regard solely from the Company.

1.2 Defined terms and headings

In this letter:

(a) capitalised terms used without definition in this letter or the schedules hereto have the meanings assigned to them in the Registration Statement unless a contrary indication appears;

(b) headings are for ease of reference only and shall not affect interpretation; and

(c) the term "**Shares**" shall include any additional ADSs registered by the Company pursuant to Rule 462(b) under the Securities Act in connection with the Offering contemplated by the Registration Statement.

Goodwin Procter (UK) LLP is a limited liability partnership registered in England and Wales with registered number OC362294. Its registered office is at 100 Cheapside, London, EC2V 6DY. A list of the names of the members of Goodwin Procter (UK) LLP is available for inspection at the registered office. Goodwin Procter (UK) LLP is authorised and regulated by the Solicitors Regulation Authority. Goodwin Procter (UK) LLP is affiliated with Goodwin Procter LLP, which operates in the United States of America.

1.3 **Legal review**

For the purpose of issuing this letter, we have examined such questions of law as we have considered appropriate to give the opinions set forth in this letter. We have reviewed such documents and conducted such enquiries and searches as we have considered appropriate to give the opinions set forth in this letter, including the following documents and the following enquiries and searches:

(a) an online search at Companies House in respect of information available for inspection on the Company's file conducted on 3 June 2019 at 10.30 a.m. (London time);

(b) an enquiry of the Central Index of Winding Up Petitions, London on 3 June 2019 at 10.30 a.m. (London time) ((a) and (b) together, the "**Searches**");

(c) a PDF executed copy of the written resolutions passed by the shareholders of the Company on 25 October 2018 which resolved, *inter alia*, to give the directors of the Company the authority to allot and issue Ordinary Shares and dis-apply pre-emptive rights on the offering, issuance and allotment of Ordinary Shares up to an aggregate nominal amount of £13,023,851.50 (the "**Shareholder Written Resolutions**");

(d) a draft copy of the minutes of a meeting of the board of directors of the Company held on 27 March 2019 (the "**Board Resolutions**") at which it was resolved, *inter alia*, to appoint a pricing committee of the board of directors of the Company (the "**Pricing Committee**");

(e) a draft copy of the minutes of a meeting of the Pricing Committee to be held resolving, *inter alia*, to allot and issue the Shares (the "**Allotment Resolutions**" and together with the Shareholder Written Resolutions and the Board Written Resolutions, the "**Corporate Approvals**");

(f) a PDF copy of the current articles of association of the Company dated 2 November 2018 (the "**Articles**"), the certificate of incorporation of the Company dated 1 August 2018 and the certificate of incorporation on re-registration of the Company as a public limited company dated 29 October 2018; and

(g) a copy of the Registration Statement.

1.4 **Applicable law**

This letter, the opinions given in it, and any non-contractual obligations arising out of or in connection with this letter and/or the opinions given in it, are governed by, and to be construed in accordance with, English law and relate only to English law as applied by the English courts, including the laws of the European Union to the extent having the force of law in England, as at today's date. In particular:

(a) we have not investigated the laws of any country other than England and we express no opinion in this letter on the laws of any jurisdiction other than England and we assume that no foreign law affects any of the opinions given below. It is assumed that no foreign law which may apply to the matters contemplated by the Registration Statement, the Offering, the Company, any document or any other matter contemplated by any document would or might affect this letter and/or the opinions given in it;

(b) we do not undertake or accept any obligation to update this letter and/or the opinions given in it to reflect subsequent changes in English law or factual matters, and

(c) we express no opinion in this letter on the laws of any jurisdiction other than England. It is assumed that no foreign law which may apply to the matters contemplated by the Registration Statement, the Offering, the Company, any document or any other matter contemplated by any document would or might affect this letter and/or the opinions given in it.

1.5 **Assumptions and reservations**

The opinions given in this letter are given on the basis of each of the assumptions set out in paragraph 1.4, schedule 1 (*Assumptions*) and are subject to each of the reservations set out in schedule 2 (*Reservations*) to this letter. The opinions given in this letter are strictly limited to the matters stated in paragraph 2 (*Opinions*) below and do not extend, and should not be read as extending, by implication or otherwise, to any other matters.

2. OPINION

Subject to paragraph 1 (*Introduction*) and the other matters set out in this letter and its schedules, and subject further to the following:

(a) the Registration Statement becoming effective under the Securities Act;

(b) the number of Shares to be allotted and issued in connection with the Offering not being greater than the aggregate nominal value specified in the Corporate Approvals;

(c) that the Board Resolutions and Allotment Resolutions were or will be (as appropriate) each passed at a meeting which was or will be duly convened and held in accordance with all applicable laws and regulations; that in particular, but without limitation, a duly qualified quorum of directors was or will be present in each case throughout the meeting and voted in favour of the resolutions; and that in relation to each meeting of the board of directors of the Company and of the Pricing Committee, each provision contained in the Companies Act 2006, as amended (the "**Act**") or the Articles relating to the declaration of the directors' interests or the power of the interested directors to vote and to count in the quorum was or will be duly observed;

(d) that the Shareholder Written Resolutions were duly constituted and all constitutional, statutory and other formalities were duly observed, the requisite majority of shareholders, as applicable, voted in favour of approving the resolutions and the resolutions passed thereby were duly adopted, have not been revoked or varied and remain in full force and effect;

(e) the receipt in full of payment for the Shares in an amount of "cash consideration" (as defined in section 583(3) of the Act) of not less than the aggregate nominal value for such Shares; and

(f) valid entries having been made in relation to the allotment and issue of the Shares in the books and registers of the Company,

it is our opinion that, as at today's date, the Shares, if and when allotted and issued, registered in the name of the recipient in the register of members of the Company and delivered as described in the Registration Statement, will be duly and validly authorised and issued, fully paid or credited as fully paid (subject to the receipt of valid consideration by the Company for the issue thereof in connection with the Offering) and will not be subject to any call for payment of further capital.

3. EXTENT OF OPINIONS

We express no opinion as to any agreement, instrument or other document other than as specified in this letter or as to any liability to tax or duty which may arise or be suffered as a result of or in connection with the Offering or the transactions contemplated thereby.

This letter only applies to those facts and circumstances which exist as at today's date and we assume no obligation or responsibility to update or supplement this letter to reflect any facts or circumstances which may subsequently come to our attention, any changes in laws which may occur after today, or to inform the addressee of any change in circumstances happening after the date of this letter which would alter our opinion.

4. DISCLOSURE AND RELIANCE

This letter is addressed to you in connection with the Registration Statement. We consent to the filing of this letter as an exhibit to the Registration Statement. We further consent to the incorporation by reference of this letter and consent into any registration statement filed pursuant to Rule 462(b) under the Securities Act with respect to the Shares. In giving such consent, we do not thereby admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations thereunder.

Other than for the purpose set out in the prior paragraph, this letter may not be relied upon, or assigned, for any purpose, without our prior written consent, which may be granted or withheld in our discretion.

Yours faithfully

/s/ Goodwin Procter (UK) LLP

Goodwin Procter (UK) LLP

SCHEDULE 1

ASSUMPTIONS

The opinions in this letter have been given on the basis of the following assumptions:

(a) the genuineness of all signatures, stamps and seals on all documents, the authenticity and completeness of all documents submitted to us as originals, and the conformity to original documents of all documents submitted to us as copies;

(b) that, where a document has been examined by us in draft or specimen form, it will be or has been duly executed in the form of that draft or specimen, and that each of the signed documents examined by us has been duly executed and, where applicable, delivered on behalf of the Company;

(c) that the Articles remain in full force and effect, and no alteration has been made or will be made to such articles of association, in each case prior to the date of allotment and issue of the Shares (the "**Allotment Date**");

(d) on the Allotment Date the Company will comply with all applicable laws to allot and issue the Shares and the Company will receive such amounts as are necessary to fully pay the nominal value of the Shares and any applicable share premium;

(e) that all documents, forms and notices which should have been delivered to the Registrar of Companies in respect of the Company have been so delivered, that information revealed by the Searches was complete and accurate in all respects and has not, since the time of the Searches, been altered and that the results of the Searches will remain complete and accurate as at the Allotment Date;

(f) that the minutes of the meetings of the board of directors of the Company and the draft minutes of the meeting of the Pricing Committee provided to us in connection with the giving of the opinions in this letter reflect a true record of the proceedings described in them in duly convened, constituted and quorate meetings in which all constitutional, statutory and other formalities were duly observed, and the resolutions set out in the minutes were or will have been validly passed and have not been and will not be revoked or varied and remain in full force and effect and will remain so as at the Allotment Date;

(g) that the resolutions set out in the Shareholder Written Resolutions were validly passed and have not been and will not be revoked or varied and remain in full force and effect and will remain so as at the Allotment Date;

(h) that in relation to the allotment and issue of the Shares, the directors of the Company have acted and will act in the manner required by section 172 of the Act (Duty to promote the success of the Company), and there has not been and will not be any bad faith, breach of trust, fraud, coercion, duress or undue influence on the part of any of the directors of the Company;

(i) following the date of this letter and prior to the issue of the Shares, the Company will validly enter into an underwriting agreement on substantially the terms and conditions described in Exhibit 1.1 of the Registration Statement;

(j) that no Shares or rights to subscribe for Shares have been or shall be offered to the public in the United Kingdom in breach of the Financial Services and Markets Act 2000, as amended ("**FSMA**") or of any other United Kingdom laws or regulations concerning offers of securities to the public, and no communication has been or shall be made in relation to the Shares in breach of section 21 of FSMA or any other United Kingdom laws or regulations relating to offers or invitations to subscribe for, or to acquire rights to subscribe for or otherwise acquire, shares or other securities; and

(k) that the Company has not taken any corporate or other action nor have any steps been taken or legal proceedings been started against the Company for the liquidation, winding up, dissolution, reorganisation or bankruptcy of, or for the appointment of a liquidator, receiver, trustee, administrator, administrative receiver or similar officer of, the Company or all or any of its assets (or any analogous proceedings in any jurisdiction) and the Company is not unable to pay its debts as they fall due within the meaning of section 123 of the Insolvency Act 1986 and will not become unable to pay its debts within the meaning of that section as a result of any of the transactions contemplated herein, is not insolvent and has not been dissolved or declared bankrupt (although the Searches gave no indication that any winding-up, dissolution or administration order or appointment of a receiver, administrator, administrative receiver or similar officer has been made with respect to the Company).

SCHEDULE 2

RESERVATIONS

The opinions in this letter are subject to the following reservations:

(a) the Searches are not capable of revealing conclusively whether or not a winding-up or administration petition or order has been presented or made, a receiver appointed, a company voluntary arrangement proposed or approved or any other insolvency proceeding commenced, and the available records may not be complete or up-to-date. In particular, the Central Registry of Winding-Up Petitions in England may not contain details of administration applications filed, or appointments recorded in or orders made by, district registries and county courts outside London. Searches at Companies House and at the Central Registry of Winding Up Petitions in England are not capable of revealing whether or not a winding up petition or a petition for the making of an administration order has been presented and, further, notice of a winding up order or resolution, notice of an administration order and notice of the appointment of a receiver may not be filed at Companies House immediately and there may be a delay in the relevant notice appearing on the file of the company concerned. Further, not all security interests are registrable, such security interests have not in fact been registered or such security interests have been created by an individual or an entity which is not registered in England. We have not made enquiries of any District Registry or County Court in England;

(b) the opinions set out in this letter are subject to: (i) any limitations arising from applicable laws relating to insolvency, bankruptcy, administration, reorganisation, liquidation, moratoria, schemes or analogous circumstances; and (ii) an English court exercising its discretion under section 426 of the Insolvency Act 1986 (*co-operation between courts exercising jurisdiction in relation to insolvency*) to assist the courts having the corresponding jurisdiction in any part of the United Kingdom or any relevant country or territory;

(c) we express no opinion as to matters of fact;

(d) we have made no enquiries of any individual connected with the Company;

(e) a certificate, documentation, notification, opinion or the like might be held by the English courts not to be conclusive if it can be shown to have an unreasonable or arbitrary basis or in the event of a manifest error; and

(f) it should be understood that we have not been responsible for investigating or verifying (i) the accuracy of the facts, including statements of foreign law, or the reasonableness of any statements of opinion, contained in the Registration Statement; or (ii) that no material facts have been omitted from it.

Exhibit 10.1

EXECUTION VERSION

DATED 2 August 2018

UNIQUE DIAMOND INVESTMENTS LIMITED (1)

F-PRIME CAPITAL PARTNERS HEALTHCARE FUND IV LP (2)

F-PRIME CAPITAL PARTNERS HEALTHCARE FUND IV-A LP (3)

SCOTTISH MORTGAGE INVESTMENT TRUST PLC (4)

TLS BETA PTE LTD (5)

COWEN HEALTHCARE INVESTMENTS II LP (6)

GLAXO GROUP LIMITED (7)

and

ORCHARD THERAPEUTICS LIMITED (8)

DEED OF AMENDMENT AND RESTATEMENT

relating to an

INVESTMENT AND SHAREHOLDERS' AGREEMENT

in respect of the entire issued share capital of

ORCHARD THERAPEUTICS LIMITED

Cooley

THIS DEED is made the 2 day of August 2018

BETWEEN:

(1) **UNIQUE DIAMOND INVESTMENTS LIMITED**, a company incorporated in the British Virgin Islands and whose registered office is at Vistra Corporate Services Centre, Wickhams Cay II, Road Town, Tortola, VG1110 British Virgin Islands ("**ORI**");

(2) **SCOTTISH MORTGAGE INVESTMENT TRUST PLC**, a public limited company incorporated in Scotland under company number SC007058 whose registered office is at Calton Square, 1 Greenside Row, Edinburgh EH1 3AN, acting through its agent, **Baillie Gifford & Co**., ("**SMIT**");

(3) **F-PRIME CAPITAL PARTNERS HEALTHCARE FUND IV LP**, a Delaware limited partnership whose principal place of business is at One Main Street, 13th Floor, Cambridge, MA 02142, United States ("**F-Prime**");

(4) **F-PRIME CAPITAL PARTNERS HEALTHCARE FUND IV-A LP**, a Delaware limited partnership whose principal place of business is at One Main Street, 13th Floor, Cambridge, MA 02142, United States ("**F-Prime A**");

(5) **TLS BETA PTE LTD.**, a Singapore company with registered number 200500368D whose office is at 60B Orchard Road #06-18 Tower 2, The Atrium@Orchard, Singapore 238891 ("**Temasek**");

(6) **COWEN HEALTHCARE INVESTMENTS II LP**, a New York limited partnership whose principal place of business is 599 Lexington Avenue, New York, NY 10022 ("**Cowen**");

(7) **GLAXO GROUP LIMITED**, a company incorporated in England and Wales under company number 305979 whose registered office is at 980 Great West Road, Brentford, Middlesex TW8 9GS ("**GSK**"); and

(8) **ORCHARD THERAPEUTICS LIMITED**, a company incorporated in England and Wales under company number 9759506 whose registered office is at Birchin Court, 20, Birchin Lane, London, England, EC3V 9DU (the "**Company**").

BACKGROUND:

(A) SMIT, F-Prime, F-Prime A, ORI, Temasek, Cowen, GSK, certain other parties and the ordinary shareholders of the Company and the Company are parties to an investment and shareholders' agreement in relation to the Company dated 29 March 2017 as amended on 18 August 2017, 26 October 2017 and 11 April 2018 (the "**ISA**").

(B) Certain new and existing investors (the "**Investors**") have agreed to subscribe for a new class of series C preferred shares of £0.00001 each in the Company (the "**Series C Shares**") pursuant to the terms of an investment agreement to be executed by the relevant parties immediately following the effective date of this deed (the "**Investment Agreement**") (the "**Transaction**").

(C) Pursuant to the Transaction, and in accordance with clause 23.4.1 of the ISA, the parties have agreed to vary the terms of the ISA on the terms set out herein.

IT IS AGREED:

1. Terms defined in the ISA

In this deed, capitalised expressions defined in the ISA and used in this deed have the meaning set out in the ISA. Expressions defined in the 'Background' section above shall have the meaning ascribed thereto. Clauses 1.2 (but not clause 1.2.4) and 1.3 of the ISA are hereby repeated and incorporated by reference into this deed *mutatis mutandis*.

2. Investor Majority Consent and Series B Investor Majority Consent

2.1 Each of the parties hereby confirms that this deed shall constitute an Investor Majority Consent, a Series B Investor Majority Consent and a Series B-2 Investor Majority Consent for the purposes of the ISA (including, but not limited to, clauses 23.4.1 and 9.3 and Schedule 3 thereof) in connection with the following matters:

2.1.1 the amendment and restatement of the ISA on the terms set out herein;

2.1.2 the amendment to the Company's articles of association in the form provided to the parties;

2.1.3 the creation of a new class of Series C Shares having the rights set out in the new articles of association to be adopted as the Company's articles of association with effect from the date of this deed;

2.1.4 the issue and allotment of 17,421,600 Series C Shares to the Investors free of any rights of pre-emption set out in article 13 of the Company's articles of association on the terms of the Investment Agreement;

2.1.5 the increase in the size of the Equity Award Pool to include such number of Ordinary Shares that represent 13.5% of the Company's issued share capital post-Transaction, calculated on a fully diluted basis; and

2.1.6 all other matters related to or required in order to give effect to the Transaction.

3. Amendment and Restatement

3.1 With effect from the date of this deed, the ISA shall be amended and restated in the form set out in Schedule 1 (the "**Restated ISA**") so that the rights and obligations of the parties to the Restated ISA shall, on and from that date, be governed by and construed in accordance with the provisions of the Restated ISA.

3.2 Save as expressly amended by this deed, the ISA and the rights and obligations of the parties thereunder shall remain in full force and effect. In particular, the rights and obligations of the parties to the ISA arising in connection with the Warranties given by the Company under the terms of the ISA shall continue in full force and effect, subject in all cases to any limitations applicable thereto as further described in the ISA, and this deed shall not operate to release or discharge the Company from any liability to any Series B Investor (as defined in the ISA) pursuant to clause 12 of the ISA.

4. General

4.1 Investment Agreement

The Company hereby agrees and undertakes that it shall not agree to vary the terms of the Investment Agreement in a manner that creates any rights in favour of the Investors that are additional or superior to the rights granted to such Investors pursuant to the Restated ISA.

4.2 Counterparts

This deed may be executed in any number of duplicates, or by the parties on separate counterparts. Each executed duplicate or counterpart shall be an original, but all the duplicates or counterparts shall together constitute one and the same instrument.

4.3 General

The provisions of the following clauses contained in the ISA are hereby repeated and incorporated by reference in this deed mutatis mutandis: 15; 16; 18; 19; 23.3; and 25.

5. Governing law

This deed or the performance, enforcement, breach or termination hereof shall be interpreted, governed by and construed in accordance with the laws of England, excluding any conflicts or choice of law rule or principle that might otherwise refer construction or interpretation of this deed to the substantive law of another jurisdiction.

6. Dispute Resolution

In relation to any legal action or proceedings arising out of or in connection with this Agreement (including any dispute relating to the existence, validity or termination of this Agreement or any contractual or non-contractual obligation) ("**Proceedings**"), each of the Parties irrevocably submits to the exclusive jurisdiction of the English courts and waives any objection to Proceedings in such courts on the grounds of venue or on the grounds that Proceedings have been brought in an inappropriate forum provided that an order or judgment of any court may be enforced in any court of competent jurisdiction.

SCHEDULE 1

Amended and Restated ISA

FINAL FORM

DATED 29 MARCH 2017 AS AMENDED AND RESTATED ON 2 AUGUST 2018

(1) THE SERIES C INVESTORS

(2) THE EXISTING INVESTORS

(3) THE ORDINARY SHAREHOLDERS

- and –

(4) ORCHARD THERAPEUTICS LIMITED

SHAREHOLDERS' AGREEMENT
RELATING TO ORCHARD THERAPEUTICS LIMITED

Cooley

TABLE OF CONTENTS

THIS AGREEMENT is dated 29 March 2017 and amended and restated on 2 August 2018 and made

1. BETWEEN:

1. **THE SERIES C INVESTORS**, whose names and addresses are set out in Part C of Schedule 1 and each of whom has adhered to this Agreement immediately following entry into of the Deed of Amendment and Restatement (the "**Series C Investors**");

2. **THE EXISTING INVESTORS,** whose names and addresses are set out in Part A of Schedule 1 (the "**Existing Investors**");

3. **THE ORDINARY SHAREHOLDERS**, whose names and addresses are set out in Part B of Schedule 1 (the "**Ordinary Shareholders**"); and

4. **ORCHARD THERAPEUTICS LIMITED**, a company incorporated in England and Wales under company number 9759506 whose registered office is at 108 Cannon Street, London EC4N 6EU (the "**Company**"),

(each a "**Party**" and together, the "**Parties**").

2. WHEREAS:

A. The Company is a private company limited by shares, incorporated in England and Wales on 2 September 2015 under the Companies Act 2006.

B. The Parties have agreed to regulate their relationship in accordance with the terms of this Agreement.

3. THE PARTIES AGREE THAT:

1. DEFINITIONS AND INTERPRETATION

1.1 Definitions

"**Act**" means the Companies Act 2006;

"**Adjustment Event**" means at any time following Completion (as defined in the Investment Agreement): (i) any return of capital, bonus issue of shares or other securities by the Company by way of capitalisation of profits or reserves (other than a capitalisation issue in substitution for or as an alternative to a cash dividend which is made available to holders of Preferred Shares); or (ii) any consolidation or sub-division, or any repurchase or redemption of Shares or any variation in the subscription price applicable to any other outstanding Shares;

"**Affiliate**" means, with respect to any specified Person, any other Person who, directly or indirectly, controls, is controlled by, or is under common control with such Person, including without limitation any general partner, managing member, limited partner, manager, member, employee, officer or director of such Person or any trust for the benefit of any of the foregoing or any Affiliate of the foregoing or any venture capital fund now or hereafter existing that is controlled by one or more general partners or managing members of, or shares the same management company with, such Person. For purposes of this definition, the term "control" when used with respect to any Person means the power to direct the management or policies of such Person, directly or indirectly, whether through ownership of voting securities, by contract or otherwise, and the terms "controlling" and "controlled" shall have meanings correlative to the foregoing;

"**APA**" means the asset purchase and licence agreement dated 11 April 2018 and entered into between, inter alia, the Company and GSK in connection with the GSK Transaction;

"**Articles**" means the articles of association of the Company from time to time;

"**As Converted Basis**" in reference to any calculation or number, means that such calculation shall be made, or number determined, on the basis that each Preferred Share is equivalent to such number of Ordinary Shares into which such Preferred Share may then be converted in accordance with the Articles;

"**Board**" means the board of Directors of the Company as constituted from time to time;

"**Business**" means the business of the Company and any Group Company from time to time, including, in particular, the development and commercialisation of *ex vivo* gene therapy products;

"**Business Day**" means any day, other than a Saturday, Sunday or a day that is a national or bank holiday in the United Kingdom or the United States on which banks are open for the transaction of non-automated general commercial banking business;

"**CHI**" means, collectively, Cowen Healthcare Investments II LP and CHI EF II LP;

"**Co-Sale Rights**" means the rights set out in article 20 of the Articles (as may be varied, supplemented, amended or replaced by similar compulsory transfer provisions from time to time);

"**Confidential Information**" means all proprietary information marked as being confidential or of a reasonably apparent confidential nature on the face of them, provided during the term of this Agreement, relating to the Company, disclosed to another Party in any form, whether in writing, orally communicated, in electronic format or otherwise, and including any such information obtained through discussions with directors, officers, the management or employees of the Group;

"**Deed of Adherence**" means a deed of adherence substantially in the form set out in Schedule 3 (*Deed of Adherence*);

"**Deerfield**" means, collectively, Deerfield Special Situations Fund, L.P., Deerfield Private Design Fund III, L.P. and Deerfield Private Design Fund IV, L.P.;

"**Director(s)**" means the directors of the Company from time to time;

"**Drag Rights**" means the rights set out in article 21 of the Articles (as may be varied, supplemented, amended or replaced by similar compulsory transfer provisions from time to time);

"**Encumbrance**" means a lien, pledge, claim, charge (whether fixed or floating), mortgage or other encumbrance or security interest of any kind or right exercisable by a third party having similar effect, including any restriction on the use, voting, transfer, receipt of income or other exercise of any attributes of ownership, whether arising by contract or by operation of law;

"**Equity Award Pool**" has the meaning given to it in clause 9.1;

"**ERISA**" means the regulations made under the United States Employee Retirement Income Security Act of 1974;

"**EU**" has the meaning given to it in the APA;

"**F-Prime A**" means F-Prime Capital Partners Healthcare Fund IV-A LP;

"**F-Prime**" means, collectively, F-Prime Capital Partners Healthcare Fund IV LP and F-Prime Capital Partners Healthcare Fund IV-A LP;

"**Founders**" means Andrea Spezzi and Nicolas Koebel;

"**Group**" means in respect of any undertaking, such undertaking together with its Affiliates, and references to a "Group Company" shall be construed accordingly;

"**GSK**" means Glaxo Group Limited, a private limited company incorporated under the laws of England and Wales under company number 00305979 having its registered office at 980 Great West Road, Brentford, Middlesex, TW8 9GS;

"**GSK Transaction**" means the purchase and licence by the Company from GSK and its affiliates of certain assets in accordance with the terms of the APA;

"**GSK Director**" means the director appointed by GSK in accordance with clause 5.2;

"**HMRC**" means Her Majesty's Revenue and Customs;

"**ICTA**" means the Income and Corporation Taxes Act 1988;

"**Intellectual Property Rights**" means any intellectual property rights of any nature, including, without limitation, inventions, trade secrets and Know-How patents, trademarks, service marks, trade names, business names, copyrights, registered designs, design rights, domain names, rights in logos and get up, rights in goodwill or to sue for passing off or unfair competition, database rights, moral rights, utility models, semi-conductor topographies, all rights of whatsoever nature in computer software and data, rights to or in confidential information, all rights of privacy and all intangible rights and privileges of a nature similar or allied to any of the foregoing, and all other intellectual property rights in each case whether registered or unregistered, together with all applications for registration of and rights to apply for, and renewals or extensions of such rights and all similar equivalent rights or forms of protection which subsist now or in the future in any part of the world;

"**Investment Agreement**" means the investment agreement entered into between the Series C Investors and the Company on the same date as this amended and restated Agreement;

"**Investor**" means a holder of Preferred Shares from time to time;

"**Investor Limited Partnership**" means any limited partnership vehicle of any Investor subject (directly or indirectly) to ERISA;

"**Investor Majority Consent**" means, subject to limbs 1 – 3 of this definition below, the prior written consent of the holders of (i) at least sixty five per cent (65%) in nominal value of the Series A Shares; (ii) at least sixty-five per cent (65%) in nominal value of the Series B Shares and the Series B-2 Shares voting as if they constituted one and the same class; and (iii) at least a majority in nominal value of the Series C Shares, save that:

1. in respect of limb (i) of this definition above and solely for the purposes of Schedule 2, part A, paragraph 6 of this Agreement and any vote or written consent sought pursuant to clause 20.3 to amend this Agreement with respect to any consent or approval right granted to a Special Director and not granted to other Directors of the Company in each case when at the relevant time F-Prime and F-Prime A hold Shares which in aggregate exceed twenty-five per cent (25%) of the Company's issued voting share capital at any time the threshold of Series A Shares for the purposes of Investor Majority Consent shall be amended to require the approval of holders of at least 1,000,000 of the Series A shares in issue at that time

2. in respect of limb (ii) of this definition above and solely for the purposes of Part A of Schedule 2, for so long as GSK, together with its Permitted Transferees, holds in excess of ten per cent (10%) of the Company's issued share capital (calculated on a fully diluted basis) and provided that GSK has not served a Restoration Notice on the Company, the calculation of an Investor Majority Consent in respect of:

    a. the matters set out in paragraphs 6, 7, 12, 18 and 19 of Part A of Schedule 2, shall not include any Series B-2 Shares held by GSK (or its Permitted Transferees); and

    b. paragraph 11 of Part A of Schedule 2, shall include Series B-2 Shares held by GSK (and its Permitted Transferees) only to the extent that the action being considered results in the sale, transfer, assignment, license, pledge or grant of any Encumbrance over Intellectual Property Rights relating to the assets divested or licensed by GSK to the Company pursuant to the GSK Transaction; and

3. when calculating an Investor Majority Consent for any matter other than an Investor Majority Consent for those matters set out in paragraphs (a) and (b) above, only one half (1/2) of the total number of Series B-2 Shares held by each Series B-2 Preferred Shareholder shall be taken into account.

Where Series B-2 Shares are excluded from the calculation of the "Investor Majority Consent" as set out in paragraphs 1—3 above, all remaining Preferred Shares shall be deemed to constitute the entire issued share capital of the Company;

"**IPO**" means the admission of all or any of the Shares or securities representing those Shares (including without limitation depositary interests, American depositary receipts, American depositary shares and/or other instruments) to or the grant of permission by any like authority for the same to be admitted to or traded or quoted on any Recognised Investment Exchange;

"**Know-How**" means all information, data, know-how and methodology including all financial, commercial, trade and business secrets of whatever nature and in whatever form and information comprising or relating to any inventions, discoveries, improvements, processes, techniques, methods, tests, component tests, instructions, drawings, diagrams, illustrations, data, specifications, lists, programs, formulae, technical information, plans, reports, manuals and all other documents, recorded information and data whatsoever and howsoever stored;

"**Law**" or "**Laws**" includes all applicable legislation, statutes, directives, regulations, judgments, decisions, decrees, orders, instruments, by-laws, and other legislative measures or decisions having the force of law, treaties, conventions and other agreements between states, or between states and the European Union or other supranational bodies, rules of common law, customary law and equity and all civil or other codes and all other laws of, or having effect in, any jurisdiction from time to time and whether before or after the date of this Agreement;

"**Liquidation Event**" has the meaning given to it in the Articles;

"**Management Accounts**" means the unaudited management accounts of the Company, comprising a balance sheet and profit and loss account to be produced by the Company at the end of every month;

"**NASDAQ**" means the NASDAQ stock market of the NASDAQ OMX Group Inc.;

"**Notice**" has the meaning given to it in clause 22.1;

"**NYSE**" means the New York Stock Exchange;

"**Observer**" means an observer appointed by the Series A Investor, Temasek or CHI in accordance with clause 7.4 and "Observers" shall be construed accordingly;

"**Option Scheme**" means the Company's share option plan entitled "Orchard Therapeutics Limited Employee Share Option Plan, with Non-Employee Sub-Plan and US Sub-Plan with California Supplement", as adopted by the Board on 14 September 2016;

"**Ordinary Shares**" means the ordinary shares of £0.00001 each in the capital of the Company, which have the rights set out in the Articles;

"**ORI**" means Unique Diamond Investments Limited, a company incorporated in the British Virgin Islands and whose registered office is at Vistra Corporate Services Centre, Wickhams Cay II, Road Town, Tortola, VG1110 British Virgin Islands;

"**Permitted Transfer**" has the meaning given to it in the Articles;

"**Permitted Transferee**" has the meaning given to it in the Articles;

"**Preferred Director**" means any of the Special Directors, ORI Director, GSK Director and Deerfield Director and "Preferred Directors" shall be construed accordingly;

"**Preferred Shares**" means the Series A Shares, the Series B Shares, the Series B-2 Shares and the Series C Shares;

"**Proceedings**" has the meaning given to it in clause 23.2;

"**Qualified Listing**" means the legal completion of a fully underwritten listing and admission of any of the Shares (or the shares of any holding company of the Company) to trading on, or the granting of permission for any such Shares to be dealt on, NASDAQ or the NYSE at a price per Share issued of the time of such listing not less than the price paid per Series C Share by the Series C Investors at Completion (as defined in the Investment Agreement and subject to appropriate adjustment to reflect any Adjustment Event) and where the gross proceeds to the Company of the listing are equal to or exceed US$50,000,000 (before the deduction of broker's commissions, discounts and fees);

"**Recognised Investment Exchange**" means a recognised investment exchange as defined by section 285 of the Financial Services and Markets Act 2000 and every statutory modification or re-enactment thereof for the time being in force, together with (whether or not falling within such definition) the Official List of the UK Listing Authority, the Main Market of the London Stock Exchange plc, the AIM market of the London Stock Exchange plc, NASDAQ and the NYSE;

"**Relevant Securities**" means in respect of the Company, any Share or other security in the capital of the Company from time to time, or any other security, agreement or instrument which contains or provides for any right to subscribe or exchange for, convert into or otherwise call for any issue of any Shares or other securities in the capital of the Company from time to time;

"**Restoration Notice**" means: a notice served on the Company by GSK requiring that (i) GSK shall cease to be prevented from voting on items identified in limb (2) of the definition of Investor Majority Consent and/or (ii) the GSK Director shall cease to be prevented from voting on the items identified in clause 5.8;

"**Sale**" means: (i) the sale or other transfer of the whole or substantially the whole of the business and assets of the Company, including the grant by the Company to any person of an exclusive licence over all or substantially all of the Company's commercially valuable intellectual property; or (ii) the sale of the entire issued share capital of the Company;

"**Series A Shares**" means the series A convertible preferred shares of £0.00001 each in the capital of the Company, which have the rights set out in the Articles;

"**Series B Shares**" means the series B convertible preferred shares of £0.00001 each in the capital of the Company, which have the rights set out in the Articles;

"**Series B-2 Investor Majority Consent**" means the prior written consent of the holders of at least sixty-five per cent (65%) in nominal value of the Series B-2 Shares;

"**Series B-2 Shares**" means the series B-2 convertible preferred shares of £0.00001 each in the capital of the Company, which have the rights set out in the Articles;

"**Series B Investor Majority Consent**" means the prior written consent of the holders of at least sixty-five per cent (65%) in nominal value of the Series B Shares;

"**Series C Shares**" means the series C convertible preferred shares of £0.00001 each in the capital of the Company, which have the rights set out in the Articles;

"**Shareholder**" means a holder of any of the Company's Shares;

"**Shares**" means the Ordinary Shares, the Series A Shares, the Series B Shares, the Series B-2 Shares and the Series C Shares (and any other classes of share (if any) comprised in the capital of the Company from time to time);

"**SMIT**" means Scottish Mortgage Investment Trust plc;

"**Special Director**" means a Director appointed pursuant to clause 5.2.1;

"**Tag Rights**" means the rights set out in article 19 of the Articles (as may be varied, supplemented, amended or replaced by similar compulsory transfer provisions from time to time);

"**Temasek**" means TLS Beta Pte Ltd., a Singapore company with registered number 200500368D whose office is at 60B Orchard Road #06-18 Tower 2, The Atrium@Orchard, Singapore 238891;

"**Transaction Agreements**" has the meaning given to it in clause 20.1.1;

"**US Shareholder**" has the meaning given to it in clause 8.6.1; and

"**VCOC**" has the meaning given to it in clause 8.5.

1.2 Interpretation

In this Agreement, where the context admits:

1.2.1 clause, Schedule and paragraph headings shall not affect the interpretation of this Agreement;

1.2.2 words and phrases the definitions of which are contained or referred to in the Act shall have the meanings thereby respectively attributed to them unless otherwise expressly defined in this Agreement;

1.2.3 every reference to a particular statutory provision or other Law shall be construed also as a reference to all other Laws made under the Law referred to and to all such Laws as amended, re-enacted, consolidated or replaced or as their application or interpretation is affected by other Laws from time to time and whether before, on or after the date of this Agreement;

1.2.4 references to "**clauses**" and "**Schedules**" are references to clauses of and schedules to this Agreement, references to paragraphs are, unless otherwise stated, references to paragraphs of the Schedule in which the reference appears;

1.2.5 references to the singular shall include the plural and vice versa and references to the masculine, the feminine and the neuter shall include each other such gender;

1.2.6 "**person**" or "**Person**" includes any individual, partnership, body corporate, corporation sole or aggregate, limited liability company, trust or other entity, state or agency of a state, and any unincorporated association or organisation, in each case whether or not having separate legal personality;

1.2.7 words introduced by the word "**other**" shall not be given a restrictive meaning because they are preceded by words referring to a particular class of acts, matters or things;

1.2.8 general words shall not be given a restrictive meaning because they are followed by words which are particular examples of the acts, matters or things covered by the general words and the word "**including**" shall be construed without limitation;

1.2.9 where the expressions "**connected persons**" and "**person connected**" and any other similar expressions are used in this Agreement any question as to whether a person is connected with another shall be determined in accordance with section 993 and section 994 of the Income Tax Act 2007 (subject to the deletion of the words from "But" to "arrangements" in sub-section (4) of the said section 993);

1.2.10 every reference to an English legal term for any action, remedy, method or judicial proceedings legal document, legal status, court, official, or any other legal concept shall, in respect of any jurisdiction other than England be deemed to include the legal term which most nearly approximates in that jurisdiction to the English legal term;

1.2.11 every reference to the "**Parties to this Agreement**", "**the Parties hereto**" or any other similar expression or like effect shall include every person who becomes party to this Agreement by entering into a Deed of Adherence;

1.2.12 any reference to "**written**" or "**writing**" includes faxes (but not e-mail) or other transitory forms;

1.2.13 any document expressed to be "**in agreed form**" means a document in a form approved by the Parties to this Agreement;

1.2.14 unless the context otherwise requires or unless otherwise defined in this Agreement, words and expressions defined in the Articles shall have the same meaning when used in this Agreement;

1.2.15 the headings and sub-headings are inserted for convenience only and shall not affect the construction of this Agreement; and

1.2.16 each of the Schedules shall have effect as if set out herein.

1.3 Several liabilities

Save where expressly stated otherwise in this Agreement, all warranties, indemnities, covenants, agreements and obligations given or entered into by more than one person in this Agreement are given or entered into severally.

2. TRANSFER AND ISSUES OF SHARES

2.1 Transfers and no Encumbrances

2.1.1 Notwithstanding the Articles, each Shareholder undertakes to the Series C Investors that he shall not, and shall not agree to create any Encumbrance over, transfer or otherwise dispose of the whole or any part of his interest in or grant any option over any Shares to any person except:

(a) with Investor Majority Consent; or

(b) where required or permitted to do so by both (i) the Articles; and (ii) this Agreement.

2.1.2 Other than pursuant to clause 9, the Company shall not issue any Shares or other Relevant Securities to any person, unless that person is a Party to this Agreement or has executed and delivered a Deed of Adherence (save where the Investors acting by Investor Majority Consent have agreed in advance that such person does not need to enter into a Deed of Adherence).

2.1.3 Except as expressly provided in this Agreement or where Shares are allotted to satisfy the exercise of an option under the Equity Award Pool, the Company shall not register any transfer or issue of shares unless a Deed of Adherence is executed by the transferee or allottee (save where the Investors acting by Investor Majority Consent have agreed in advance that such transferee or allottee does not need to enter into a Deed of Adherence).

3. REGISTRATION RIGHTS AND IPO

3.1 Registration rights

The Company grants to each of the Investors the registration rights set forth in Schedule 5. No IPO shall take place unless all Preferred Shares are converted into Ordinary Shares and the provisions set out in the Articles are complied with. Notwithstanding anything to the contrary in this Agreement, Schedule 5 shall survive termination of this Agreement due to an IPO and, for the avoidance of doubt, shall terminate in accordance with paragraph 14 thereof.

3.2 Actions on a Qualified Listing

3.2.1 Each Shareholder and the Company agrees to comply with the provisions of Schedule 6 (*IPO*). Notwithstanding anything to the contrary in this Agreement, Schedule 6 shall survive termination of this Agreement due to an IPO.

3.2.2 In the event that a reorganisation of the Company's issued share capital (the terms of which are supported by Investor Majority Consent) is to be implemented prior to an IPO, the effect of which is that the Company becomes a wholly-owned subsidiary of a new holding company (the "**Newco**") and the shareholders of the Newco and their respective percentage holdings of shares in Newco are the same as the Shareholders and their respective percentage holdings of Shares prior to such reorganisation, then:

(a) the Company shall procure that the Newco shall execute a deed of adherence to this Agreement in such form as is approved by an Investor Majority pursuant to which the Newco shall agree to be bound by and comply with the terms of this Agreement;

(b) following the due execution of the deed of adherence referred to in clause 3.2.2(a) above, any reference to "the Company" in this Agreement shall be construed as a reference to the Newco; and

(c) the parties (other than the Company) shall continue to be bound by and comply with the terms of this Agreement *mutatis mutandis* in their capacity as holders of shares in Newco as if they were holders of Shares until completion of the IPO.

3.3 Variations to the Articles

Each Series B-2 Preferred Shareholder hereby agrees with the other Investors that in the event there is any variation or abrogation proposed to be made to both the Series B Shares and the Series B-2 Shares where the effect on both such classes of share is in all material respects the same, and such variation or abrogation is approved by Series B Investor Majority Consent, then they will sign all documents, deeds and resolutions and vote in favor of any such variation or abrogation (including pursuant to clause 20.3.1(c)) and including but not limited to passing any resolution in connection with article 12.1.1 of the Articles in respect of such variation or abrogation.

4. EFFECT OF CEASING TO HOLD SHARES

4.1 Effect of ceasing to hold Shares

In the event that any Shareholder ceases to hold any Shares or other Relevant Securities in the Company, then such Shareholder shall cease to have any right to enforce any provision of this Agreement (including any requirement that its consent be obtained to any termination, amendment, variation, or supplement to this Agreement), provided always that nothing in this clause shall prejudice any right or obligation of such Shareholder which accrued in respect of the period prior to the time at which it ceased to hold any such Shares or other Relevant Securities.

5. THE BOARD

5.1 Members of the Board

The members of the Board as at the date of this amended and restated Agreement shall be:

Mark Rothera	- *Chief Executive Officer*
Alexander Pasteur	- *Special Director (non-executive)*
Jonathan Ellis	- *GSK Director (non-executive)*
Hong Fang Song	- *ORI Director (non-executive)*
Elise Wang	- *Deerfield Director (non-executive)*
Hubert Gaspar	- *(non-executive)*
Charles Rowland Jr.	- *(non-executive)*
James Geraghty	- *(non-executive)*
Marc Dunoyer	- *(non-executive)*
Joanne Beck	- *(non-executive)*

5.2 Director appointment rights

5.2.1 For so long as F-Prime, together with its Permitted Transferee(s), holds Preferred Shares, F-Prime shall be entitled to appoint any two (2) persons holding office at any one time to act as Special Directors of the Company and to remove from office any person so appointed and to appoint another person in his place.

5.2.2 For as long as Deerfield, together with its respective Permitted Transferee(s), holds Shares representing not less than two per cent. (2%) (calculated on a undiluted basis) of the Company's issued share capital, Deerfield shall be entitled to appoint one person holding office at any one time to act as a director of the Company and to remove from office any person so appointed and to appoint another person in his place. The first such person appointed from the date of this amended and restated Agreement shall be Elise Wang until such time as Deerfield and the Company identify a mutually satisfactory replacement.

5.2.3 For so long as ORI, together with its Permitted Transferee(s), holds Shares representing not less than two per cent. (2%) (calculated on a undiluted basis) of the Company's issued share capital, ORI shall be entitled to appoint one person holding office at any one time to act as a director of the Company and to remove from office any person so appointed and to appoint another person in his place.

5.2.4 For so long as GSK, together with its Permitted Transferees, holds Series B-2 Shares representing not less than five per cent. (5%) of the Company's issued share capital (calculated on an undiluted basis), or, if longer, until the date on which in respect of at least one (1) WAS Royalty Product (as defined in the APA) and one (1) MLD Royalty Product (as defined in the APA), in respect of which the Company has (i) obtained a marketing authorisation or biologics licence application; (ii) made the first commercial sale for which revenue has been recognised; and (iii) obtained pricing reimbursement for such products, in each of the EU and the United States, GSK shall be entitled to appoint one person to act as a director of the Company and to remove from office any person so appointed and to appoint another person in his or her place.

5.2.5 The right to appoint a Director pursuant to this clause 5.2 shall be exercised by the appointing Investor(s) serving notice on the Company, specifying the Director(s) to be appointed. The removal of a Director so appointed shall be effected by the appointing Investor(s) who requested the appointment of the relevant Director serving notice on the Company or procuring the resignation of the relevant Director.

5.2.6 The Preferred Directors have the right to receive notice of, and to attend, all meetings of directors and the meetings of any committee(s) of the Board (whether in person, by telephone or otherwise). The Company will procure the provision to the Preferred Directors concurrently with the relevant directors or committee members, and in the same manner, notice of such meetings and a copy of all materials provided to such persons.

5.2.7 F-Prime shall have the right to appoint one (1) Special Director (if then appointed to each committee of the Board.

5.3 Independent director appointment rights

The holders of Preferred Shares and Ordinary Shares (voting together as if the Preferred Shares and Ordinary Shares constitute the same class and on an As Converted Basis) shall be entitled by notice in writing to the Company to appoint any two persons holding office at any one time to act as non-executive Directors and to remove from office by notice to the Company any person so appointed and to appoint another person in his place.

5.4 Observer appointment rights

5.4.1 For so long as F-Prime, together with its Permitted Transferee(s), holds Shares, F-Prime shall be entitled by notice to the Company to appoint, remove and replace one representative to attend as an observer at each and any meeting of the Board and at each and any committee of the Board.

5.4.2 For so long as Temasek, together with its Permitted Transferee(s), holds Shares, Temasek shall be entitled by notice to the Company to appoint, remove and replace one representative to attend as an observer at each and any meeting of the Board and at each and any committee of the Board.

5.4.3 For so long as CHI, together with their Permitted Transferee(s), holds Shares, CHI shall be entitled by notice to the Company to appoint, remove and replace one representative to attend as an observer at each and any meeting of the Board and at each and any committee of the Board.

5.5 Fees and expenses

The Company shall reimburse commercially reasonable expenses of the Preferred Directors, any other Director and any Observers for out-of-pocket costs incurred in attending meetings of the Board (or meetings of any committee thereof) and other meetings or events attended on behalf of the Company.

5.6 Quorum at Board meetings

5.6.1 No resolution may be passed at a meeting of the Board (or a meeting of a committee of the Board) unless the nature of the business has been specified in an agenda circulated to all members of the Board (or all members of the committee of the Board) and all Observers at least five (5) Business Days in advance of the meeting.

5.6.2 However, if any Director who is required for the quorum is not present within half an hour of the time at which the meeting was due to start, the chairperson of the Board may adjourn the meeting by forty-eight (48) hours, to be held at the same time of the day and place, and shall give written notice of the same to all Directors. If the same Director is not present within half an hour of the time at which the adjourned meeting was due to start, then the chairperson of the Board may declare a quorum present, notwithstanding that the quorum requirements set out in clause 5.6.1 have not been fully satisfied.

5.7 Conduct of meetings of the Board and committees

5.7.1 Meetings of the Board shall be held as often as may be necessary but not less than four (4) times in each calendar year (or with such lesser frequency as the Board shall agree in writing) and shall be convened in accordance with the Articles.

5.7.2 No business shall be transacted at any meeting of the Board (or a committee of the Board) save for that specified in the agenda referred to in clause 5.6.1.

5.7.3 The quorum at any meeting of the Board shall be as set out in clause 5.6 and, subject to clause 7.1, clause 7.2, Schedule 4 (*Matters Requiring Consent*) and the Articles, decisions shall be taken by a majority vote. The chairperson of the Board shall have a casting vote in the event of a tied vote.

5.8 GSK Director

For so long as GSK, together with its Permitted Transferees, holds Series B-2 Shares representing ten per cent. (10%) or more of the Company's issued share capital (calculated on an undiluted basis), the GSK Director shall not, unless GSK has served a Restoration Notice on the Company, be permitted to vote on any matters requiring: (i) the consent of the Board pursuant to paragraphs 4, 5, 6, 9, 12, 13, 15, 16, 17, 18, 19 and 20 of Part B of Schedule 2; and (ii) the consent of the Board pursuant to paragraphs 8 and 9 if the matter relates to any of the assets which are the subject of the GSK Transaction.

6. INFORMATION RIGHTS

6.1 Provision of information to Investors

Subject to clause 6.2.3, the Company undertakes to each Investor that is not an individual that:

6.1.1 the Company shall keep the Investors informed of all material matters relating to the progress of the Business to such extent and in such form and detail as the Investors may from time to time reasonably require and shall supply to the Investors such written particulars of any matters concerned with and arising out of the activities of the Company as the Investors may from time to time reasonably require;

6.1.2 the Company shall deliver, as soon as practicable, but in any event within one hundred and twenty (120) days after the end of each financial year of the Company (i) a balance sheet as of the end of such year; (ii) statements of income and of cash flows for such year, and a comparison between (x) the actual amounts as of and for such financial year and (y) the comparable amounts for the prior year and as included in any Budget (as defined in clause 6.1.5) for such year with an explanation of any material difference between such amounts and a schedule as to the sources and applications of funds for such year; and (iii) a statement of shareholders' equity as of the end of such year, all such financial statements to be audited by accountants approved by the Board;

6.1.3 the Company shall deliver, as soon as practicable, but in any event within thirty (30) days after the end of each of the first three quarters of each financial year of the Company, unaudited statements of income and cash flows for such financial quarter, and an unaudited balance sheet and a statement of shareholders' equity as of the end of such financial quarter, all prepared in accordance with UK GAAP (except that such financial statements may (i) be subject to normal year end audit adjustments; and (ii) not contain all notes thereto that may be required in accordance with UK GAAP), as well as the Management Accounts for the relevant period along with a report providing summary details of the progress of the Company and its business and details of the Company's expenditure throughout the course of such period;

6.1.4 the Company shall deliver, as soon as practicable, but in any event within thirty (30) days of the end of each month, an unaudited income statement and statement of cash flows for such month, and an unaudited balance sheet and statement of shareholders' equity as of the end of such month, all prepared in accordance with UK GAAP (except that such financial statements may (i) be subject to normal year-end audit adjustments and (ii) not contain all notes thereto that may be required in accordance with UK GAAP), as well as the Management Accounts for that month along with a report providing summary details of the progress of the Company and its business and details of the Company's expenditure throughout the course of that month;

6.1.5 the Company shall deliver, as soon as practicable, but in any event thirty (30) days before the end of each financial year, a detailed operating and capital budget and business plan for the next financial year, which shall include a cash flow forecast for such period along with the Board's and management's forecasts and projections for the Business for the next financial year (collectively, the "**Budget**"), approved by the Board and prepared on a monthly basis, including balance sheets, income statements, and statements of cash flow for such months and, promptly after prepared, any other budgets or revised budgets prepared by the Company;

6.1.6 at the same time as audited accounts of the Company are provided pursuant to clause 6.1.2, the Company shall provide all relevant audit and management letters and all correspondence between the Company and the auditors of the Company concerning such accounts unless doing so would, in the opinion of the Board acting reasonably, jeopardize legal privilege between the Company and its legal advisers;

6.1.7 each of the Preferred Directors appointed pursuant to clause 5.2 and any Observer appointed pursuant to clause 5.4 may, from time to time, make full but confidential disclosure to its appointing Shareholder of any information relating to the Company;

6.1.8 notwithstanding clause 12, each Investor shall be at liberty from time to time to make such disclosure:

(a) to its partners, trustees, shareholders, unit holders and other participants and/or to any member of the same Group as the Investor for the purposes of, but not limited to, reviewing existing investments and investment proposals;

(b) to any lender to the Company and/or to any shareholder of any member of the Company's Group;

(c) about any member of the Company's Group as shall be required by law and any regulatory authority to which the Investor is subject;

(d) to the Company's auditors and/or any other professional advisors of the Company; and

(e) to the Investor's professional advisers and to the professional advisers of any person to whom the Investors is entitled to disclose information pursuant to this clause,

in relation to the business affairs or financial position of the Company as it may in its reasonable discretion think fit provided that any Person to whom information is disclosed is subject to an obligation of confidentiality substantially similar to the obligation of confidentiality contained in this Agreement; and

6.1.9 upon being given a reasonable amount of notice in writing, the Company shall permit any Investor to enter the Company's premises and to make reasonable inspection of its books and records and to have reasonable access to the Company's employees and advisers for the purposes of ascertaining the progress of the Business.

6.1.10 Subject to clause 6.2, the Company undertakes to UCLB (for so long as it together with any of its Permitted Transferees hold not less than five per cent. (5%) in nominal value of the Shares) that it shall, upon receipt of written notice from UCLB, provide to UCLB the information set out in clauses 6.1.2—6.1.6 above at the same time as it is provided to the Investors.

6.2 Provision of additional information to F-Prime, SMIT, ORI, Temasek, GSK, CHI and Deerfield

Subject to clause 6.2.3, the Company undertakes to F-Prime, SMIT, ORI, Temasek, GSK, CHI and Deerfield that for so long as they (or any of their Permitted Transferees) each hold any Shares that, in addition to the information to be provided pursuant to clause 6.1 above:

(a) the Company shall deliver to F-Prime, SMIT, ORI, Temasek, GSK, CHI and Deerfield copies of all Board materials and the agenda for meetings of the Board and, following such meetings, the final form minutes of the meeting, in each case at the same time such materials are distributed to the Directors; and

(b) the Company shall deliver to F-Prime, SMIT, ORI, Temasek, GSK, CHI and Deerfield as soon as practicable, but in any event within forty-five (45) days after the end of each calendar quarter, an up to date capitalisation table showing (i) the number of Shares of each class and Relevant Securities convertible into or exercisable in respect of Shares outstanding at the end of the relevant period; (ii) the Shares to be issued upon the conversion or exercise of any Relevant Securities and the exchange ratio and exercise price applicable thereto; and (iii) the number of Ordinary Shares outstanding in the Equity Award Pool over which the Company may grant awards or options, in each case in sufficient detail as to permit F-Prime, SMIT, ORI, Temasek, GSK, CHI and Deerfield (or any of its/or their Permitted Transferees as applicable) to calculate their percentage equity ownership in the Company and certified by the chief financial officer or chief executive officer of the Company as being true, accurate and complete.

6.2.2 If the Company fails to comply with any of its obligations to provide information to the Investors (that are not individuals) pursuant to clause 6.1 or to F-Prime, SMIT, ORI, Temasek, GSK, CHI and Deerfield pursuant to clause 6.2, then the Investors (who are not individuals) (acting by Investor Majority Consent) or F-Prime, SMIT, ORI, Temasek, GSK, CHI and Deerfield (as the case may be) will be entitled to instruct a firm of accountants to prepare the relevant information and provide it to the Investors (who are not individuals), F-Prime, SMIT, ORI, Temasek, GSK, CHI and Deerfield (as the case may be). The Company will permit full access to its books and records and its premises for this purpose. The reasonable costs of, and incidental to, any such appointment (plus any VAT) will be paid by the Company.

6.2.3 The Company's obligations under clauses 6.1 and 6.2 shall not apply in respect of an Investor (other than an Institutional Investor (as defined in the Articles)) where the Company reasonably determines that such information or materials include trade secrets or contain other proprietary information that is commercially sensitive, or in respect of any Investor where the Company reasonably determines that such information is subject to legal privilege between the Company and its legal advisors.

7. BUSINESS CONDUCT OBLIGATIONS

7.1 The Company's undertakings

7.1.1 The Company agrees and undertakes that, save with the prior approval of the various categories of persons as further particularised in Schedule 2 (*Matters Requiring Consent*), for so long as the Investors and their Permitted Transferees hold Shares, it shall not effect or propose (by way of resolution) any of the actions referred to in Schedule 2 (*Matters Requiring Consent*).

7.1.2 The Company agrees and undertakes that it will run the Business in compliance with applicable Law in all material respects.

7.1.3 The Company shall maintain directors and officers insurance policies for each member of the Board (and their affiliated funds) and the officers of the Company in the amount of at least £1,000,000 and, subject to approval by the Board, will increase such coverage immediately prior to an IPO to at least £5,000,000, on terms reasonably acceptable to F-Prime.

7.2 Shareholder undertakings

Each Shareholder that is a party to this Agreement agrees and undertakes that, save with the prior approval of the various categories of persons as further particularised in Schedule 2 (*Matters Requiring Consent*), for so long as the Investors and their Permitted Transferees hold Shares, it shall exercise its rights and powers under this Agreement and as a holder of Shares to procure, in so far as it is lawfully able by the exercise of such rights and powers, that no Group Company will effect or propose (by way of resolution) any of the actions referred to in Schedule 2 (*Matters Requiring Consent*).

7.3 Consents and approvals

Any consent or approval given pursuant to Schedule 2 (*Matters Requiring Consent*) hereunder may be given on such terms and subject to such conditions (if any) as such persons (acting together as a group) may in their absolute discretion determine and no such consent or approval shall be held to have been validly given unless and until all such terms and conditions have been complied with.

8. ERISA

8.1 Exercise of rights by Investor Limited Partnerships

The Parties agree that, whatever rights an Investor Limited Partnership may have, or elect to acquire, or designate to one or more Directors, any rights of such Investor Limited Partnership under this Agreement may be exercised by such Investor Limited Partnership acting through its respective general partner or, if any current or subsequent general partner is removed as the general partner of such an Investor Limited Partnership, the successor or replacement general partner of that partnership.

8.2 Directors and observers

The investment vehicles comprising the Investors hereby agree that, insofar as such vehicles are Investor Limited Partnerships, their respective rights (if any) to appoint and/or nominate a Director pursuant to clause 5.2 or the Articles shall be exercised by the respective general partners of such Investor Limited Partnerships. In the event that an Investor Limited Partnership has not exercised its rights (if any) to appoint and/or nominate a Director pursuant to clause 5.2 or the Articles, then any such partnership shall have the right to appoint a representative to attend as a non-voting observer at each meeting. The appointment and removal of such representative shall be by written notice from the relevant Investor Limited Partnership to the Company, which shall take effect on delivery at the Company's registered office or at any meeting of the Board or any committee thereof.

8.3 Provision of information

Any Investor Limited Partnership acting through their general partner shall have the right to receive on reasonable written request to the Company:

8.3.1 Management Accounts of the Company (and each Group Company), including a balance sheet and profit and loss account;

8.3.2 on an annual basis, budgets and cash flow forecasts of the Company and each Group Company; and

8.3.3 such additional information as such Investor Limited Partnership may at any time reasonably request (including any information provided to a Preferred Director).

8.4 Meetings with management

The Investor Limited Partnerships all acting through their respective general partners shall each have the right to meet on a regular basis with such management personnel of the Company as may reasonably be designated by such partnerships, on reasonable notice to the Company, for the purpose of consulting with management, obtaining information regarding the business and prospects of the Company or expressing the views of such partnerships and advising Company management on such matters.

8.5 Alteration of rights

The Parties agree that if legal counsel for any Investor Limited Partnership reasonably concludes that the rights granted to it by this clause 8 should be altered to preserve the qualifications of an Investor Limited Partnership as a "venture capital operating company" (a "**VCOC**"), or otherwise to ensure that the assets of such Investor Limited Partnership are not considered "plan assets" of such Investor Limited Partnership for the purposes of ERISA, the Parties hereto will agree such amendments to this Agreement as may be reasonably required by such Investor Limited Partnership to effect such alterations with such expense being shared by the Company and the relevant Investor Limited Partnership.

8.6 Passive foreign investment or controlled foreign corporation

8.6.1 Not later than forty-five (45) days after the date of this amended and restated Agreement, the Company will determine whether it constitutes a "passive foreign investment company" (a "**PFIC**") or a "controlled foreign corporation" (a "**CFC**") as defined for U.S. tax purposes for the current financial year up to the date of such determination and will so advise any Shareholder who so requires (each, a "**US Shareholder**"). In the event that the Company determines it constitutes a CFC, it shall provide all information available to it that is necessary for a US Shareholder to complete IRS Form 5471 (or successor form).

8.6.2 Not later than forty-five (45) days after the end of each financial year of the Company, the Company will determine whether it constitutes a PFIC or a CFC as defined for U.S. tax purposes for such financial year and will so advise F-Prime and any other US Shareholder who so requires. For each financial year of the Company, commencing with the first financial year for which it is determined to be a PFIC, the Company shall no later than 45 days after the end of such fiscal year, furnish each US Shareholder with all information necessary for such US Shareholder to make a qualified electing fund ("**QEF**") election pursuant to Section 1295(b) of the U.S. Internal Revenue Code, as amended (the "**Code**") and to file its U.S. federal income tax returns in connection with such QEF election. Without limiting the generality of the foregoing, the Company shall provide (a) a PFIC Annual Information Statement as described in Treas. Reg. 1.1295-1(g) and (b) all information necessary for the US Shareholder to complete IRS Form 8621 (or successor form). The Company will obtain the advice of one of the "big four" accounting firms to make the determinations and provide the information and statements as described in this paragraph.

8.6.3 The Company will (1) provide or cause its affiliates to provide sufficient information to enable each US Shareholder to accurately complete its annual U.S. tax reporting and payment obligations as a 10% shareholder of the Company and each of its subsidiaries under the Code, and (2) if necessary, permit each US Shareholder (or its authorised representatives) to examine and copy the books of account, records, and other documentation of the Company and each of its affiliates in order to verify the required information. In addition, the Company will covenant to retain all records relevant for calculating the earnings and profits of and taxes paid by each US Shareholder and each of its subsidiaries for as long as such US Shareholder and its affiliates own in the aggregate 10% or more of the Company and will provide such information to the relevant US Shareholder (or its authorised representative) upon such US Shareholder's request within 30 days after the end of the Company's financial year in which the calculation of a deemed paid foreign tax credit becomes relevant to such US Shareholder under the Code.

8.6.4 Any third party costs incurred by the Company in respect of its obligations under this clause 8.6 will be borne by the Company.

9. EQUITY AWARD POOL

9.1 Size and nature of Equity Award Pool

The Company shall establish and operate a pool for the granting of equity incentives with respect to Ordinary Shares, which, for the avoidance of doubt shall include any Ordinary Shares issued to the Founders (the "**Equity Award Pool**"). The number of Ordinary Shares comprised in the Equity Award Pool and the rules of any share option scheme (or other terms of grant or arrangement) applicable in respect of the grant of options or other award of equity incentives (including if deemed appropriate share awards) from the Equity Award Pool shall be subject to approval of the Remuneration Committee (or if such committee is not then constituted, the Board) (provided always that the size of the Equity Award Pool (including both shares and options previously issued and shares and options available to be issued thereunder) shall not exceed thirteen point five per cent. (13.5%) (the "**Equity Award Pool Cap**") of the Company's fully diluted share capital following Completion; *provided that* if upon Completion (as defined in the Investment Agreement) the Company has issued Series C Shares for aggregate subscription proceeds in excess of US$150,000,000, the Equity Award Pool Cap shall be based on Completion (as defined in the Investment Agreement) assuming the issue of Series C Shares with an aggregate subscription price of US$150,000,000 only. Any grant of options or other award of equity incentives from the Equity Award Pool shall be in such number, at such price and otherwise on terms as may be decided by the Remuneration Committee (or if such committee is not then constituted, the Board).

9.2 No further consents required

For the avoidance of doubt, Investor Majority Consent shall not be required prior to the allotment of any share or grant of any option over shares from the Equity Award Pool or the allotment and issue of any Ordinary Shares on a valid exercise of any such option; *provided that* such allotment of any share or grant of any option over shares is within the Equity Award Pool Cap. If the Company wishes to increase the size of the Equity Award Pool beyond the Equity Award Pool Cap, such increase shall require Investor Majority Consent, it being acknowledged that following Completion (as defined in the Investment Agreement) the Board shall conduct a review of incentivisation practices of similar companies operating in the same sector as the Company (taking into account, among other factors, valuation, headcount and stage of development), and, depending on the outcome of such review, may recommend an increase to the Equity Award Pool. For the avoidance of doubt, the Investor Majority shall be under no obligation to approve any such increase.

9.3 Pre-emption rights

Each Party hereby irrevocably waives all rights of pre-emption contained in the Articles or otherwise in respect of the grant of options or the allotment and issue of Ordinary Shares on exercise of options granted, in each case in accordance with the provisions of this clause 9 (including without limitation with respect to the Equity Award Pool Cap).

9.4 Power of Attorney

Prior to issuing any Ordinary Shares following the exercise of options or other award of equity incentives from the Equity Award Pool, the Company shall procure that the recipient enters into a power of attorney in the form set out at Schedule 4 (*Power of Attorney*) in respect of those Ordinary Shares.

10. COMPLIANCE WITH THE DRAG, CO-SALE AND TAG RIGHTS

Each Party acknowledges that the Drag Rights, Co-Sale Rights and the Tag Rights may result in a transfer of Shares or other Relevant Securities held by it and agrees and approves the application of the Drag Rights, Co-Sale Rights and Tag Rights in accordance with their terms.

11. ADHERENCE TO THIS AGREEMENT

11.1 Provision of Deeds of Adherence

Notwithstanding the provisions of the Articles:

11.1.1 no Shareholder shall effect any transfer or disposal in respect of any Shares or other Relevant Securities to any person who is not a Party to this Agreement; and

11.1.2 the Company shall not issue any Shares or other Relevant Securities, to any person who is not a Party to this Agreement,

unless in either case, such person has first executed and delivered to the Company for itself and on behalf of the other Shareholders a Deed of Adherence.

11.2 Service of Transfer Notices

On each occasion when the Board is permitted to serve a Transfer Notice (as defined in and in accordance with the provisions of the Articles) the Board shall serve such a Transfer Notice as soon as reasonably practicable after being requested to do so by the Investors acting by Investor Majority Consent.

12. CONFIDENTIALITY

12.1 Confidentiality obligations

Each of the Parties hereto (other than the Company) undertakes to the Company that unless otherwise agreed to in writing by the Company, all Confidential Information disclosed to such Party (and its Permitted Transferees and any Preferred Director or Observer appointed by it) as well as the terms of this Agreement, the Investment Agreement and investment by the Series C Investors made pursuant to the Investment Agreement will:

12.1.1 be kept strictly confidential and not disclosed to any person by such Party (other than disclosure to another Party to this Agreement or disclosure specifically permitted herein);

12.1.2 be used solely for the purpose of evaluating, monitoring and managing such Party's interest in the Company or otherwise used in the conduct of the business and affairs of the Company;

12.1.3 be securely retained such that the Party receiving such information shall not part with the possession, custody or control of Confidential Information provided to it unless specifically permitted herein; and

12.1.4 be afforded a level of protection and security against unauthorised access not less than that level of protection and security which the Party receiving such information affords to its own equivalent confidential information.

12.2 Exclusions

The obligations set out in clause 12.1 shall not apply:

12.2.1 to any disclosures made by:

(a) any Party in the bona fide course of the Company's business activities, subject to entering into an appropriate non-disclosure agreement prior to doing so;

(b) a Party (other than an Investor) if the information disclosed relates to the Company or a member of the Company's Group and a Preferred Director has consented to its disclosure;

(c) an Investor (that is not an individual) to actual or prospective bona fide lenders to such Investor (or to any person referenced in clause 12.2.6 in respect of that Investor); or

(d) a Party to its professional advisers or to the professional advisers of a member of such Party's Group or, where the party is an Investor, to any person referenced in clause 12.2.6 in respect of that Investor;

12.2.2 to any information which at the time of disclosure or thereafter is generally available to or known by the public (other than as a result of its disclosure by the relevant Party to this Agreement (or any of its Permitted Transferees or any Preferred Director or Observer appointed by it) in breach of any obligation of confidentiality);

12.2.3 to any information which was or becomes available to the relevant Party to this Agreement on a non-confidential basis from a person other than the Company (or any of its directors, employees, agents, consultants, representatives or advisers) and who is not bound by an obligation of confidentiality in respect of such information;

12.2.4 to any information which the Company agrees in writing is not Confidential Information;

12.2.5 to the disclosure of information between the Preferred Directors and any Observer and the Investors to the extent reasonably necessary;

12.2.6 to the disclosure of information by the Investors to their management committees, general partners, limited partners, shareholders, professional advisors and any Permitted Transferee of such Investors, in each case provided that such recipient has agreed to receive and hold such Confidential Information subject to terms limiting the further disclosure and use of such information no less onerous than the terms set out in this clause 12; and

12.2.7 where information is disclosed in accordance with clause 12.3.

12.3 Compulsory disclosure

In the event that a Party to this Agreement (or any person acting on its behalf) becomes legally compelled to disclose any Confidential Information (by discovery, request for documents, subpoena, civil investigation, demand, interrogatory, deposition, order or similar process or otherwise pursuant to any applicable Law, rule or regulation (including the rules of any investment exchange or Authority regulating the issue or sale of securities to which the relevant party is subject)), the Company agrees that such Party to this Agreement (and, as relevant, its Permitted Transferees and any Preferred Director or Observer appointed by it) may do so without liability, but provided that such Party to this Agreement agrees, so far as is reasonably practicable to do so:

12.3.1 promptly to notify the Company prior to any such disclosure to the extent practicable; and

12.3.2 to co-operate with the Company (at the Company's expense provided any costs are reasonably and properly incurred) in any attempt it may make to limit the amount and extent of such disclosure or to obtain a protective order or other appropriate assurance that confidential treatment will be afforded to the Confidential Information.

12.4 Right to conduct activities

12.4.1 The Company acknowledges that Baillie Gifford & Co. and F-Prime each provides investment management and advisory services and/or is a private equity fund and, as such, neither F-Prime nor SMIT nor their respective Affiliates shall be restricted in any way from investing in any company or entity which may be deemed as competitive with the business of the Company or any Group Company.

12.4.2 Subject always to clause 12, the Company hereby agrees and acknowledges that its shareholders that are Institutional Investors (as defined in the Articles), together with their respective Affiliates, (collectively, the "**Fund Investors**", and each a "**Fund Investor**") are professional investment funds, and as such invest in numerous portfolio companies, some of which may be deemed competitive with the Company's business (as currently conducted or as currently proposed to be conducted). The Company hereby agrees that, to the extent permitted under applicable law, no Fund Investor shall be liable to the Company for any claim arising out of, or based upon, (i) the investment by such Fund Investor in any entity competitive with the Company, or (ii) actions taken by any partner, officer or other representative of such Fund Investor to assist any such competitive company, whether or not such action was taken as a member of the board of directors of such competitive company or otherwise, and whether or not such action has a detrimental effect on the Company; provided, however, that the foregoing shall not relieve (x) any of the Fund Investors from liability associated with the unauthorized disclosure of the Company's confidential information obtained pursuant to this Agreement, or (y) any director or officer of the Company from any liability associated with his or her fiduciary duties to the Company.

The Company acknowledges that the Fund Investors are in the business of venture capital investing and therefore review the business plans and related proprietary information of many enterprises, including enterprises which may have products or services which compete directly or indirectly with those of the Company. Nothing in this Agreement shall preclude, create an obligation or duty, or in any way restrict the Fund Investors from evaluating or purchasing securities, including publicly traded securities, of a particular enterprise, or investing or participating in any particular enterprise, whether or not such enterprise has products or services which compete with those of the Company. The Company acknowledges that the Fund Investors, their Affiliates, and any of their respective representatives currently may be invested in, may invest in or may consider investments in public and private companies some of which may compete either directly or indirectly with the Company, and that the execution of this Agreement, the terms hereof and the access to confidential information hereunder shall in no way be construed to prohibit or restrict the Fund Investors, their Affiliates, or any of their respective representatives from maintaining, making or considering such investments or from otherwise operating in the ordinary course of business. Further, the Company understands and acknowledges that the confidential information may be used by the Fund Investors, their Affiliates, or any of their respective representatives in connection with evaluating investment opportunities, trading securities in the public markets and participating in private investment transactions, but specifically excluding disclosing or otherwise providing confidential information (or any derivatives, extracts or summaries thereof) to anyone other than the Fund Investors, their Affiliates, or any of their respective representatives in violation of this Agreement.

12.5 The Company

The Company shall keep secret and confidential and not disclose or divulge to any third party or cause any person to become aware of any information regrinding the terms of this Agreement, the Investment Agreement and the investment made by the Series C Investors pursuant to the Investment Agreement, save where such disclosure is necessary or desirable in the bona fide course of the Company's business, or where such disclosure is made pursuant to any applicable Law, rule or regulation (including the rules of any investment exchange or Authority), or where the provisions of clauses 12.2.2 or 12.2.3 apply.

13. NO PARTNERSHIP

Nothing in this Agreement shall be deemed to constitute a partnership between the Parties hereto.

14. AGREEMENT PREVAILS

Save as expressly provided in this Agreement, in the case of any conflict between the terms of this Agreement and the provisions of the Articles the terms of this Agreement shall prevail as between the Parties. In such circumstances, the Parties shall procure that such modifications as are necessary are made to the Articles.

15. BINDING NATURE OF THIS AGREEMENT

Each Party hereto hereby warrants and undertakes to each other Party hereto that this Agreement has been duly executed by it and comprises a valid and legally binding obligation enforceable against it in accordance with the terms of this Agreement.

16. SEVERANCE

If any provision of this Agreement shall be held to be illegal, void, invalid or unenforceable under the Laws of any jurisdiction, the legality, validity and enforceability of the remainder of this Agreement in that jurisdiction shall not be affected, and the legality, validity and enforceability of the whole of this Agreement in any other jurisdiction shall not be affected.

17. COUNTERPARTS

This Agreement may be executed in any number of counterparts and by the Parties in separate counterparts, each of which when executed and delivered is an original and all of which together evidence one and the same agreement. Signatures provided by any photocopy and transmitted by facsimile or other electronic means will be deemed to be original signatures.

18. ASSIGNMENT

18.1.1 Save as provided in this clause 18, this Agreement may not be assigned, in whole or in part, by operation of Law or otherwise, and no Party may assign, or grant any Encumbrance or security interest over, any of its rights under this Agreement or any document referred to in it, without the prior written consent of the other Parties.

18.1.2 Each Shareholder may assign the benefit (but not the obligations) of this Agreement (including the Warranties) to any person to whom it may transfer any right or interest in Shares in accordance with the Articles.

18.1.3 On an assignee or transferee of any Shares or other Relevant Securities executing a Deed of Adherence and delivering the same to the Company for itself and on behalf of the other Shareholders, each Party hereto agrees that this Agreement shall enure for the benefit of such assignee or transferee and shall be enforceable by such assignee or transferee, to the extent any such rights were vested in its assignor or transferor pursuant to this Agreement, as if such assignee or transferee had been a party hereto and named herein as a Shareholder and, if the definition of “Investor” or “Series C Investor” applies to the relevant assignee or transferee, as if that assignee or transferee was named as an Investor or Series C Investor, as the case may be, herein.

18.2 Registration of new shareholders

The Parties hereto, other than the Company, undertake to each other that they shall, to the extent of their respective rights and the rights of their respective nominees from time to time, vote (or procure that their respective nominees vote) as Investors, Shareholders and/or as Directors of the Company, as the case may be, so as to procure that no person is registered as holder of any Shares (whether on transfer or transmission or by issue) in breach of the Articles or this Agreement.

19. TERMINATION

Save as set out herein, this Agreement shall terminate without liability on any party hereto immediately on the earliest of the completion of: (i) an IPO; (ii) a Sale; or (iii) completion of the liquidation of the Company, where, in each case, the applicable provisions in the Articles have been duly complied with.

20. MISCELLANEOUS

20.1 Entire agreement

20.1.1 This Agreement together with the Shareholders' Agreement and the Articles (together, the "**Transaction Agreements**") constitutes the whole agreement between the Parties relating to its subject matter and supersedes and extinguishes any prior drafts, agreements, and undertakings, whether in writing or oral, relating to such subject matter, except to the extent that the same are repeated in the Transaction Agreements.

20.1.2 Each Shareholder acknowledges that it has not been induced to enter into this Agreement by any representation, warranty, promise or assurance by the Company or any other person save for those contained in the Transaction Agreements.

20.2 Further assurance

Each Party shall (at their own expense) promptly execute and deliver, or cause to be executed and delivered, all such documents and instruments, and do all such things or cause to do all such things, as any other Party may from time to time reasonably require for the purpose of giving full effect to and the full benefit of the provisions of this Agreement.

20.3 Variation and waiver

20.3.1 Any variation of this Agreement is valid only if it is in writing and signed by the Company and Shareholders comprising an Investor Majority Consent, in which event such change shall be binding against all of the Parties hereto, provided that:

(a) if such change would impose any new obligations on a Party or increase any existing obligation, the prior written consent of the affected Party to such change shall be specifically required; and

(b) if such change would:

(i) alter or change the rights, preferences or privileges of the Series B Shares or Series C Shares in a manner that is different than the effect on the rights, preferences or privileges of the other Preferred Shares; or

(ii) reclassify, alter or amend any existing security that is junior to or on parity with the Series B Shares or Series C Shares, if such reclassification, alteration or amendment would render such other security senior to or on parity with the Series B Shares or Series C Shares; or

(iii) increase or decrease the authorised number of Series B Shares or Series C Shares, then prior written Series B Investor Majority Consent to such variation or alteration shall be required in respect of the Series B Shares and prior written consent of the holders of at least a majority of the Series C Shares shall be required in respect of the Series C Shares.

(c) if such change would:

(i) alter or change the rights, preferences or privileges of the Series B-2 Shares in a manner that is different than the effect on the rights, preferences or privileges of the Series B Shares; or

(ii) reclassify, alter or amend any existing security that is junior to or on parity with the Series B-2 Shares, if such reclassification, alteration or amendment would render such other security senior to or on parity with Series B Shares; or

(iii) increase or decrease the authorised number of Series B-2 Shares unless the same increase or decrease is also being made to the number of Series B Shares,

then prior written Series B-2 Investor Majority Consent to such variation or alteration shall be required.

20.3.2 Any waiver of any right, power, privilege or remedy under this Agreement is only effective if it is in writing and it applies only to the Party to whom the waiver is addressed and to the circumstances for which it is given and shall not prevent the Party who has given the waiver from subsequently relying on the provision it has waived.

20.3.3 A Party that waives a right, power, privilege or remedy in relation to one Party, or takes or fails to take any action against that Party, does not affect its rights, powers, privileges or remedies in relation to any other Party.

20.3.4 The failure to exercise or delay in exercising a right, power, privilege or remedy provided by this Agreement or by law does not impair or constitute a waiver of the right, power, privilege or remedy or an impairment of or a waiver of other rights or remedies. No single or partial exercise of a right, power, privilege or remedy provided by this Agreement or by Law shall prevent, preclude or impair the further exercise of the right, power, privilege or remedy or the exercise of another right, power, privilege or remedy.

20.3.5 The rights, powers, privileges and remedies contained in this Agreement are cumulative and not exclusive of rights or remedies provided by Law.

20.4 Investor Restrictions

The Parties acknowledge and agree that in the event of a Sale or IPO, each Investor shall not be required to give any warranties, indemnities or covenants other than warranties as to title to the Shares held by them and capacity to enter into legally binding documentation. For the avoidance of doubt there shall be no obligation on the Investors to give any non-solicitation or non-competition covenants in the event of a Sale.

20.5 Legal Representation

Each Party to this Agreement acknowledges that Cooley (UK) LLP ("**Cooley**"), the Company's Solicitors, has in the past performed and is or may now or in the future represent one or more Shareholders or their affiliates in matters unrelated to the transactions contemplated by this Agreement (the "**Financing**"), including representation of such Shareholders or their affiliates in matters of a similar nature to the Financing. The applicable rules of professional conduct require that Cooley inform the parties hereunder of this representation and obtain their consent. Cooley has served as outside general counsel to the Company and has negotiated the terms of the Financing solely on behalf of the Company. The Company and each Shareholder hereby (a) acknowledge that they have had an opportunity to ask for and have obtained information relevant to such representation, including disclosure of the reasonably foreseeable adverse consequences of such representation; (b) acknowledge that with respect to the Financing, Cooley has represented solely the Company, and not any Shareholder or any stockholder, director or employee of the Company or any Shareholder; and (c) gives its informed consent to Cooley's representation of the Company in the Financing.

21. COSTS

Each Party shall bear their own costs arising out of or in connection with the preparation, negotiation and implementation of this Agreement.

22. NOTICES

22.1 Manner in which to give notice

A notice or other communication under or in connection with this Agreement (a "**Notice**") shall be in writing and shall be delivered personally or sent by first class post (and air mail if overseas) or by fax or by email to the Party due to receive the Notice to the registered office address set out in:

22.1.1 Part A of Schedule 1 (*Details of the Company*) in the case of the Existing Investors;

22.1.2 Part B of Schedule 1 (*Details of the Company*) in the case of the Ordinary Shareholders;

22.1.3 Part C of Schedule 1 (*Details of the Company*) in the case of the Company; and

22.1.4 The Investment Agreement in the case of the Series C Investors,

or, in each case, to such fax number or email address that is supplied by the Party to the other Parties hereto for the purpose of giving Notice to the Party or to an alternative address, person, fax number or email address specified by that Party by not less than five (5) Business Days' written notice to the other Party received before the Notice was dispatched.

22.2 Deemed delivery of notice

Unless there is evidence that it was received earlier, a Notice is deemed given if:

22.2.1 delivered personally, when left at the address referred to in clause 22.1;

22.2.2 sent by mail, except air mail, two (2) Business Days after posting it;

22.2.3 sent by air mail, six (6) Business Days after posting it;

22.2.4 sent by fax, when confirmation of its transmission has been recorded by the sender's fax machine; or

22.2.5 sent by email, when the sender receives an email acknowledging receipt of the sender's email.

23. LAW AND JURISDICTION

23.1 English law

This Agreement and any disputes and/or claims arising out of or in connection with it or its subject matter or formation (including non-contractual disputes or claims) shall be governed by and construed in accordance with English law.

23.2 Jurisdiction

In relation to any legal action or proceedings arising out of or in connection with this Agreement (including any dispute relating to the existence, validity or termination of this Agreement or any contractual or non-contractual obligation) ("**Proceedings**"), each of the Parties irrevocably submits to the exclusive jurisdiction of the English courts and waives any objection to Proceedings in such courts on the grounds of venue or on the grounds that Proceedings have been brought in an inappropriate forum provided that an order or judgment of any court may be enforced in any court of competent jurisdiction.

23.3 Contracts (Rights of Third Parties) Act 1999

23.3.1 Except pursuant to clause 23.3.2, a person who is not a Party to this Agreement shall not have any right under the Contracts (Rights of Third Parties) Act 1999 to enforce any term of this Agreement.

23.3.2 The general partner of an Investor or the management company authorised from time to time to act on behalf of that Investor or another person or persons nominated by that Investor, shall be entitled to enforce all of that Investor's rights and benefits under this Agreement at all times as if it or they were a party to this Agreement.

24. F-PRIME WAIVER

24.1 In the event that F-Prime and F-Prime A retain Shares which in aggregate exceed twenty five per cent (25%) (the "**Threshold**") of the Company's issued voting share capital at the relevant time, each of F-Prime and F-Prime A irrevocably waive any right to vote (whether at a meeting, pursuant to a written consent or otherwise) in respect to the portion of such Shares which exceed the Threshold in respect of the following:

24.1.1 any matter relating to clause 5.3 of this Agreement;

24.1.2 any matter relating to Schedule 3 Part A, paragraph 6 of this Agreement;

24.1.3 pursuant to clause 20.3, to amend this Agreement with respect to clause 5.3 or Schedule 3, Part A, paragraph 6 of this Agreement; and

24.1.4 any future provision of this Agreement or any other governing document of the Company that grants new rights to the holders of Shares with respect to matters relating to membership on and /or the size of the Board.

24.2 Clause 24.1 is irrevocable and may not be waived or amended. Clause 24.1 shall survive termination of this Agreement.

24.3 Each of F-Prime and F-Prime A agree and confirm that the provisions of 24.1 shall apply on a pro rata basis as between F-Prime and F-Prime A at the relevant time according to the number of Shares held by each of them and their respective Affiliates to whom any Shares may be transferred after the date of this Agreement.

24.4 F-Prime and F-Prime A hereby notify the Company that they will not seek to exercise their right to appoint the second of their two Special Directors unless the total number of Directors changes such that having a second Special Director would result in the total number of Special Directors representing 25% or less of the total number of Directors. For as long as F-Prime and F-Prime A do not exercise their right to appoint two Special Directors because having a second Special Director would result in the total number of Special Directors representing more than 25% of the total number of Directors, F-Prime will have the right to appoint one additional Observer. This clause 24.4 is irrevocable and may not be waived or amended.

SCHEDULE 1: DETAILS OF THE COMPANY

Part A: The Existing Investors

Name	Address
4B-P01 Ltd.	Georgiou Katsounotou 6, 3036, Limassol, Cyprus
Agent Capital Fund I LP	204 Drakes Drum Drive, Bryn Mawr, PA 19010, United States
CHI EF II LP	599 Lexington Avenue, New York City, NY 10022, United States
Cowen Healthcare Investments II LP	599 Lexington Avenue, New York City, NY 10022, United States
F-Prime Capital Partners Healthcare Fund IV LP	One Main Street, 13th Floor, Cambridge, MA 02142, United States
F-Prime Capital Partners Healthcare Fund IV-A LP	One Main Street, 13th Floor, Cambridge, MA 02142, United States
Glaxo Group Limited	980 Great West Road, Brentford, Middlesex TW8 9GS
Highfly Global Investments Limited	Vistra Corporate Services Centre, Wickhams Cay II, Road Town, Tortola, VG1110 British Virgin Islands
Juda Capital Inc.	Start Chambers, Wickham's Cay II, PO Box 2221, Road Town, Tortola, British Virgin Islands
Pav Investments Pte. Ltd.	3 Fraser Street, #10-23, Duo Tower, Singapore 189352
RTW Innovation Master Fund, Ltd.	250 West 55th Street, 16th Floor Suite A, New York City, NY 10019, United States
RTW Master Fund, Ltd.	250 West 55th Street, 16th Floor Suite A, New York City, NY 10019, United States
Scottish Mortgage Investment Trust plc (acting through its agent, Baillie Gifford & Co)	Calton Square, 1 Greenside Row, Edinburgh EH1 3AN
TLS Beta Pte Ltd.	60B Orchard Road #06-18 Tower 2, The Atrium@Orchard, Singapore 23889
UCL Technology Fund LP	1 Kings Arms Yard, London EC2R 7AF
Unique Diamond Investments Limited	Vistra Corporate Services Centre, Wickhams Cay II, Road Town, Tortola, VG1110 British Virgin Islands

Adam Seymour	41a West Street, Oundle, Peterborough
Adrien Lemoine	Flat 7, 4 Acton Street, London WC1X 9NA
Andrea Spezzi	Angel Southside, Flat 9, 1 Owen Street, London EC1V 7JW
Mark Rothera	42 Cambridge Street, London SW17 4QH
Tom Abbey	The Rectory, Croft Lane, Newton Kyme LS24 9LR

Part B: The Ordinary Shareholders

Name	Address
Central Manchester University Hospitals NHS Foundation Trust	Central Manchester University Hospitals NHS Foundation Trust
Children’s Medical Center Corporation (aka Boston Children’s Hospital)	300 Longwood Avenue, Boston, MA 02115, United States
F-Prime Capital Partners Healthcare Fund IV LP	One Main Street, 13th Floor, Cambridge, MA 02142, United States
F-Prime Capital Partners Healthcare Fund IV-A LP	One Main Street, 13th Floor, Cambridge, MA 02142, United States
Généthon	1 bis, rue de l’internationale, 91002 Evry, Cedex, France
Oxford BioMedica (UK) Limited	Windrush Court, Transport Way, Oxford OX4 6LT
The University of Manchester	c/o UMI3 Ltd., CTF, 46 Grafton Street, Manchester M13 9NT
UCL Business plc	The Network Building, 97 Tottenham Court Road, London W1T 4TP
Adrian Thrasher	Blaysworth Manor, Colmworth, Bedfordshire MK44 2LD
Andrea Spezzi	Angel Southside, Flat 9, 1 Owen Street, London EC1V 7JW
Brian Bigger	104 Manchester Road, Manchester M27 5FQ
Hubert Gasper	5 Ardburg Road, London SE24 9JL
Kristopher Wood	333 1st Street, Unit 1501, San Francisco, CA 94105, United States
Nicolas Koebel	5 Warwick House, Windsor Way, London W14 0UQ
Robert Wynn	c/o Central Manchester University Hospitals NHS Foundation Trust, Trust Headquarters, Cobbett House, Manchester Royal Infirmary, Oxford Road, Manchester, M13 9WL
Simon Jones	127 Blackburn Road. Haslingdon, Lancashire BB4 5HN
Sue Wraith	Flat 1, 26 Sandwich Road, Ellesmere Park, Eccles M30 9DX

Part C: The Series C Investors

Name	Address
Deerfield Special Situations Fund, L.P.	c/o Deerfield Management Company, Attn: General Counsel, 780 Third Avenue, 37th Floor, New York, NY 10017, United States
Deerfield Private Design Fund III, L.P.	c/o Deerfield Management Company, Attn: General Counsel, 780 Third Avenue, 37th Floor, New York, NY 10017, United States
Deerfield Private Design Fund IV, L.P.	c/o Deerfield Management Company, Attn: General Counsel, 780 Third Avenue, 37th Floor, New York, NY 10017, United States
RA Capital Healthcare Fund, L.P.	20 Park Plaza, Suite 1200, Boston, MA 02116, United States
Baker Brothers Life Sciences, L.P.	860 Washington Street, 3rd Floor, New York, NY 10014, United States
667, L.P.	860 Washington Street, 3rd Floor, New York, NY 10014, United States
Scottish Mortgage Investment Trust plc	Calton Square, 1 Greenside Row, Edinburgh EH1 3AN
TLS Beta Pte Ltd.	60B Orchard Road #06-18 Tower 2, The Atrium@Orchard, Singapore 238891
Cowen Healthcare Investments II LP	599 Lexington Avenue, New York, NY 10022, United States
CHI EF II LP	599 Lexington Avenue, New York, NY 10022, United States
Agent Capital Fund I LP	204 Drakes Drum Drive, Bryn Mawr, PA 19010, United States
Pav Investments Pte. Ltd.	3 Fraser Street, #10-23, Duo Tower, Singapore 189352
RTW Innovation Master Fund, Ltd.	250 West 55th Street, 16th Floor Suite A, New York City, NY 10019, United States

RTW Master Fund, Ltd.	250 West 55th Street, 16th Floor Suite A, New York City, NY 10019, United States
Venrock Healthcare Capital Partners III, L.P.	7 Bryant Park, 23rd Floor, New York, NY 10018, United States
VHCP Co-Investment Holdings III, LLC	7 Bryant Park, 23rd Floor, New York, NY 10018, United States
Foresite Capital Fund IV, L.P.	600 Montgomery St., Suite 4500, San Francisco, CA 94111, United States
Perceptive Life Sciences Master Fund LTD	51 Astor Place 10th Floor, New York, NY 10003, United States
Adage Capital Partners, LP	200 Clarendon St, 52nd Floor, Boston, MA 02116, United States
Cormorant Private Healthcare Fund I, LP	200 Clarendon St, 52nd Floor, Boston, MA 02116, United States
Cormorant Global Healthcare Master Fund, LP	200 Clarendon St, 52nd Floor, Boston, MA 02116, United States
Meridian Small Cap Growth Fund	100 Fillmore Street, Suite 325, Denver, CO 80206, United States
ArrowMark Life Science Fund, LP	100 Fillmore Street, Suite 325, Denver, CO 80206, United States
Sphera Global Healthcare Master Fund	C/o Sphera Global Healthcare Management, 21 Ha'arbaa street, 4th floor, Tel Aviv, Israel
NR 2 SP, a Segregated Portfolio of North Rock SPC	Maples Corporate Services Limited, Ugland House, P.O. Box 309, Grand Cayman KY1-1104, Cayman Islands
Ghost Tree Master Fund, LP	Maples Corporate Services Limited, Ugland House, P.O. Box 309, Grand Cayman KY1-1104, Cayman Islands
Medison Ventures Ltd.	Hashiloach 10, Petach Tikva, 4917002, Israel
Driehaus Event Driven Fund, A Series of Driehaus Mutual Funds	Driehaus Event Driven Fund, 25 East Erie Street, Chicago, IL 60611, United States

SCHEDULE 2: MATTERS REQUIRING CONSENT

Part A: Investor Consents

Investor Majority Consent shall be required for any action which:

4. creates or reclassifies any new or existing class or series of shares having rights, preferences or privileges senior to or on a parity with the Preferred Shares;

5. increases or decreases the authorised number of Ordinary Shares or Preferred Shares or the number of shares reserved for issuance under the Equity Award Pool, unless (in the case of Shares reserved for issuance under the Equity Award Pool) approved by the Board;

6. results in any material amendment to or adoption of new share option scheme rules relating to the Equity Award Pool, unless approved by the Board;

7. results in any public offering (other than a Qualified Listing, which, for the avoidance of doubt, shall not require Investor Majority Consent), merger, licence or sale of all or substantially all assets, intellectual property or other corporate reorganisation or acquisition of the Company;

8. results in the redemption or repurchase of any Ordinary Shares or Preferred Shares (other than a repurchase of Shares held by a Leaver pursuant to the Articles);

9. increases or decreases the authorised size of the Board (unless approved by the Board);

10. results in the payment or declaration of any dividend on any Ordinary Shares or Preferred Shares, or any other distribution (as defined under sections 209, 418 and 419 of ICTA);

11. results in any liquidation or dissolution of the Company;

12. alters, varies or otherwise changes the rights attaching to the Preferred Shares;

13. adopts new, or amends the then current, Articles or waives any provision of the Articles in a manner adverse to the holders of Preferred Shares;

14. results in the sale, transfer, assignment, license, pledge or grant of any Encumbrance over any of the Company's material Intellectual Property Rights;

15. results in the factoring of any of its debts, borrowing monies, accepting credit (other than normal trade credit) or otherwise incurring indebtedness in excess of £500,000 in any one transaction or series of related transactions;

16. results in any capital expenditures in excess of £750,000 or series of capital expenditures in excess of £2,000,000 for any fiscal year (calculated on a cumulative and aggregated basis during such fiscal year) that are not otherwise contemplated by the Company's then applicable business plan, unless approved by the Board;

17. results in the incorporation of subsidiary undertaking, the entry into of a partnership or joint venture;

18. requires any material change in the Company's lines of business or business model;

19. other than where expressly contemplated by this Agreement, the entry into or variation of any transaction or arrangement with, or for the benefit of any of its directors or shareholders or any other person who is a "connected person" with any of its directors or shareholders (save where such transaction or arrangement has a value of less than £400,000);

20. results in the allotment and/or issuance of any Shares or other securities, or grant or entry into any arrangement (including any warrant, option or other right) conferring on any person any right (whether or not conditional) to acquire any interest in any Shares or other securities, except as set out in clause 9.2;

21. results in the acquisition or disposal by the Company of any securities issued by any person, or any business or undertaking of any person or the entry into or withdrawal from any partnership, consortium, joint venture or any other unincorporated association;

22. results in the capitalisation of any of the Company's reserves or application of any amount thereof for any purpose;

23. any material change to jurisdiction in which the Business is managed and controlled; and

24. the entry into any transaction or the making of any payment other than on an arm's length basis for the benefit of the Company.

Part B: Board Consents

In addition to any Investor Majority Consent required, the Company shall require the consent of the Board acting by simple majority for:

1. the making of any loan or advance to any person or entity, or acquisition of any stock or other securities of any entity unless it is wholly-owned by the Company;

2. incorporation of any subsidiary undertaking;

3. the guarantee, directly or indirectly, of any indebtedness or obligations except for trade accounts of a subsidiary arising in the ordinary course of business;

4. the factoring of any of its debts, borrowing monies or accepting credit (other than normal trade credit);

5. the entry into of any business arrangement that exceeds £750,000;

6. the establishment of any new branch, agency, trading establishment or business or closing of any such branch, agency, trading establishment or business;

7. any act or thing outside the ordinary course of the business carried on by it;

8. the execution of any document, undertaking of any action, or approval of any matter which is material to the business, assets and/or affairs of the Company;

9. any change to:

    (i) its lawyers;

    (ii) its auditors;

    (iii) its bankers or the terms of the mandate given to such bankers;

    (iv) its accounting reference date or accounting policies (other than as recommended by the Company's auditors); or

    (v) any budget approved by the Investors;

10. any change to any budget approved by the Investors;

11. the engagement of a financial advisor in connection with a potential, proposed or actual public offering or Sale;

12. the engagement of any employee or consultant on terms that either his contract cannot be terminated by three (3) months' notice or less or his emoluments and/or commissions or bonuses are or are likely to be at the rate of £175,000 per annum or more or the increase of the emoluments and/or commissions or bonuses of any employee or consultant to more than £80,000 per annum or the variation of the terms of employment of any employee earning (or so that after such variation he will, or is likely to earn) more than £175,000 per annum;

13. the variation or making of any binding decisions on the terms of employment and service of any director or company secretary of the Company earning (or after such variation will or is likely to earn) more than £175,000 per annum, the increase or variation of the salary or other benefits of any such director or company secretary, or the appointment or dismissal of any such director or company secretary;

14. the mortgage or charge or the creation of or the suffering to subsist any mortgage or fixed or floating charge, lien (other than a lien arising by operation of law) or other Encumbrance over the whole or any part of its undertaking, property or assets;

15. the making of any loan or advance or the giving of any credit (other than in the ordinary course of business) to any person or the acquisition of any loan capital of any corporate body (wherever incorporated);

16. save in connection with the appointment of any Special Director, the appointment of any person as a CEO or a Director;

17. the creation of any committee of the Board, or subcommittees thereof, and delegation of matters to such committees and subcommittees;

18. conducting any litigation material to the Company, save for the collection of debts arising in the ordinary course of the business carried on by the Company or any application for an interim injunction or other application or action (including interim defence) which is urgently required in the best interests of the Company in circumstances in which it is not reasonably practicable to obtain prior consent as aforesaid;

19. the taking, agreement to take or disposal of any leasehold interest in or licence over any real property; and

20. the making of any gifts or charitable donations provided that these are not or could not reasonably be construed or otherwise interpreted to be in breach of any applicable Laws. No gifts or charitable donations shall be permitted to be made by the Company in any other circumstances.

SCHEDULE 3: DEED OF ADHERENCE

THIS DEED is dated [•] 20[•]

WHEREAS:

A. This Deed is entered into in compliance with and is supplemental to the Investment and Shareholders' Agreement dated 29 March 2017 as amended and restated on **[•]** 2018 and made between **[•]** (the "**Investment and Shareholders' Agreement**"); and

B. [***Name***] of [***Address***] [a company incorporated in England and Wales (registered [•])] (the "**New Shareholder**") has agreed to execute this Deed in accordance with clause [•] of the Investment and Shareholders' Agreement, pursuant to which it shall adhere to and be bound by the Investment and Shareholders' Agreement.

IT IS AGREED as follows:

1. Terms and expressions defined in the Investment and Shareholders' Agreement shall have the same meanings in this Deed unless the context otherwise expressly requires. The "**Effective Date**" means the date of this Deed.

2. The New Shareholder acknowledges, undertakes and covenants with each of the parties to the Investment and Shareholders' Agreement that with effect from Effective Date the New Shareholder shall be bound by and will observe and perform all the terms and conditions and obligations of and included in the Investment and Shareholders' Agreement as if the New Shareholder had been a Party and was named in the Investment and Shareholders' Agreement as an Investor or Shareholder, as the case may be.

3. The provisions of this Deed are made for the benefit of and shall be enforceable by each of the parties to the Investment and Shareholders' Agreement and any other person or persons who may after the date of the Investment and Shareholders' Agreement (and whether or not prior to the Effective Date) assume any rights or obligations under the Investment and Shareholders' Agreement and be permitted to do so by the terms thereof and this Deed shall, subject to clause [•] of the Investment and Shareholders' Agreement, be irrevocable without the written consent of the Company.

4. The Investment and Shareholders' Agreement shall enure for the benefit of the New Shareholder and shall be enforceable by the New Shareholder, to the extent any such rights are vested in the New Shareholder pursuant to the Investment and Shareholders' Agreement, as if it had been a Party thereto.

5. This Deed shall be governed by and construed in accordance with the laws of England.

6. None of the Investors:

   (a) make any representation or warranty or assume any responsibility with respect to the legality, validity, effectiveness adequacy or enforceability of the Investment and Shareholders' Agreement (or any agreement entered into pursuant thereof); or

   (b) make any representation or warranty or assume any responsibility with respect to the content of any information regarding the Company or any Group Company or otherwise relating to the [acquisition/subscription] of Shares; or

(c) assume any responsibility for the financial condition of the Company or any Group Company or any other party to the Investment and Shareholders' Agreement or any other document or for the performance and observance by the Company or any other party to the Investment and Shareholders' Agreement or any other document (save as may be expressly provided therein);

and any and all conditions and warranties, whether express or implied by law or otherwise, are excluded.

IN WITNESS WHEREOF this Deed has been executed and delivered as a deed on the date first before written.

EXECUTED and DELIVERED	)
as a **DEED** by	)
[***New Shareholder***]	)
Acknowledged and received by	)
ORCHARD THERAPEUTICS LIMITED	)

SCHEDULE 4: POWER OF ATTORNEY

To: The Directors
Orchard Therapeutics Limited (the "**Company**")
108 Cannon Street
London EC4N 6EU

[Date]

Dear Sirs

Deed of Power of Attorney

1. I refer to the [•] ordinary shares of £0.00001 each in the Company held by me and to all further shares in the capital of the Company held by me on or after the date of this deed (collectively, the "**Shares**").

2. I hereby irrevocably appoint any director from time to time of the Company as my attorney and agent (the "**Attorney**") with full power and authority in my name or otherwise, and on my behalf to do and perform all acts and things and to approve, execute or sign and deliver in my name all deeds, documents, resolutions, consents, forms or agreements which the Attorney in his absolute discretion considers necessary or desirable in connection with:

2.1 the entering into of an election under section 431 of the Income Tax Earnings and Pension Act 2003 election (a "**section 431 election**") or under section 83(b) of the United States Internal Revenue Code (a "**section 83(b) election**") in respect of any Shares;

2.2 the sale of all or any of my Shares as part of a proposed sale of more than 50% of the issued share capital of the Company;

2.3 any admission of shares in the capital of the Company or securities representing such shares (including without limitation depositary interests, American depositary receipts, American depositary shares and/or other instruments) to the Nasdaq National Stock Market of the NASDAQ OMX Group Inc., to the New York Stock Exchange or to the Official List of the UK Listing Authority and to trading on the Main Market of the London Stock Exchange plc. and such admission becoming effective, or the grant of permission for any shares in the capital of the Company or securities representing such shares to be dealt with on any recognised investment exchange (as defined in section 285 Financial Services and Markets Act 2000) or any other public securities market, and such permission becoming effective; or

2.4 any other reorganisation of the Company or any of its parent or subsidiary undertakings which the Attorney considers in his sole discretion should involve the transfer, sale, re-designation, consolidation or cancellation of the Shares,

(2.2, 2.3 and 2.4 together with all matters ancillary to such a transaction (an "**Exit**"), where the holders of a majority of the issued share capital of the Company have agreed to such proposed Exit).

3. Without limiting the generality of paragraph 2 above, the Attorney shall have power:

3.1 to appoint any person(s) as their attorney to exercise any one or more of the powers given to the Attorney by me under this deed;

3.2 to give any warranties in respect of my Shares;

3.3 to agree the form and content of, negotiate, vary or approve, and execute deliver and sign in my name or otherwise and on my behalf any document or deed relating to any Exit, including:

3.3.1 a share purchase agreement, share exchange agreement, reorganisation agreement or any other agreement governing or otherwise relating to the sale and/or transfer of my Shares;

3.3.2 any other agreements, consents, resolutions, deeds or documents whatsoever which may have to be executed by me in connection with the Exit or any other arrangements to be made in connection with the Exit (including any arrangement regarding vesting or other restrictions prior to, at the time of or after the Exit in relation to my Shares);

3.4 in relation to any shares in the Company registered in my name or in respect of which I am otherwise able to procure such action:

3.4.1 to consent on my behalf to the holding of any general meeting or class meeting of the Company at short notice and complete and return any proxy cards;

3.4.2 to receive notice of, attend and vote on my behalf in favour of any resolution proposed at any general meeting or class meeting, and all or any adjournments of such meetings of the Company or to receive and sign any written resolution of the Company; and

3.4.3 to deal with and give directions as to any moneys, securities, benefits, documents, notices or other communications (in whatever form) arising by right of the Shares or received in connection with the Shares from the Company or any other person,

in each case in which the Attorney in their absolute discretion considers necessary or desirable.

4. I undertake that, where any proposed Exit is in the form of a reorganisation as contemplated by paragraph 2.4 above, I will execute a deed on the same terms as this deed in respect of any shares or other securities issued to me in the capital of any new company to which my shareholding is transferred.

5. The authority given by me shall be by way of security and shall be irrevocable in accordance with section 4 of the Powers of Attorney Act 1971.

6. The Attorney is authorised to deliver on my behalf at the appropriate time to the relevant party all deeds and other documents signed or executed by him on my behalf.

7. I undertake to:

7.1 ratify and confirm anything that the Attorney does or lawfully causes to be done in good faith in my name or on my behalf under the powers contained in this deed;

7.2 to indemnify the Attorney on demand against all liabilities, losses, claims, costs, and expenses which the Attorney may suffer and incur arising from or in connection with anything done or omitted to be done in good faith under this authority (including any cost incurred in enforcing this indemnity);

7.3 to act promptly in accordance with the Attorney's instructions in relation to any rights exercisable or anything received by me in my capacity as registered holder of the Shares; and

7.4 not to exercise any rights attaching to the Shares or exercisable in my capacity as registered holder of the Shares without the Attorney's prior written consent

8. In any case where the Company or any subsidiary or other person is obliged to account for Employee Taxation as a result of or in respect of the following:

8.1 the acquisition of the Shares; or

8.2 the entering into of a section 431 election or a section 83(b) election in respect of the Shares; or

8.3 any actual or deemed action, event or thing done following the acquisition of Shares which gives rise to a liability to Employee Taxation in respect of the Shares including without limitation any Exit, any element of a reorganisation or a reconstruction or anything giving rise to a charge to Employee Taxation pursuant to any section of Income Tax (Earnings and Pensions) Act 2003 (or equivalent legislation), or

8.4 any failure by me to reimburse the Company (or any subsidiary or other person) for any amount of Employee Taxation within any particular time frame regardless of whether due amount has been demanded or not,

9. I agree that such company or person may recover the Employee Taxation from me in such manner as the Company shall think fit and (without limitation to the foregoing) that such company or person may, to the extent permitted by law, recover the Employee Taxation via deductions from future payments (including but not limited to salary or bonuses) and that, to the extent that such deductions or proceeds are insufficient to cover the Employee Taxation, I shall pay to such company or person the balance within 5 working days following receipt of a demand in writing.

10. For the purposes of this paragraph 8 "Employee Taxation" means the amount for which any Group Company becomes liable to account to HM Revenue & Customs (or equivalent authority) under Pay As You Earn in respect of income tax and primary class 1 (employees') national insurance contributions (or equivalent charges outside of the UK) together with any corresponding amount of interest or penalties.

11. This deed (and any dispute, claim or matter of whatever nature arising out of or in any way relating to this deed or its formation) shall be governed by and construed in accordance with the law of England and Wales. The Attorney and I each irrevocably submit to the exclusive jurisdiction of the courts of England and Wales over any dispute, claim or matter of whatever nature arising out of or in any way relating to this deed or its formation.

IN WITNESS WHEREOF this power of attorney has been EXECUTED as a deed and DELIVERED)

By **[ ]**)

in the presence of:

Witness's

Signature _____

Print Name _____

Address _____

_____

___

Occupation _____

SCHEDULE 5: REGISTRATION RIGHTS

Applicability of Rights:

The Investors shall be entitled to the following rights and shall be subject to the following restrictions with respect to any potential public offering of the Company's Shares in the United States. Unless waived by Investor Majority Consent, in the event that the Company undertakes a public offering of its Shares outside of the United States in a jurisdiction where registration rights are issued in connection with a public offering, the Company shall apply this Schedule 5 *mutatis mutandis* to such public offering, subject always to applicable law.

1. **Definitions**

For the purposes of this Schedule 5:

1.1 "**Applicable Definitive Documents**" means this Agreement, together with any ancillary documents or agreements required to give effect to the transactions contemplated hereby and thereby.

1.2 "**Exchange Act**" means the United States Securities Exchange Act of 1934, as amended, or any similar successor federal statute, and the rules and regulations of the SEC thereunder, all as the same shall be in effect at the time;

1.3 "**Excluded Registration**" means (i) a registration relating to the sale or grant of securities to employees of the Company or a subsidiary pursuant to a stock option, stock purchase, equity incentive or similar plan; (ii) a registration relating to an SEC Rule 145 transaction; (iii) a registration on any form that does not include substantially the same information as would be required to be included in a registration statement covering the sale of the Registrable Securities; or (iv) a registration in which the only Ordinary Shares being registered are Ordinary Shares issuable upon conversion of debt securities that are also being registered.

1.4 "**Form F-1**" means such form under the Securities Act as in effect on the date hereof or any successor registration form under the Securities Act subsequently adopted by the SEC.

1.5 "**Form F-3**" means such respective form under the Securities Act as is in effect on the date hereof or any successor registration form under the Securities Act subsequently adopted by the SEC which permits inclusion or incorporation of substantial information by reference to other documents filed by the Company with the SEC;

1.6 "**Form S-1**" means such form under the Securities Act as in effect on the date hereof or any successor registration form under the Securities Act subsequently adopted by the SEC.

1.7 "**Form S-3**" means such form under the Securities Act as in effect on the date hereof or any successor or similar registration form under the Securities Act subsequently adopted by the SEC which permits inclusion or incorporation of substantial information by reference to other documents filed by the Company with the SEC;

1.8 "**Holder**" means, for purposes of this Schedule 5, any person owning Registrable Securities or any permitted assignee of record of such Registrable Securities to whom rights under this Schedule 5 have been duly assigned in accordance with this Agreement;

1.9 "**IPO**" means the Company's first underwritten public offering of its Ordinary Shares under the Securities Act.

1.10 "**Registration**", "**register**", "**registered**" or "**registration**" refer to a registration effected by preparing and filing a registration statement which is in a form which complies with, and is declared effective by the SEC in accordance with, the Securities Act;

1.11 "**Registrable Securities**" means: (i) the Series A Shares; (ii) the Series B Shares; (iii) the Series B-2 Shares; (iv) the Series C Shares; (v) any Ordinary Shares issued on conversion of Series A Shares, Series B Shares, Series B-2 Shares or Series C Shares; and (vi) the Ordinary Shares. Notwithstanding the foregoing, "**Registrable Securities**" shall exclude any Registrable Securities sold by a person in a transaction in which rights under this Schedule 5 are not assigned in accordance with this Agreement, and any Registrable Securities which are sold in a registered public offering under the Securities Act or analogous statute of another jurisdiction, or sold pursuant to Rule 144 promulgated under the Securities Act or analogous rule of another jurisdiction;

1.12 "**Registrable Securities Then Outstanding**" means the number of Ordinary Shares that are Registrable Securities and are then issued and outstanding or issuable upon conversion of the Preferred Shares then issued and outstanding;

1.13 "**Registration Expenses**" means all expenses incurred by the Company in complying with paragraphs 2, 3 and 4 hereof, including, without limitation, all registration and filing fees, printing expenses, Financial Industry Regulatory Authority fees, fees and disbursements of counsel for the Company, reasonable fees and disbursements of counsel for the Holders (not to exceed US$100,000 per registration), Blue Sky fees and expenses and the expense of any special audits incident to or required by any such registration (but excluding the compensation of regular employees of the Company which shall be paid in any event by the Company);

1.14 "**SEC**" means the U.S. Securities and Exchange Commission;

1.15 "**SEC Rule 144**" means Rule 144 promulgated under the SEC by the Securities Act;

1.16 "**SEC Rule 145**" means Rule 145 promulgated under the SEC by the Securities Act;

1.17 "**Securities Act**" means the United States Securities Act of 1933, as amended, or any similar successor federal statute, and the rules and regulations of the SEC thereunder, all as the same shall be in effect at the time; and

1.18 "**Selling Expenses**" means all underwriting discounts, selling commissions and stock transfer taxes applicable to the sale of Registrable Securities pursuant to paragraphs 2, 3 and 4 hereof, and fees and disbursements of counsel for any Holder, except for the fees and disbursements of counsel for the Holders selling Registrable Securities borne and paid by the Company as provided in Section 5.1 of this Schedule 5.

2. **Demand Registration**

2.1 Request by Holders. Subject to the conditions of this paragraph 2.1, if the Company shall receive at any time after the earlier of: (i) five (5) years after the date of this Agreement; or (ii) one hundred eighty (180) days following its IPO, a written request from the Holders of at least a majority or more of the Registrable Securities then outstanding that the Company shall file a registration statement covering the registration of all or some of the Registrable Securities (a "**Demand Notice**") in accordance with this paragraph 2.1, then the Company shall, as soon as practicable, and in any event within sixty (60) days after the date such request is given, effect such a registration statement. Within ten (10) business days of the receipt of a Demand Notice, the Company shall give written notice of such proposed registration to all Holders (a "**Request Notice**") and shall offer to include in such proposed registration any Registrable Securities requested to be included in such proposed registration by such Holders who respond in writing to the Company's notice within thirty (30) days after delivery of such

notice (which response shall specify the number of Registrable Securities proposed to be included in such registration). The Company shall use its commercially reasonable efforts to effect, as soon as practicable, but in any event within sixty (60) days from the date of such request, such registration on an appropriate form under the Securities Act of the Registrable Securities which the Company has been so requested to register; *provided*, *however*, that the Company shall not be obligated to effect any registration under the Securities Act except in accordance with the following provisions:

(A) The Company shall not be obligated to effect more than two (2) such demand registrations pursuant to this paragraph 2; and

(B) The Company shall not be obligated to effect, or to take any action to effect, any registration pursuant to Subsection 2.1 on Form S-1 or Form F-1 during the period that is sixty (60) days before the Company's good faith estimate of the date of filing of, and ending on a date that is one hundred eighty (180) days after the effective date of, a Company-initiated registration; *provided*, that the Company is actively employing in good faith commercially reasonable efforts to cause such registration statement to become effective; *provided*, *further*, that if the Company does not effect such registration statement, the Company shall effect the registration pursuant to Subsection 2.1 on Form S-1 on the sixty-first (61st) day after its notice to the Holders describing the delay in this subparagraph B of this paragraph 2.1.

2.2 Underwriting. If the Holders initiating the registration request under this paragraph 2 (the "**Initiating Holders**") intend to distribute the Registrable Securities covered by their request by means of an underwriting, then they shall so advise the Company as a part of their Demand Notice and the Company shall include such information in the Request Notice. In such event, the right of any Holder to include its Registrable Securities in such registration shall be conditioned upon such Holder's participation in such underwriting and the inclusion of such Holder's Registrable Securities in the underwriting to the extent provided herein. All Holders proposing to distribute their securities through such underwriting shall enter into an underwriting agreement in customary form with the managing underwriter or underwriters selected for such underwriting by the Holders of a majority of the Registrable Securities being registered and reasonably acceptable to the Company. Notwithstanding any other provision of this paragraph 2, if the underwriter(s) advise(s) the Company in writing that marketing factors require a limitation of the number of securities to be underwritten, then the Company shall so advise all Holders of Registrable Securities which would otherwise be registered and underwritten pursuant hereto, and the number of Registrable Securities that may be included in the underwriting shall be reduced as required by the underwriter(s) and allocated among the Holders of Registrable Securities on a *pro rata* basis according to the number of Registrable Securities Then Outstanding held by each Holder requesting registration (including the Initiating Holders); *provided*, *however*, that the number of shares of Registrable Securities to be included in such underwriting and registration shall not be reduced unless all other securities are first entirely excluded from the underwriting and registration including, without limitation, all shares that are not Registrable Securities and are held by any other person, including, without limitation, any person who is an employee, officer or director of the Company or any subsidiary of the Company. If any Holder disapproves of the terms of any such underwriting, such Holder may elect to withdraw therefrom by written notice to the Company and the underwriter(s), delivered at least ten (10) business days prior to the effective date of the registration statement. Any Registrable Securities excluded or withdrawn from such underwriting shall be excluded and withdrawn from the registration. For purposes of the provision in this Subsection 2.3 concerning apportionment, for any selling Holder that is a partnership, limited liability company, or corporation, the partners, members, retired partners, retired members, stockholders, and Affiliates of such Holder, or the estates and family members of any such partners, retired partners, members, and retired members and any trusts for the benefit of any of the foregoing persons, shall be deemed to be a single "selling Holder," and any pro rata reduction with respect to such "selling Holder" shall be based upon the aggregate number of Registrable Securities owned by all persons included in such "selling Holder," as defined in this sentence.

2.3 Deferral. Notwithstanding the foregoing, if the Company shall furnish to Holders requesting registration pursuant to this paragraph 2, a certificate signed by the President or Chief Executive Officer of the Company stating that in the good faith judgment of the Board, it would be materially detrimental to the Company and its shareholders for such registration statement to be filed because such action would (i) materially interfere with a significant acquisition, corporate reorganization, or other similar transaction involving the Company; (ii) require premature disclosure of material information that the Company has a bona fide business purpose for preserving as confidential; or (iii) render the Company unable to comply with requirements under the Securities Act or Exchange Act, then the Company shall have the right to defer such filing for a period of not more than sixty (60) days after receipt of the Demand Notice; *provided*, *however*, that the Company may not utilise this right more than once in any twelve (12) month period; and *provided*, *further*, that the Company shall not register any securities for its own account or that of any other stockholder during such sixty (60) day period, other than an Excluded Registration.

2.4 Effectiveness of Demand Registration.

(A) A registration shall not be counted as "effected" for purposes of this paragraph 2 until such time as the applicable registration statement has been declared effective by the SEC, unless the Initiating Holders withdraw their request for such registration, elect not to pay the registration expenses therefor, in which case such withdrawn registration statement shall be counted as "effected" for the purposes of this paragraph 2 and as such the Holders shall forfeit their right to one demand registration statement pursuant to this paragraph 2 provided, that if such withdrawal is during a period the Company has deferred taking action to file a registration statement, then the Initiating Holders may withdraw their request for registration and such registration statement will not be counted as effected.

(B) A registration shall not be counted as "effected" if, as a result of an exercise of the underwriter's cutback provisions in paragraph 2.2, fewer than fifty percent (50%) of the total number of Registrable Securities that Holders have requested to be included in such registration statement are actually included.

3. **Piggyback Registrations**

3.1 Offering by Company. The Company shall notify all Holders of Registrable Securities in writing at least thirty (30) days prior to filing any registration statement under the Securities Act for purposes of effecting a public offering of securities of the Company (including, but not limited to, registration statements relating to secondary offerings of securities of the Company, but excluding Excluded Registrations), and shall afford each such Holder an opportunity to include in such registration statement all or any part of the Registrable Securities then held by such Holder. Each Holder desiring to include in any such registration statement all or any part of the Registrable Securities held by it shall within twenty (20) days after receipt of the above described notice from the Company, so notify the Company in writing, and in such notice shall inform the Company of the number of Registrable Securities such Holder wishes to include in such registration statement. If a Holder decides not to include all of its Registrable Securities in any registration statement thereafter filed by the Company, such Holder shall nevertheless continue to have the right to include any Registrable Securities in any subsequent registration statement or registration statements as may be filed by the Company with respect to offerings of its securities, all upon the terms and conditions set forth herein. The Company shall have the right to terminate or withdraw any registration initiated by it under this paragraph 3 before the effective date of such registration, whether or not any Holder has elected to include Registrable Securities in such registration. The expenses (other than Selling Expenses) of such withdrawn registration shall be borne by the Company in accordance with paragraph 5.

3.2 Underwriting. If a registration statement under which the Company gives notice under this paragraph 3 is for an underwritten offering, then the Company shall so advise the Holders of Registrable Securities. In such event, the right of any such Holder's Registrable Securities to be included in a registration pursuant to this paragraph 3 shall be conditioned upon such Holder's participation in such underwriting and the inclusion of such Holder's Registrable Securities in the underwriting to the extent provided herein. All Holders proposing to distribute their Registrable Securities through such underwriting shall enter into an underwriting agreement in customary form with the managing underwriter or underwriters selected for such underwriting. Notwithstanding any other provision of this Agreement, if the managing underwriter(s) determine(s) in good faith that marketing factors require a limitation of the number of shares to be underwritten, then the managing underwriter(s) may exclude shares from the registration and the underwriting, and the number of shares that may be included in the registration and the underwriting shall be allocated among the Holders of Registrable Securities on a *pro rata* basis according to the number of Registrable Securities Then Outstanding held by each Holder requesting registration; *provided, however*, that the number of shares of Registrable Securities held by the Holders to be included in such underwriting and registration shall not be reduced unless all other securities are first entirely excluded from the underwriting and registration including, without limitation, all shares that are not Registrable Securities and are held by any other person, including, without limitation, any person who is an employee, officer or director of the Company or any subsidiary of the Company. If any Holder disapproves of the terms of any such underwriting, such Holder may elect to withdraw therefrom by written notice to the Company and the underwriter(s), delivered at least ten (10) business days prior to the effective date of the registration statement. Any Registrable Securities excluded or withdrawn from such underwriting shall be excluded and withdrawn from the registration. For purposes of the provision in this Subsection 3.2 concerning apportionment, for any selling Holder that is a partnership, limited liability company, or corporation, the partners, members, retired partners, retired members, stockholders, and Affiliates of such Holder, or the estates and family members of any such partners, retired partners, members, and retired members and any trusts for the benefit of any of the foregoing persons, shall be deemed to be a single "selling Holder," and any pro rata reduction with respect to such "selling Holder" shall be based upon the aggregate number of Registrable Securities owned by all persons included in such "selling Holder," as defined in this sentence. A registration shall not be counted as "effected" if, as a result of an exercise of the underwriter's cutback provisions in this paragraph 3.2, fewer than fifty percent (50%) of the total number of Registrable Securities that Holders have requested to be included in such registration statement are actually included.

3.3 Not Demand Registration. Registration pursuant to this paragraph 3 shall not be deemed to be a demand registration as described in paragraph 2 above. There shall be no limit on the number of times the Holders may request registration of Registrable Securities under this paragraph 3.

4. **Form F-3 and Form S-3 Registration**

If at any time when it is eligible to use a Form F-3 or S-3 registration statement, the Company receives a request from Holders of at least 20% of all Registrable Securities then outstanding a written request or requests that the Company effect a registration on Form F-3 or Form S-3 and any related qualification or compliance with respect to all or a part of the Registrable Securities owned by such Holder or Holders, then the Company will:

4.1 Notice. Promptly give written notice of the proposed registration and the Holder's or Holders' request therefor, and any related qualification or compliance, to all other Holders of Registrable Securities; and

4.2 Registration. As soon as practicable and in any event within forty-five (45) days after the date the written request is delivered to the Company, effect such registration and all such qualifications and compliances as may be so requested and as would permit or facilitate the sale and distribution of all or such portion of such Holders or Holders' Registrable Securities as are specified in such request, together with all or such portion of the Registrable Securities of any other Holder or Holders joining in such request as are specified in a written request given within twenty (20) days after the Company provides the notice contemplated by paragraph 4.1 *provided, however*, that the Company shall not be obligated to effect any such registration, qualification or compliance pursuant to this paragraph 4:

(A) if Form F-3 or Form S-3 is not available for such offering by the Holders;

(B) if the Holders, together with the holders of any other securities of the Company entitled to inclusion in such registration, propose to sell Registrable Securities and such other securities (if any) at an aggregate price to the public of less than US$5,000,000;

(C) if the Company shall furnish to the Holders a certificate signed by the President or Chief Executive Officer of the Company stating that in the good faith judgment of the Board, it would be materially detrimental to the Company and its shareholders for such Form F-3 or Form S-3 Registration to be effected because such action would (i) materially interfere with a significant acquisition, corporate reorganization, or other similar transaction involving the Company; (ii) require premature disclosure of material information that the Company has a bona fide business purpose for preserving as confidential; or (iii) render the Company unable to comply with requirements under the Securities Act or Exchange Act, in which event the Company shall have the right to defer the filing of the Form F-3 or Form S-3 registration statement no more than once during any twelve (12) month period for a period of not more than sixty (60) days after receipt of the request of the Holder or Holders under this paragraph 4; *provided that* the Company shall not register any of its other shares during such sixty (60) day period other than an Excluded Registration; or

(D) during the period that is thirty (30) days before the Company's good faith estimate of the date of filing of, and ending on a date that is ninety (90) days after the effective date of, a Company-initiated registration; *provided*, that the Company is actively employing in good faith commercially reasonable efforts to cause such registration statement to become effective; *provided, further*, that if the Company does not effect such registration statement, the Company shall effect such registration on the thirty-first (31st) day after its notice to the Holders describing the delay in this paragraph 4.2.

4.3 Not Demand Registration. Form F-3 or Form S-3 registrations shall not be deemed to be demand registrations as described in paragraph 2 above. Except as otherwise provided herein, there shall be no limit on the number of times the Holders may request registration of Registrable Securities under this paragraph 4; *provided that* the Company shall not be required to file more than two (2) Form F-3 or Form S-3 registration statements in any twelve (12) month period.

4.4 Underwriting. If the Holders of Registrable Securities requesting registration under this paragraph 4 intend to distribute the Registrable Securities covered by their request by means of an underwriting, the provisions of paragraph 2.2 shall apply to such registration.

5. **Expenses**

5.1 All Registration Expenses incurred in connection with any registration pursuant to paragraphs 2, 3 or 4, including in connection with filings, qualification fees, printers' fees and accounting fees (but excluding Selling Expenses and expenses for the special counsel of the selling Holders that exceed US$100,000) shall be borne by the Company. Each Holder participating in a registration pursuant to paragraphs 2, 3 or 4 shall bear such Holder's proportionate share (based on the total number of shares sold in such registration other than for the account of the Company or persons or entities that are not Holders) of all Selling Expenses or other amounts payable to underwriter(s) or brokers, in connection with such offering by the Holders.

6. **Obligations of the Company**

6.1 Whenever required to effect the registration of any Registrable Securities under this Agreement the Company shall, as expeditiously as reasonably possible:

(A) Registration Statement. Prepare and file with the SEC a registration statement with respect to such Registrable Securities and use its best efforts to cause such registration statement to become effective, and, upon the request of the Holders of a majority of the Registrable Securities registered thereunder, keep such registration statement effective for a period of up to one hundred twenty (120) days or, in the case of Registrable Securities registered under Form F-3 or Form S-3 in accordance with Rule 415 under the Securities Act or a successor rule, for a period of up to one hundred and twenty (120) days; provided, however, that: (i) such one hundred twenty (120) day period shall be extended for a period of time equal to the period any Holder refrains from selling any securities included in such registration at the request of the underwriter(s); and (ii) in the case of any registration of Registrable Securities on Form F-3 or Form S-3 which are intended to be offered on a continuous or delayed basis, such one hundred and twenty (120) day period shall be extended, if necessary, to keep the registration statement effective until all such Registrable Securities are sold.

(B) Amendments and Supplements. Prepare and file with the SEC such amendments and supplements to such registration statement and the prospectus used in connection with such registration statement as may be necessary to comply with the provisions of the Securities Act with respect to the disposition of all securities covered by such registration statement.

(C) Prospectuses. Furnish to the Holders such number of copies of a prospectus, including a preliminary prospectus, in conformity with the requirements of the Securities Act, and such other documents as they may reasonably request in order to facilitate the disposition of the Registrable Securities owned by them that are included in such registration.

(D) Blue Sky. Use its best efforts to register and qualify the securities covered by such registration statement under such other securities or Blue Sky laws of such jurisdictions as shall be reasonably requested by the Holders; provided that the Company shall not be required in connection therewith or as a condition thereto to qualify to do business or to file a general consent to service of process in any such states or jurisdictions, unless the Company is already subject to service in such jurisdiction and except as may be required by the Securities Act.

(E) Underwriting. In the event of any underwritten public offering, enter into and perform its obligations under an underwriting agreement in usual and customary form (including without limitation in respect of comfort letter(s) and legal opinion(s)), with the managing underwriter(s) of such offering.

(F) Notification. Notify each Holder of Registrable Securities covered by such registration statement of: (i) the time when such registration statement has been declared effective; (ii) after such registration statement becomes effective, of any request by the SEC that the Company amend or supplement such registration statement or prospectus; (iii) when a prospectus relating to a registration statement is required to be delivered under the Securities Act, the time when a supplement to any prospectus forming a part of such registration statement has been filed; (iv) the issuance of any stop order by the SEC in respect of such registration statement; and (v) the happening of any event as a result of which the prospectus included in such registration statement, as then in effect, includes an untrue statement of a material fact or omits to state a material fact required to be stated therein or necessary to make the statements therein not misleading in the light of the circumstances then existing.

(G) Listing. Cause all such Registrable Securities registered pursuant hereunder to be listed on each securities exchange on which similar securities issued by the Company are then listed.

(H) CUSIP Number. Provide a transfer agent and registrar for all Registrable Securities registered pursuant hereunder and a CUSIP number for all such Registrable Securities, in each case not later than the effective date of such registration.

(I) Inspection. Promptly make available for inspection by the selling Holders, any underwriter(s) participating in any registration of Registrable Securities made under this Agreement, and any attorney or accountant or other agent retained by any such underwriter or selected by the selling Holders, all financial and other records, pertinent corporate documents, and properties of the Company, and cause the Company's officers, directors, employees, and independent accountants to supply all information reasonably requested by any such Holder, underwriter, attorney, accountant, or agent, in each case, as necessary or advisable to verify the accuracy of the information in such registration statement and to conduct appropriate due diligence in connection therewith.

(J) Withdrawal of Suspensions. Use its reasonable best efforts to obtain the withdrawal of any order suspending the effectiveness of any registration statement, or the lifting of any suspension of the qualification or exemption from qualification of any Registrable Securities for sale in any jurisdiction in in which such securities are qualified;

(K) Opportunity to Comment. Before filing a registration statement or prospectus or any amendments or supplements thereto, to the extent the Company is reasonably able to do so, furnish copies of such documents to each participating Holder, any underwriter(s) or other distributor(s) identified by any Holder and counsel for the Holders and for such underwriter(s) or distributor(s) a reasonable period prior to filing and consider in good faith any comments provided by any such persons.

6.2 Furnish Information. It shall be a condition precedent to the obligations of the Company to take any action pursuant to paragraphs 2, 3 or 4 that the selling Holders shall furnish to the Company such information regarding themselves, the Registrable Securities held by them and the intended method of disposition of such securities as shall be required to timely effect the Registration of their Registrable Securities.

6.3 10b5-1 Trading Program. The Company shall ensure that, at all times after any registration statement covering a public offering of securities of the Company under the Securities Act shall have become effective, its insider trading policy shall provide that the Company's directors may implement a trading program under Rule 10b5-1 of the Exchange Act.

7. **Indemnification**

In the event any Registrable Securities are included in a registration statement under paragraphs 2, 3 or 4:

7.1 By the Company. To the extent permitted by law, the Company will indemnify and hold harmless each Holder, its partners, members, stockholders, officers, directors, legal counsel, investment advisors, accountants, any underwriter (as defined in the Securities Act) for such Holder and each person, if any, who controls such Holder or underwriter within the meaning of the Securities Act or the Exchange Act, against any losses, claims, damages, or liabilities (joint or several) to which they may become subject under the Securities Act, the Exchange Act, or applicable securities law, insofar as such losses, claims, damages, or liabilities (or actions in respect thereof) arise out of or are based upon any of the following statements, omissions or violations (collectively a "**Violation**"):

(A) any untrue statement or alleged untrue statement of a material fact contained in such registration statement, including any preliminary prospectus or final prospectus contained therein or any amendments or supplements thereto;

(B) the omission or alleged omission to state therein a material fact required to be stated therein, or necessary to make the statements therein not misleading; or

(C) any violation or alleged violation by the Company of the Securities Act, the Exchange Act, any United States federal or state securities law, or any rule or regulation promulgated under the Securities Act, the Exchange Act, or any United States federal or any applicable securities laws in connection with the offering covered by such registration statement;

and the Company will reimburse each such Holder, its partner, member, stockholder, officer, director, legal counsel, investment advisor, accountants, underwriter or controlling person for any legal or other expenses reasonably incurred by them, as incurred, in connection with investigating or defending any such loss, claim, damage, liability or action; *provided, however*, that the indemnity agreement contained in this paragraph 7.1 shall not apply to amounts paid in settlement of any such loss, claim, damage, liability or action if such settlement is effected without the consent of the Company (which consent shall not be unreasonably withheld), nor shall the Company be liable in any such case for any such loss, claim, damage, liability or action to the extent that it arises out of or is based upon a Violation which occurs in reliance upon and in conformity with written information furnished expressly for use in connection with such registration by such Holder, or any partner, member, stockholder, officer, director, legal counsel, investment advisor, accountant, underwriter or controlling person of such Holder.

7.2 By Selling Holders. To the extent permitted by law, each selling Holder will, severally and not jointly, if Registrable Securities held by such Holder are included in the securities as to which such registration qualifications or compliance is being effected, indemnify and hold harmless the Company, each of its directors, each of its officers who has signed the registration statement, each person, if any, who controls the Company within the meaning of the Securities Act, any underwriter and any other Holder selling securities under such registration statement or any of such other Holder's partners, directors, officers, legal counsel or any person who controls such Holder within the meaning of the Securities Act or the Exchange Act, against any losses, claims, damages or liabilities (joint or several) to which the Company or any such director, officer, legal counsel, controlling person, underwriter or other such Holder, partner or director, officer or controlling person of such other Holder may become subject under the Securities Act, the Exchange Act or other applicable securities law, insofar as such losses, claims, damages or liabilities (or actions in respect thereto) arise out of or are based upon any Violation, in each case to the extent (and only to the extent) that such Violation occurs in reliance upon and in conformity with written information furnished by such

Holder expressly for use in connection with such registration; and each such Holder will reimburse any legal or other expenses reasonably incurred by the Company or any such director, officer, controlling person, underwriter or other Holder, partner, officer, director or controlling person of such other Holder in connection with investigating or defending any such loss, claim, damage, liability or action; *provided, however*, that the indemnity agreement contained in this paragraph 7.2 shall not apply to amounts paid in settlement of any such loss, claim, damage, liability or action if such settlement is effected without the consent of the Holder, which consent shall not be unreasonably withheld; and *provided, further, that* in no event shall any indemnity under this paragraph 7.2 exceed the net proceeds received by such Holder in the registered offering out of which the applicable Violation arises, except in the case of fraud or wilful misconduct by such Holder.

7.3 Notice. Promptly after receipt by an indemnified party under this paragraph 7 of notice of the commencement of any action (including any governmental action), such indemnified party will, if a claim in respect thereof is to be made against any indemnifying party under this paragraph 7, deliver to the indemnifying party a written notice of the commencement thereof and the indemnifying party shall have the right to participate in, and, to the extent the indemnifying party so desires, jointly with any other indemnifying party similarly noticed, to assume the defence thereof with counsel mutually satisfactory to the parties; *provided, however*, that an indemnified party (together with all other indemnified parties that may be represented without conflict by one counsel) shall have the right to retain one separate counsel, with the fees and expenses to be paid by the indemnifying party, if representation of such indemnified party by the counsel retained by the indemnifying party would be inappropriate due to actual or potential conflict of interests between such indemnified party and any other party represented by such counsel in such proceeding. The failure to deliver written notice to the indemnifying party within a reasonable time of the commencement of any such action shall relieve such indemnifying party of liability to the indemnified party under this paragraph 7 to the extent the indemnifying party is prejudiced as a result thereof, but the omission to so deliver written notice to the indemnifying party will not relieve it of any liability that it may have to any indemnified party otherwise than under this paragraph 7.

7.4 Contribution. In order to provide for just and equitable contribution to joint liability under the Securities Act in any case in which either: (i) any indemnified party makes a claim for indemnification pursuant to this paragraph 7 but it is judicially determined (by the entry of a final judgment or decree by a court of competent jurisdiction and the expiration of time to appeal or the denial of the last right of appeal) that such indemnification may not be enforced in such case notwithstanding the fact that this paragraph 7 provides for indemnification in such case; or (ii) contribution under the Securities Act may be required on the part of any indemnified party in circumstances for which indemnification is provided under this paragraph 7; then, and in each such case, the indemnified party and the indemnifying party will contribute to the aggregate losses, claims, damages or liabilities to which they may be subject (after contribution from others) in such proportion as is appropriate to reflect the relative fault of each of the indemnifying party and the indemnified party in connection with the statements, omissions, or other actions that resulted in such loss, claim, damage, liability, or expense, as well as to reflect any other relevant equitable considerations. The relative fault of the indemnifying party and of the indemnified party shall be determined by a court of law by reference to, among other things, whether the untrue or alleged untrue statement of a material fact or the omission to state a material fact relates to information supplied by the indemnifying party or by the indemnified party and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such statement or omission; *provided, however,* that, in any such case: (A) no Holder will be required to contribute any amount in excess of the public offering price of all such Registrable Securities offered and sold by such Holder pursuant to such registration statement, except in the case of fraud or wilful misconduct by such Holder; and (B) no person or entity guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Securities Act) will be entitled to

contribution from any person or entity who was not guilty of such fraudulent misrepresentation, and *provided further* that in no event shall a Holder's liability pursuant to any of the paragraphs 7, exceed the proceeds from the offering received by such Holder, except in the case of fraud or wilful misconduct by such Holder

7.5 Notwithstanding the foregoing, to the extent that the provisions on indemnification and contribution contained in the underwriting agreement entered into in connection with the underwritten public offering are in conflict with the foregoing provisions, the provisions in the underwriting agreement shall control. Unless otherwise superseded by an underwriting agreement entered into in connection with the underwritten public offering, the obligations of the Company and Holders under this paragraph 7 shall survive the completion of any offering of Registrable Securities in a registration, and otherwise shall survive the termination of this Agreement.

7.6 Survival; Consents to Judgments and Settlements. The obligations of the Company and Holders under this paragraph 7 shall survive the completion of any offering of Registrable Securities in a registration statement, regardless of the expiration of any statutes of limitation or extensions of such statutes. No indemnifying party, in the defence of any such claim or litigation, shall, except with the consent of each indemnified party, consent to entry of any judgment or enter into any settlement which does not include as an unconditional term thereof the giving by the claimant or plaintiff to such indemnified party of a release from all liability in respect to such claim or litigation. In addition, if any settlement contains any statement as to or an admission of fault, culpability or a failure to act, by or on behalf of any indemnified party, then the consent of such indemnified party is required prior to entry into such settlement.

8. **No Registration Rights to Third Parties**

From and after the date of this Agreement, the Company shall not, without the prior written consent of the Holders of [a majority] of the Registrable Securities Then Outstanding, enter into any agreement with any holder or prospective holder of any securities of the Company that would (i) allow such holder or prospective holder to include such securities in any registration unless, under the terms of such agreement, such holder or prospective holder may include such securities in any such registration only to the extent that the inclusion of such securities will not reduce the number of the Registrable Securities of the Holders that are included; or (ii) allow such holder or prospective holder to initiate a demand for registration of any securities held by such holder or prospective holder; provided that this limitation shall not apply to Registrable Securities acquired by any additional Holder that becomes a party to this Agreement in accordance with the terms hereof.

9. **Market Stand-Off**

Each Holder agrees that, so long as it holds any voting securities of the Company, upon request by the Company or the underwriters managing the Company's IPO, it will not sell or otherwise transfer or dispose of any securities of the Company (other than those permitted to be included in the registration and other transfers to affiliates permitted by law) or enter into any hedging or similar transaction with the same economic effect as a sale of securities, in each case held by such Holder immediately before the effective date of the registration statement for the Company's IPO without the prior written consent of the Company or such underwriters, as the case may be, for a period of time specified by the representative of the underwriters not to exceed one hundred and eighty (180) days from the effective date of the registration statement covering such IPO. The foregoing provision of this paragraph 9 shall not apply to the sale of any securities of the Company to an underwriter pursuant to any underwriting agreement, and shall only be applicable to the Holders if all officers, directors and holders of one per cent (1%) or more of the Company's outstanding share capital enter into similar agreements, and if the Company with Investor Majority Consent or any

underwriter releases any officer, director or holder of one per cent (1%) or more of the Company's outstanding share capital from his or her sale restrictions so undertaken, then each Holder shall be notified prior to such release and shall itself be simultaneously released to the same proportional extent. The foregoing provisions of this paragraph 9 shall only apply to the first such registration statement of the Company which covers securities to be sold on its behalf to the public in an underwritten offering but not to Registrable Securities sold pursuant to such registration statement. The Company shall require all future acquirers of the Company's securities holding at least one per cent (1%) of the then outstanding share capital of the Company to execute prior to its initial public offering a market stand-off agreement containing substantially similar provisions as those contained in this paragraph 9.

10. **Transfer of Registration Rights**

The rights to cause the Company to register Registrable Securities pursuant to this Agreement may be assigned by a Holder to a transferee or assignee of such securities that: (i) is an Affiliate, nominee, subsidiary, parent, partner, limited partner, retired partner, retired limited partner, employee, member, retired member, shareholder or related party of a Holder; (ii) is a Holder's family member or trust for the benefit of an individual Holder; or (iii) after such assignment or transfer, holds at least 250,000 shares of Registrable Securities (subject to appropriate adjustment for stock splits, stock dividends, combinations and other recapitalisations), provided that the Company is, within a reasonable time after such transfer, furnished with written notice of the name and address of such transferee or assignee and the securities with respect to which such registration rights are being assigned, and, provided further, that such transferee agrees to become a signatory to the Applicable Definitive Documents.

11. **Rule 144 Reporting**

With a view to making available to the Holders the benefits of certain rules and regulations of the SEC which may at any time permit the sale of the Registrable Securities to the public without registration or pursuant to a registration on Form F-3 or Form S-3, after such time as a public market exists for the Ordinary Shares, the Company agrees to:

11.1 Make and keep adequate public information available, as those terms are understood and defined in Rule 144 under the Securities Act, at all times after the effective date of the first registration under the Securities Act filed by the Company for an offering of its securities to the general public;

11.2 File with the SEC in a timely manner all reports and other documents required of the Company under the Securities Act and the Exchange Act (at any time after it has become subject to such reporting requirements); and

11.3 So long as a Holder owns any Registrable Securities, to furnish to such Holder forthwith upon request: (i) a written statement by the Company as to its compliance with the reporting requirements of Rule 144 (at any time after ninety (90) days after the effective date of the Company's IPO), the Securities Act and the Exchange Act (at any time after it has become subject to such reporting requirements), or its qualification as a registrant whose securities may be resold pursuant to Form F-3 or Form S-3 (at any time after it so qualifies); (ii) a copy of the most recent annual or quarterly report of the Company and such other reports and documents so filed by the Company; and (iii) such other reports, documents and information regarding the Company as a Holder may reasonably request in availing itself of any rule or regulation of the SEC that permits the selling of any such securities without registration or pursuant to Form F-3 or Form S-3.

12. **Restrictions on Transfer**

12.1 The Registrable Securities shall not be sold, pledged, or otherwise transferred, and the Company shall not recognize and shall issue stop-transfer instructions to its transfer agent with respect to any such sale, pledge, or transfer, except upon the conditions specified in this Agreement, which conditions are intended to ensure compliance with the provisions of the Securities Act. A transferring Holder will cause any proposed purchaser, pledgee, or transferee of the Registrable Securities held by such Holder to agree to take and hold such securities subject to the provisions and upon the conditions specified in this Agreement.

12.2 Each certificate, instrument, or book entry representing (i) the Registrable Securities and (ii) any other securities issued in respect of the Registrable Securities, upon any stock split, stock dividend, recapitalization, merger, consolidation, or similar event ((i) and (ii) together, the "**Restricted Securities**"), shall (unless otherwise permitted by the provisions of paragraph 12.3) be notated with a legend substantially in the following form:

"THE SECURITIES REPRESENTED HEREBY HAVE BEEN ACQUIRED FOR INVESTMENT AND HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933. SUCH SHARES MAY NOT BE SOLD, PLEDGED, OR TRANSFERRED IN THE ABSENCE OF SUCH REGISTRATION OR A VALID EXEMPTION FROM THE REGISTRATION AND PROSPECTUS DELIVERY REQUIREMENTS OF SAID ACT.

THE SECURITIES REPRESENTED HEREBY MAY BE TRANSFERRED ONLY IN ACCORDANCE WITH THE TERMS OF AN AGREEMENT BETWEEN THE COMPANY AND THE STOCKHOLDER, A COPY OF WHICH IS ON FILE WITH THE SECRETARY OF THE COMPANY."

The Holders consent to the Company making a notation in its records and giving instructions to any transfer agent of the Restricted Securities in order to implement the restrictions on transfer set forth in this paragraph 12.

12.3 The holder of such Restricted Securities, by acceptance of ownership thereof, agrees to comply in all respects with the provisions of this Schedule 5. Before any proposed sale, pledge, or transfer of any Restricted Securities, unless there is in effect a registration statement under the Securities Act covering the proposed transaction, the Holder thereof shall give notice to the Company of such Holder's intention to effect such sale, pledge, or transfer. Each such notice shall describe the manner and circumstances of the proposed sale, pledge, or transfer in sufficient detail and, if reasonably requested by the Company, shall be accompanied at such Holder's expense by either (i) a written opinion of legal counsel who shall, and whose legal opinion shall, be reasonably satisfactory to the Company, addressed to the Company, to the effect that the proposed transaction may be effected without registration under the Securities Act; (ii) a "no action" letter from the SEC to the effect that the proposed sale, pledge, or transfer of such Restricted Securities without registration will not result in a recommendation by the staff of the SEC that action be taken with respect thereto; or (iii) any other evidence reasonably satisfactory to counsel to the Company to the effect that the proposed sale, pledge, or transfer of the Restricted Securities may be effected without registration under the Securities Act, whereupon the Holder of such Restricted Securities shall be entitled to sell, pledge, or transfer such Restricted Securities in accordance with the terms of the notice given by the Holder to the Company. The Company will not require such a legal opinion or "no action" letter (x) in any transaction in compliance with SEC Rule 144; or (y) in any transaction in which such Holder distributes Restricted Securities to an Affiliate of such Holder for no consideration; *provided* that each transferee agrees in writing to be subject to the terms of this paragraph 12. Each certificate, instrument, or book entry representing the Restricted Securities transferred as above provided shall be notated with, except if such transfer is made pursuant to SEC Rule 144, the appropriate restrictive legend set forth in paragraph 12.2, except that such certificate instrument, or book entry shall not be notated with such restrictive legend if, in the opinion of counsel for such Holder and the Company, such legend is not required in order to establish compliance with any provisions of the Securities Act.

13. Delay of Registration. No Holder shall have any right to obtain or seek an injunction restraining or otherwise delaying any registration pursuant to this Agreement as the result of any controversy that might arise with respect to the interpretation or implementation of this Schedule 5.

14. **Termination of Registration Rights**

The right of any Holder to request registration or inclusion of Registrable Securities in any registration pursuant to paragraphs 2, 3 and 4 herein, shall terminate on the earlier to occur of: (i) the closing of a Liquidation Event, as such term is defined in the Articles other than a Liquidation Event undertaken in connection with effecting an IPO; and (ii) the fifth (5th) anniversary of an IPO.

SCHEDULE 6 : IPO

1. **Structural considerations**

At any time prior to, and in contemplation of, an IPO, with, in the case of an IPO that is a Qualified Listing, the consent of the Board and, in the case of an IPO that is not a Qualified Listing, with the consent of the Board and upon receipt of an Investor Majority Consent in accordance with the requirements of clause 7.1 and Part A of Schedule 2, the Company may carry out any actions as may be necessary, appropriate or desirable to liquidate, dissolve or wind up, merge, reorganise, recapitalise or otherwise restructure any member of its Group, in each case, so as to optimise the corporate structure of its Group as is appropriate in light of tax, legal or other considerations provided that any such Restructuring does not (i) abrogate any Shareholder's rights provided for in this Agreement or the Articles or (ii) result in any material adverse tax impact upon any Investor.

2. **Determination of structure and participation**

The Company, acting by decision of the Board and in consultation with the investment bank advising the Company in respect of the IPO, shall approve the selection of the managing underwriters.

3. **Co-operation**

3.1 The Company shall, and shall procure that each other member of the Group from time to time shall, take all steps reasonably necessary, appropriate or desirable to effect the IPO and to expedite or facilitate the disposition of all securities included therein, including cooperation in the preparation of any offering document, providing access to the books and records of the Group, Group's auditors and management, and participation in road shows and other marketing efforts as determined by the Board. If, at any time after determining to pursue an IPO and prior to the completion of such IPO, such IPO is terminated or otherwise not completed, the Company shall give written notice of such termination or failure to complete to each Investor, but none of the Shareholders shall be relieved from their obligations in respect of another IPO as set out in this schedule.

3.2 In the event of an IPO, each Shareholder shall fully cooperate with the Company, including coordination with respect to any applicable laws or regulations in any relevant jurisdiction relating to publicly listed or traded securities.

3.3 Each Shareholder shall take, and shall instruct its representative(s), nominee(s) or designee(s), as the case may be, on the Board or any other board (or any committee thereof) to take any and all action within its power and in accordance with applicable law as may be necessary, appropriate or desirable to effect, and to cause the Company and each other member of its Group to take any and all action as may be necessary, appropriate or desirable to effect, the transactions described in this schedule.

3.4 Subject to, in respect of a Qualified Listing, the prior consent of the Board and, in respect of an IPO that is not a Qualified Listing, receipt of Investor Majority Consent and the prior consent of the Board, the parties agree to amend, supplement or otherwise modify this Agreement as may be necessary to comply with the laws, regulations and rules of the relevant regulatory authority and the rules of the securities exchange in connection with an IPO.

4. **Execution of underwriting agreement and lock-up agreement**

In the event of an IPO, each Shareholder agrees that it would have to execute a customary underwriting agreement with the managing underwriters of such offering (taking into account market practice at the time of the IPO), which, in the case of a Qualified Listing, is approved by the Board and in the case of an IPO that is not a Qualified Listing, is approved by the Board and Investor Majority Consent. The parties acknowledge and agree that, in connection with any such agreement, the same terms and shall apply to each Shareholder equally. The parties agree that in connection with such underwriting agreement they will also agree to be subject to a market standoff agreement according to the terms of Schedule 5 of this Agreement.

IN WITNESS whereof this Agreement has been executed and delivered as a Deed on the date first before written.

IN WITNESS WHEREOF this document has been executed as a deed and is delivered and takes effect on the date stated at the beginning of it.

EXECUTED and **DELIVERED** as a **DEED** by **ORCHARD THERAPEUTICS** **LIMITED** acting by a director	))))	/s/ Mark Rothera
In the presence of:		*Director*
Signature of witness:		/s/ John Ilett
Name of witness:		John Ilett
Address of witness:		108 Cannon Street, London, EC4N6EU
Occupation of witness:		Solicitor

EXECUTED and **DELIVERED** as a **DEED** by **SCOTTISH MORTGAGE INVESTMENT TRUST PLC** acting through its agent **BAILLIE GIFFORD & CO.** by)

In the presence of: /s/ Tom Slatter

Name: Tom Slatter

Signature of Witness: /s/ Christopher Smith

Name of Witness: Christopher Smith

Address of Witness: Baillie Gifford and Co., Calton Square

1 Greenside Row, Edinburgh EH13AN, UK

Occupation of Witness: Corporate Lawyer

EXECUTED and **DELIVERED** as a **DEED** by **F-PRIME CAPITAL PARTNERS HEALTHCARE FUND IV LP**	)
By: F-Prime Capital Partners Healthcare Advisors Fund IV LP, its General Partner	)
By: Impresa Holdings LLC, its General Partner	)
By: Impresa Management LLC, its Managing Member	)

In the presence of: /s/ Mary Pendergast

Mary Pendergast, Vice President

Signature of Witness: /s/ Allan S. Galper

Name of Witness: Allan S. Galper

Address of Witness: One Main Street, 13th Floor

Cambridge, MA 02142 USA

Occupation of Witness: Attorney

EXECUTED and DELIVERED as a DEED by F-PRIME CAPITAL PARTNERS HEALTHCARE FUND IV-A LP	)))))
By: F-Prime Capital Partners Healthcare Advisors Fund IV-A LP, its General Partner	)))))
By: Impresa Holdings LLC, its General Partner	)))
By: Impresa Management LLC, its Managing Member	)

In the presence of: /s/ Mary Pendergast

Mary Pendergast, Vice President

Signature of Witness: /s/ Allan S. Galper

Name of Witness: Allan S. Galper

Address of Witness: One Main Street, 13th Floor

Cambridge, MA 02142 USA

Occupation of Witness: Attorney

EXECUTED and **DELIVERED** as a **DEED** by **UNIQUE DIAMOND INVESTMENTS LIMITED** acting by a director	)))	/s/ Simone Song *Authorised Signatory*
In the presence of:		
Signature of Witness:		/s/ Alice Wong
Name of Witness:		Alice Wong
Address of Witness:		Rooms 5028-5032, Sun Hung Kai Centre, 30 Harbour Rd., Wan Chai, Hong Kong
Occupation of Witness:		Company Secretary

EXECUTED and **DELIVERED** as a **DEED** by **TLS BETA PTE LTD** acting by a Director	)))	/s/ Christina Choo *Director*
In the presence of:		
Signature of Witness:		/s/ Yvette Chen Yuefei
Name of Witness:		Yvette Chen Yuefei
Address of Witness:		60B Orchard Road #06-18 Tower 2 The Atrium at Orchard Singapore 238891
Occupation of Witness:		Witness

EXECUTED and **DELIVERED** as a **DEED** by **COWEN HEALTHCARE INVESTMENTS II LP** By: Cowen Healthcare Investments II GP LLC, its General Partner By: Kevin Raidy, Managing Partner	)))))))	/s/ Kevin Raidy
Signature of Witness:		/s/ Michael Baxter
Name of Witness:		Michael Baxter
Address of Witness:		599 Lexington Ave., 19th Fl New York, NY 10022 USA
Occupation of Witness:		Attorney

EXECUTED and **DELIVERED** as a)
DEED by **GLAXO GROUP LIMITED**)
acting by a director / authorised signatory)

/s/ Sarah Ghinn

Director / Authorised Signatory

In the presence of:

Signature of Witness: /s/ Raman Kaur

Name of Witness: Raman Kaur

Address of Witness: 980 Great West Road

Brentford, TW89GS UK

Occupation of Witness: Company Secretary

Dated 19 October 2018

THE SEVERAL PERSONS LISTED IN SCHEDULE 1

THE COMPANY

DEED OF VARIATION

relating to a

SHAREHOLDERS' AGREEMENT RELATING TO

ORCHARD THERAPEUTICS LIMITED DATED 29 MARCH 2017 AS AMENDED AND RESTATED ON 2 AUGUST 2018

THIS DEED (the or this "**Deed**") is made on 19 October 2018

BETWEEN:

(1) **THE SEVERAL PERSONS** whose names and addresses are set out in Schedule 1, together constituting an Investor Majority Consent (as defined under the Shareholders' Agreement); and

(2) **ORCHARD THERAPEUTICS LIMITED**, a private limited liability company incorporated in England and Wales with registered number 09759506 and whose registered office is at 108 Cannon Street, London, EC4N 6EU (the "**Company**"),

(each a "**Party**" and together, the "**Parties**").

WHEREAS:

(A) The Series C Investors, the Existing Investors, the Ordinary Shareholders (each as defined therein) and the Company executed a shareholders' agreement relating to the Company dated 29 March 2017, as amended and restated on 2 August 2018 (the "**Shareholders' Agreement**").

(B) Pursuant to Section 3 of Schedule 5 of the Shareholders' Agreement, the holders of Registrable Securities (as defined therein) have certain rights of notice to and rights to include for registration their Registrable Securities (such rights, the "**Registration Rights**").

(C) Orchard Rx Limited, a company incorporated in England and Wales (the "**Holding Company**"), is in the process of registering ordinary shares, represented by American depositary shares with the United States Securities and Exchange Commission in connection with its proposed initial public offering (the "**IPO**"). In connection with and prior to the completion of the IPO, (i) all of the outstanding equity interests in the Company will be exchanged for the same number and classes of shares in the Holding Company, such that the holders of ordinary shares of the Company will hold ordinary shares of the Holding Company and (ii) the Holding Company will enter into a deed of adherence to the Shareholders' agreement in accordance with clause 3.2.2 of the Shareholders' Agreement.

(D) The Parties wish to vary the Shareholders' Agreement such that the Registration Rights, including, without limitation, any and all rights of notice and rights of registration, in connection with the IPO, do not apply to this contemplated IPO.

(E) In accordance with clause 20.3.1 of the Shareholders' Agreement, the Shareholders' Agreement may be varied if such variation is in writing and signed by the Company and shareholders comprising an Investor Majority Consent, in which event such changes shall be binding against all the parties to the Shareholders' Agreement.

IT IS AGREED as follows:

1. **DEFINITIONS AND INTERPRETATION**

1.1 In this Deed:

(a) capitalised terms used and not expressly defined herein shall bear their respective meaning in the Shareholders' Agreement; and

(b) clauses 1.2.1 to 1.2.16 of the Shareholders' Agreement shall be incorporated into this Deed as if set out in full in this Deed and as if references to "this Agreement" were references to "this Deed".

2. **VARIATION**

2.1 In order to give effect to the variation set out in paragraph (D) above, the Parties, representing an Investor Majority Consent as required under clause 20.3.1 of the Shareholders' Agreement, hereby agree that the Shareholders' Agreement shall be varied as follows:

(a)	Clause 1.1	this definition is inserted into the agreement: "**NASDAQ IPO**" means the proposed initial public offering of the ordinary shares of Orchard Rx Limited (a newly incorporated holding company of the Company) in the form of American depositary shares on the NASDAQ Stock Market, such initial public offering to be completed on or before 31 December 2018;
(b)	Para. 3.4 of Schedule 5	this paragraph is inserted into the agreement: 3.4 The rights granted under paragraphs 3.1 and 3.2 shall not apply in the context of the NASDAQ IPO.

2.2 Except as set out in clause 2.1, the Shareholders' Agreement shall continue in full force and effect.

2.3 References in the Shareholders' Agreement to the "Agreement", "hereof", "hereunder" and expressions of similar import shall be deemed to be references to the Varied Shareholders' Agreement as varied by this Deed

3. **FURTHER ASSURANCE**

Each Party shall from time to time, at the reasonable request of another Party, as soon as reasonable practicable do all such acts and things, and execute and deliver all documents, in either case, necessary or desirable to give effect to the amendments effected or to be effected pursuant to this Deed.

4. **THIRD PARTY RIGHTS**

A person who is not a Party shall not have any rights under the Contracts (Rights of Third Parties) Act 1999 to enforce or to enjoy the benefit of any term of this Deed.

5. **MISCELLANEOUS**

The provisions of clauses 22 (*Notices*) and 23 (*Law and Jurisdiction*) of the Shareholders' Agreement shall be incorporated into this Deed as if set out in full in this Deed and as if references to "this Agreement" were references to this Deed.

[*Intentionally left blank, Schedules 1 and the signature pages follow.*]

SCHEDULE 1

(1) Name	(2) Address
F-Prime Capital Partners Healthcare Fund IV LP	One Main Street, 13th Floor, Cambridge, MA 02142, United States
F-Prime Capital Partners Healthcare Fund IV-A LP	One Main Street, 13th Floor, Cambridge, MA 02142, United States
Glaxo Group Limited	980 Great West Road, Brentford, Middlesex TW8 9GS
Scottish Mortgage Investment Trust Plc	Calton Square, 1 Greenside Row, Edinburgh EH1 3AN
Unique Diamond Investments Limited	Vistra Corporate Services Centre, Wickhams Cay II, Road Town, Tortola, VG1110 British Virgin Islands
Cowen Healthcare Investments II LP	599 Lexington Avenue, New York City, NY 10022, United States
CHI EF II LP	599 Lexington Avenue, New York City, NY 10022, United States
TLS Beta Pte Ltd.	60B Orchard Road #06-18 Tower 2, The Atrium@Orchard, Singapore 23889
Deerfield Special Situations Fund, L.P.	c/o Deerfield Management Company, Attn: General Counsel, 780 Third Avenue, 37th Floor New York, NY 10017, United States
Deerfield Private Design Fund III, L.P	c/o Deerfield Management Company, Attn: General Counsel, 780 Third Avenue, 37th Floor New York, NY 10017, United States
Deerfield Private Design Fund IV, L.P.	c/o Deerfield Management Company, Attn: General Counsel, 780 Third Avenue, 37th Floor New York, NY 10017, United States

THIS DEED has been duly executed and delivered as a deed on the date stated above.

EXECUTED as a **DEED** and delivered by **F-PRIME CAPITAL PARTNERS HEALTHCARE FUND IV LP** By: F-Prime Capital Partners Healthcare Advisors Fund IV LP, its General Partner By: Impresa Holdings LLC, its General Partner By: Impresa Management LLC, its Managing Member	)	/s/ Mary Pendergast *Mary Pendergast, Vice President*

In the presence of:

Witness signature:	/s/ Debbie Griffin
Name of Witness:	Debbie Griffin
Address of Witness:	25 Sackville St Charlestown, MA 02129
Occupation of Witness:	VP of Finance

EXECUTED as a **DEED** and delivered by **F-PRIME CAPITAL PARTNERS HEALTHCARE FUND IV-A LP** By: F-Prime Capital Partners Healthcare Advisors Fund IV-A LP, its General Partner By: Impresa Holdings LLC, its General Partner By: Impresa Management LLC, its Managing Member	)))))))))	/s/ Mary Pendergast *Mary Pendergast, Vice President*

In the presence of:

Witness signature:	/s/ Debbie Griffin
Name of Witness:	Debbie Griffin
Address of Witness:	25 Sackville St Charlestown, MA 02129
Occupation of Witness:	VP of Finance

EXECUTED as a **DEED** and delivered by)
GLAXO GROUP LIMITED)
acting by an authorised signatory)

/s/ Sarah Ghinn
Director/Authorised Signatory

In the presence of:

Witness signature: /s/ Raman Kaur

Name of Witness: Raman Kaur

Address of Witness: 980 Great West Road
Brentford,TW89GS UK

Occupation of Witness: Company Secretary

EXECUTED as a **DEED** and delivered by)
SCOTTISH MORTGAGE INVESTMENT TRUST PLC)
acting through its agent **BAILLIE GIFFORD & CO.**)
)

/s/ Tom Slater

Name: Tom Slater

In the presence of:

Witness signature: /s/ C.D. Smith

Name of Witness: Christopher Smith

Address of Witness: Baillie Gifford & Co.
Calton Square, 1 Greenside Row
Edinburgh, EH1 3AN

Occupation of Witness: Corporate Lawyer

EXECUTED as a **DEED** and delivered by)
UNIQUE DIAMOND INVESTMENTS LIMITED)
acting by a director)
)

/s/ Simone Song
Authorised Signatory

In the presence of:

Witness signature: /s/ Alice Wong

Name of Witness: Alice Wong

Address of Witness: Rooms 5028-5032, Sun Hung Kai Centre,.
30 Harbour Rd, Wan Chai, Hong Kong

Occupation of Witness: Company Secretary

EXECUTED as a **DEED** and delivered by)
COWEN HEALTHCARE INVESTMENTS II LP)
)
By: Cowen Healthcare Investments II GP LLC, its)
General Partner

/s/ Kevin Raidy
Name: Kevin Raidy

In the presence of:

Witness signature: /s/ Michael Baxter

Name of Witness: Michael Baxter

Address of Witness: c/o Cowen Investment Management
599 Lexington Avenue, 19th Floor
New York, NY USA

Occupation of Witness: Attorney

EXECUTED as a **DEED** and delivered by)
CHI EF II LP)
)
By: Cowen Healthcare Investments II GP LLC,
Its General Partner)

/s/ Kevin Raidy
Name: Kevin Raidy

In the presence of:

Witness signature: /s/ Michael Baxter

Name of Witness: Michael Baxter

Address of Witness: c/o Cowen Investment Management
599 Lexington Avenue, 19th Floor
New York, NY USA

Occupation of Witness: Attorney

EXECUTED as a **DEED** and delivered by)
TLS BETA PTE LTD acting by a director)
)

/s/ Christina Choo
Name: Christina Choo

In the presence of:

Witness signature: /s/ Chan Yan Wei

Name of Witness: Chan Yan Wei

Address of Witness: 60B Orchard Road
#60-18 Tower 2, The Atrium at Orchard
Singapore 238891

Occupation of Witness: Investment Associate

EXECUTED as a **DEED** and delivered by)
DEERFIELD PRIVATE DESIGN FUND III, L.P.)
)
By: Deerfield Mgmt III, L.P., its General Partner)
By: J.E. Flynn Capital III, LLC, its General Partner)

/s/ David J. Clark
Name: David J. Clark

In the presence of:

Witness signature: /s/ Lawrence Atinsky

Name of Witness: Lawrence Atinsky

Address of Witness: 780 3rd Avenue, 37th Floor
New York, NY 10017

Occupation of Witness: Attorney

EXECUTED as a **DEED** and delivered by)
DEERFIELD PRIVATE DESIGN FUND IV, L.P.)
)
By: Deerfield Mgmt IV, L.P., its General Partner)
By: J.E. Flynn Capital IV, LLC, its General Partner)

/s/ David J. Clark
Name: David J. Clark

In the presence of:

Witness signature: /s/ Lawrence Atinsky

Name of Witness: Lawrence Atinsky

Address of Witness: 780 3rd Avenue, 37th Floor
New York, NY 10017

Occupation of Witness: Attorney

EXECUTED as a **DEED** and delivered by)
DEERFIELD SPECIAL SITUATIONS FUND, L.P.)
)
By: Deerfield Mgmt, L.P., its General Partner)
By: J.E. Flynn Capital, LLC, its General Partner)

/s/ David J. Clark
Name: David J. Clark

In the presence of:

Witness signature: /s/ Lawrence Atinsky

Name of Witness: Lawrence Atinsky

Address of Witness: 780 3rd Avenue, 37th Floor
New York, NY 10017

Occupation of Witness: Attorney

EXECUTED and **DELIVERED** as a **DEED** by)

ORCHARD THERAPEUTICS LIMITED) /s/ Mark Rothera
acting by a director

in the presence of

Witness:

Signature: /s/ John Ilett

Name: John Ilett

Address: 108 Cannon Street
London EC4N 6EU

Occupation: Solicitor

Dated 31 May 2019

THE SEVERAL PERSONS LISTED IN SCHEDULE 1

THE COMPANY

DEED OF VARIATION

relating to a

SHAREHOLDERS' AGREEMENT RELATING TO

ORCHARD THERAPEUTICS PLC

DATED 29 MARCH 2017

AS AMENDED AND RESTATED ON 2 AUGUST 2018
AND AS VARIED AND ADHERED TO BY THE COMPANY ON 19 OCTOBER 2018

THIS DEED (the or this "**Deed**") is made on 31 May 2019

BETWEEN:

(1) **THE SEVERAL PERSONS** whose names and addresses are set out in Schedule 1, together constituting an Investor Majority Consent (as defined under the Shareholders' Agreement); and

(2) **ORCHARD THERAPEUTICS PLC** a private limited liability company incorporated in England and Wales with registered number 11494381 and whose registered office is at 108 Cannon Street, London, EC4N 6EU (the "**Company**"),

(each a "**Party**" and together, the "**Parties**").

WHEREAS:

(A) The Series C Investors, the Existing Investors, the Ordinary Shareholders (each as defined therein) and Orchard Therapeutics Limited executed a shareholders' agreement relating to Orchard Therapeutics PLC dated 29 March 2017, as amended and restated on 2 August 2018 and as varied and adhered to by the Company on 19 October 2018 (the "**Shareholders' Agreement**").

(B) The Parties wish to vary the Shareholders' Agreement (i) to amend and restate paragraph 14 of Schedule 5 of the Shareholders' Agreement as set forth herein, (ii) in connection with such amendment, to amend the definition of "Registrable Securities" as set out in paragraph 1.11 of Schedule 5 of the Shareholders' Agreement, and (iii) to remove the thresholds for exercising registration rights.

(C) In accordance with clause 20.3.1 of the Shareholders' Agreement, the Shareholders' Agreement may be varied if such variation is in writing and signed by the Company and shareholders comprising an Investor Majority Consent, in which event such changes shall be binding against all the parties to the Shareholders' Agreement.

IT IS AGREED as follows:

1. **DEFINITIONS AND INTERPRETATION**

1.1 In this Deed:

(a) capitalised terms used and not expressly defined herein shall bear their respective meaning in the Shareholders' Agreement; and

(b) clauses 1.2.1 to 1.2.16 of the Shareholders' Agreement shall be incorporated into this Deed as if set out in full in this Deed and as if references to "this Agreement" were references to "this Deed".

2. **VARIATION**

2.1 In order to give effect to the variation set out in paragraph (B) above, the Parties, representing an Investor Majority Consent as required under clause 20.3.1 of the Shareholders' Agreement, hereby agree that the Shareholders' Agreement shall be varied as follows:

(a)	Para. 1.11 of Schedule 5	this paragraph is hereby deleted in its entirety and amended and restated as follows: "**Registrable Securities**" means: (i) the Series A Shares; (ii) the Series B Shares; (iii) the Series B-2 Shares; (iv) the Series C Shares; (v) any Ordinary Shares issued on conversion of Series A Shares, Series B Shares, Series B-2 Shares or Series C Shares; and (vi) the Ordinary Shares. Notwithstanding the foregoing, "**Registrable**

		Securities" shall exclude (i) any Registrable Securities sold by a person in a transaction in which rights under this Schedule 5 are not assigned in accordance with this Agreement, (ii) any Registrable Securities sold in a registered public offering under the Securities Act or analogous statute of another jurisdiction, (iii) any Registrable Securities sold pursuant to Rule 144 promulgated under the Securities Act or analogous rule of another jurisdiction, and (iv) any securities previously deemed to be Registrable Securities and held by a person for which or for whom the right to request registration or inclusion of Registrable Securities in any registration pursuant to paragraphs 2, 3 and 4 herein has terminated pursuant to Paragraph 14 of this Schedule 5;
(b)	Para. 2.1 of Schedule 5	The phrase "a written request from the Holders of at least a majority or more of the Registrable Securities then outstanding" in the first sentence of paragraph 2.1 shall be replaced with the phrase "a written request from any Holder of Registrable Securities then outstanding".
(c)	Para. 4 of Schedule 5	The phrase "a request from Holders of at least 20% of all Registrable Securities then outstanding" in the first sentence of paragraph 4 shall be replaced with the phrase "a request from any Holder of Registrable Securities then outstanding".
(d)	Para. 14 of Schedule 5	this paragraph is hereby deleted in its entirety and amended and restated as follows: 14. Termination of Registration Rights The right of any Holder to request registration or inclusion of Registrable Securities in any registration pursuant to paragraphs 2, 3 and 4 herein, shall terminate on the earliest to occur of: (i) the closing of a Liquidation Event, as such term is defined in the Articles other than a Liquidation Event undertaken in connection with effecting an IPO; (ii) the fifth (5th) anniversary of an IPO; and (iii) such time as SEC Rule 144 under the Securities Act or another similar exemption under the Securities Act is available for the sale of all of such Holder's shares without limitation during a three-month period without registration.

2.2 References in the Shareholders' Agreement to the "Agreement", "hereof", "hereunder" and expressions of similar import shall be deemed to be references to the Varied Shareholders' Agreement as varied by this Deed

3. **BINDING AGREEMENT**

Except as expressly amended, modified, supplemented or waived hereby, the provisions of Schedule 5 of the Shareholders' Agreement are and will remain in full force and effect.

4. **FURTHER ASSURANCE**

Each Party shall from time to time, at the reasonable request of another Party, as soon as reasonably practicable do all such acts and things, and execute and deliver all documents, in either case, necessary or desirable to give effect to the amendments effected or to be effected pursuant to this Deed.

5. **THIRD PARTY RIGHTS**

A person who is not a Party shall not have any rights under the Contracts (Rights of Third Parties) Act 1999 to enforce or to enjoy the benefit of any term of this Deed.

6. **COUNTERPARTS**

This Deed may be executed in any number of counterparts, each of which when executed and delivered shall constitute a duplicate original, but all the counterparts shall together constitute the one deed.

7. **GOVERNING LAW AND JURISDICTION**

7.1 This Deed and any dispute or claim arising out of or in connection with it or its subject matter or formation (including non-contractual disputes or claims) shall be governed by and construed in accordance with the law of England and Wales.

7.2 Each Party irrevocably agrees that the courts of England and Wales shall have exclusive jurisdiction to settle any dispute or claim arising out of or in connection with this Deed or its subject matter or formation (including non-contractual disputes or claims).

[*Intentionally left blank, Schedules 1 and the signature pages follow.*]

SCHEDULE 1

(1) Name	(2) Address
F-Prime Capital Partners Healthcare Fund IV LP	One Main Street, 13th Floor, Cambridge, MA 02142, United States
F-Prime Capital Partners Healthcare Fund IV-A LP	One Main Street, 13th Floor, Cambridge, MA 02142, United States
Glaxo Group Limited	980 Great West Road, Brentford, Middlesex TW8 9GS
Scottish Mortgage Investment Trust Plc	Calton Square, 1 Greenside Row, Edinburgh EH1 3AN
Unique Diamond Investments Limited	Vistra Corporate Services Centre, Wickhams Cay II, Road Town, Tortola, VG1110 British Virgin Islands
Cowen Healthcare Investments II LP	599 Lexington Avenue, New York City, NY 10022, United States
CHI EF II LP	599 Lexington Avenue, New York City, NY 10022, United States
Deerfield Special Situations Fund, L.P.	c/o Deerfield Management Company, Attn: General Counsel, 780 Third Avenue, 37th Floor New York, NY 10017, United States
Deerfield Private Design Fund III, L.P	c/o Deerfield Management Company, Attn: General Counsel, 780 Third Avenue, 37th Floor New York, NY 10017, United States
Deerfield Private Design Fund IV, L.P.	c/o Deerfield Management Company, Attn: General Counsel, 780 Third Avenue, 37th Floor New York, NY 10017, United States
RA Capital Healthcare Fund, L.P.	20 Park Plaza, Suite 1200, Boston, MA 02116, United States

THIS DEED has been duly executed and delivered as a deed on the date stated above.

EXECUTED as a **DEED** and delivered by **F-PRIME CAPITAL PARTNERS HEALTHCARE** FUND IV LP By: F-Prime Capital Partners Healthcare Advisors Fund IV LP, its General Partner By: Impresa Holdings LLC, its General Partner By: Impresa Management LLC, its Managing Member	)))))))))	/s/ Mary F. Pendergast Name: Mary F. Pendergast

In the presence of:

Witness signature:	/s/ Allan S. Galper.
Name of Witness:	Allan S. Galper
Address of Witness:	One Main Street, 13th Floor Cambridge, MA 02142 USA
Occupation of Witness:	Attorney

EXECUTED as a **DEED** and delivered by **F-PRIME CAPITAL PARTNERS HEALTHCARE FUND IV-A LP** By: F-Prime Capital Partners Healthcare Advisors Fund IV-A LP, its General Partner By: Impresa Holdings LLC, its General Partner By: Impresa Management LLC, its Managing Member	)))))))))	/s/ Mary F. Pendergast Name: Mary F. Pendergast

In the presence of:

Witness signature:	/s/ Allan S. Galper.
Name of Witness:	Allan S. Galper
Address of Witness:	One Main Street, 13th Floor Cambridge, MA 02142 USA
Occupation of Witness:	Attorney

EXECUTED as a **DEED** and delivered by)
GLAXO GROUP LIMITED)
acting by an authorised signatory)

/s/ John Sadler
Name: John Sadler

In the presence of:

Witness signature: /s/ Thomas Goodman

Name of Witness: Thomas Goodman

Address of Witness: 980 Great West Road
Brentford, Middlesex, TW89GS

Occupation of Witness: Corporate Secretariat Associate

EXECUTED as a **DEED** and delivered by)
SCOTTISH MORTGAGE INVESTMENT TRUST PLC)
acting through its agent **BAILLIE GIFFORD & CO.**)
)

/s/ John MacDougall

Name: John MacDougall

In the presence of:

Witness signature: /s/ Eilidh Gillanders

Name of Witness: Eilidh Gillanders

Address of Witness: Calton Square, 1 Greenside Row
Edinburgh, EH1 3AN, UK

Occupation of Witness: Solicitor

EXECUTED as a **DEED** and delivered by)
UNIQUE DIAMOND INVESTMENTS LIMITED)
acting by a director)
)

/s/ Song Hong Fang
Name: Song Hong Fang

In the presence of:

Witness signature: /s/ Dicky To

Name of Witness: Dicky To

Address of Witness: Room 5028-5032
Sun Hung Kai Centre
30 Harbour Road, Wan Chai, Hong Kong

Occupation of Witness: Director

EXECUTED as a **DEED** and delivered by)
COWEN HEALTHCARE INVESTMENTS II LP)
)
By: Cowen Healthcare Investments II GP LLC, its)
General Partner

/s/ Michael Benwitt
Name: Michael Benwitt

In the presence of:

Witness signature: /s/ Michael Baxter

Name of Witness: Michael Baxter

Address of Witness: c/o Cowen Advisors
599 Lexington Ave, 19th Floor
New York, NY 10022

Occupation of Witness: Attorney

EXECUTED as a **DEED** and delivered by)
CHI EF II LP)
)
By:)

/s/ Michael Benwitt
Name: Michael Benwitt

In the presence of:

Witness signature: /s/ Michael Baxter

Name of Witness: Michael Baxter

Address of Witness: c/o Cowen Advisors
599 Lexington Ave, 19th Floor
New York, NY 10022

Occupation of Witness: Attorney

EXECUTED as a **DEED** and delivered by)
DEERFIELD PRIVATE DESIGN FUND III, L.P.)
)
By: Deerfield Mgmt III, L.P., its General Partner)
By: J.E. Flynn Capital III, LLC, its General Partner)

/s/ David J. Clark

Name: David J. Clark, Authorized Signatory

In the presence of:

Witness signature: /s/ Robert Snetiker

Name of Witness: Robert Snetiker

Address of Witness: 780 Third Avenue, 37th Floor
New York, NY 10017
USA

Occupation of Witness: Attorney

EXECUTED as a **DEED** and delivered by)
DEERFIELD PRIVATE DESIGN FUND IV, L.P.)
)
By: Deerfield Mgmt IV, L.P., its General Partner)
By: J.E. Flynn Capital IV, LLC, its General Partner)

/s/ David J. Clark

Name: David J. Clark, Authorized Signatory

In the presence of:

Witness signature: /s/ Robert Snetiker

Name of Witness: Robert Snetiker

Address of Witness: 780 Third Avenue, 37th Floor
New York, NY 10017
USA

Occupation of Witness: Attorney

EXECUTED as a **DEED** and delivered by)
DEERFIELD SPECIAL SITUATIONS FUND, L.P.)
)
By: Deerfield Mgmt, L.P., its General Partner)
By: J.E. Flynn Capital, LLC, its General Partner)

/s/ David J. Clark

Name: David J. Clark, Authorized Signatory

In the presence of:

Witness signature: /s/ Robert Snetiker

Name of Witness: Robert Snetiker

Address of Witness: 780 Third Avenue, 37th Floor
New York, NY 10017
USA

Occupation of Witness: Attorney

EXECUTED as a **DEED** and delivered by)
RA CAPITAL HEALTHCARE FUND, L.P.)
)
By: RA Capital Management, LLC)
Its: General Partner)
)

/s/ James Schneider

Name: James Schneider
Title: Authorised Signatory

In the presence of:

Witness signature: /s/ Natasha Kassin

Name of Witness: Natasha Kassin

Address of Witness: c/o 20 Park Plaza
Suite 1200
Boston, MA 02116

Occupation of Witness: General Counsel and Chief Compliance Officer

EXECUTED and **DELIVERED** as a **DEED** by)

ORCHARD THERAPEUTICS PLC) /s/ Mark Rothera
acting by a director

in the presence of

Witness:

Signature: /s/ Linda Lauren Deleon

Name: Linda Lauren Deleon

Address: 2 Seaport Lane, 8th Floor
Boston, MA 02210

Occupation: Executive Assistant.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in this Registration Statement on Form F-1 of Orchard Therapeutics plc of our report dated March 22, 2019 relating to the financial statements, which appears in Orchard Therapeutics plc's Annual Report on Form 20-F for the year ended December 31, 2018. We also consent to the reference to us under the heading "Experts" in such Registration Statement.

/s/ PricewaterhouseCoopers LLP
Reading, United Kingdom
June 3, 2019