424B4 1 d708154d424b4.htm 424B4

Table of Contents

**Prospectus**

**Filed pursuant to Rule 424(b)(4)**
**Registration No. 333-231916**

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

Orchard therapeutics

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 $14.25 per ADS. Our ADSs are listed on the Nasdaq Global Select Market under the symbol "ORTX." On June 5, 2019, the last reported sale price of our ADSs on the Nasdaq Global Select Market was $15.04 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 | $ 14.25 | $128,250,000 |
| Underwriting discount(1) | $ 0.855 | $ 7,695,000 |
| Proceeds to Orchard Therapeutics plc, before expenses | $ 13.395 | $120,555,000 |

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

Delivery of the ADSs is expected to be made on or about June 10, 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 discount payable by us will be $8.9 million, and the total proceeds available to us, before expenses, will be $138.7 million.

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

*Lead Manager*

**Guggenheim Securities**

*Co-Manager*

**Wedbush PacGrow**

Prospectus dated June 5, 2019

Table of Contents

# Table of contents


| | Page |
|---|---|
| Market, industry and other data | 1 |
| About this prospectus | 2 |
| Presentation of financial information | 3 |
| Prospectus summary | 4 |
| The offering | 19 |
| Risk factors | 21 |
| Special note regarding forward-looking statements | 26 |
| Use of proceeds | 28 |
| Dividend policy | 29 |
| Capitalization | 30 |
| Dilution | 31 |
| Selected consolidated financial data | 32 |
| Management | 34 |
| Related party transactions | 35 |
| Principal shareholders | 39 |
| Description of share capital and articles of association | 42 |
| Description of American depositary shares | 59 |
| Shares and ADSs eligible for future sale | 72 |
| Material income tax considerations | 74 |
| Underwriting | 85 |
| Expenses of this offering | 94 |
| Legal matters | 95 |
| Experts | 96 |
| Service of process and enforcement of liabilities | 97 |
| Where you can find additional information | 99 |
| Incorporation by reference of certain documents | 100 |


*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

Table of Contents

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.

Table of Contents

# 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."

Table of Contents

# 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.

Table of Contents

# 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.

Table of Contents

# 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.

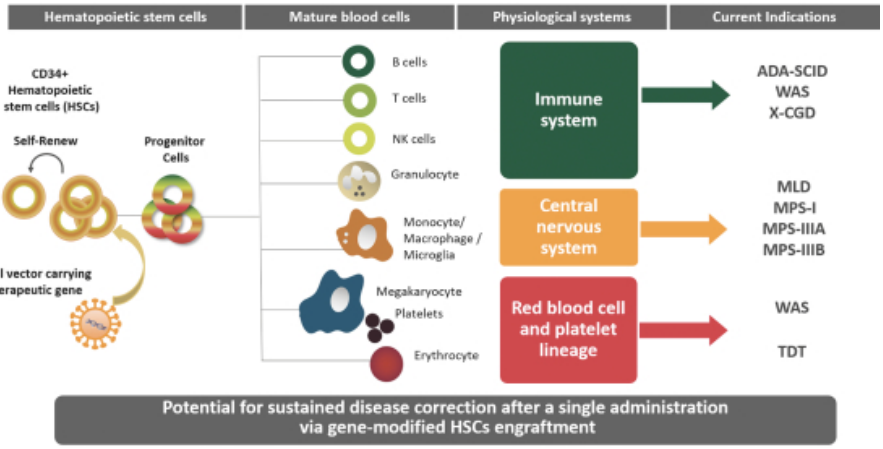
We are initially focusing our *ex vivo* autologous HSC gene therapy approach on three therapeutic rare disease franchise areas: primary immune deficiencies, neurometabolic disorders and hemoglobinopathies. Our portfolio currently includes Strimvelis, our commercial-stage gammaretroviral-based product 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

Table of Contents

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.

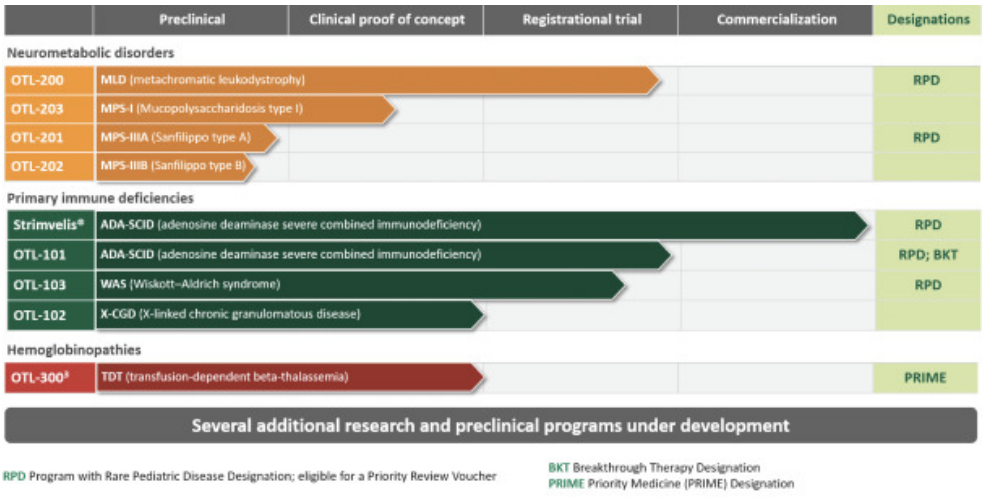



We have a broad and advanced portfolio of commercial- and development-stage products and product candidates. In April 2018, we strengthened our portfolio with our acquisition of Strimvelis for ADA-SCID, OTL-200 for MLD, OTL-103 for WAS and OTL-300 for TDT from Glaxo Group Limited and GlaxoSmithKline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

Table of Contents

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

Table of Contents

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.

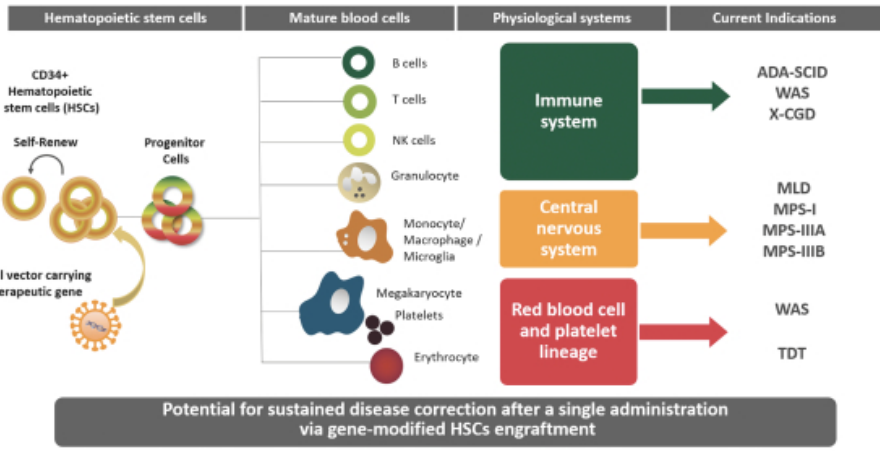
## Our *ex vivo* autologous HSC gene therapy approach

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-

Table of Contents

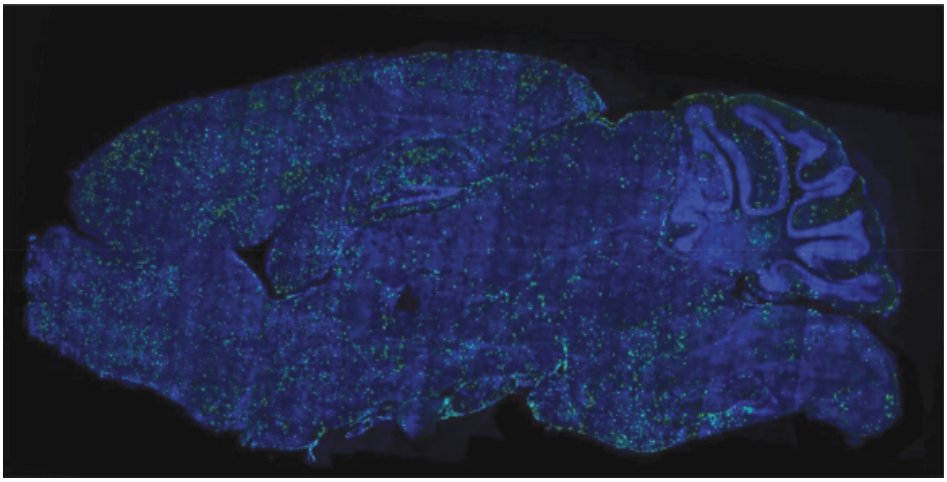
matched donors and the risk of graft-versus-host disease, transplant-related rejection and mortality from these and other complications, and is therefore typically only offered on a limited basis. Our approach is intended to address the significant limitations of HSCT.




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.

Table of Contents

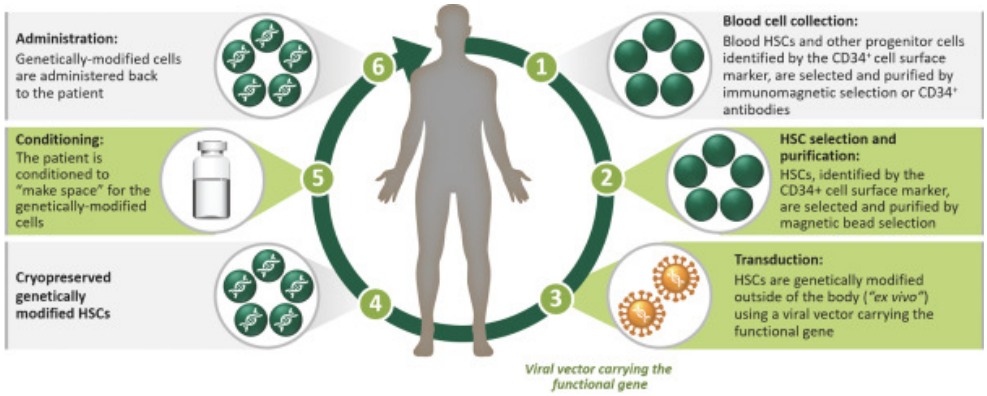
**Transgene distribution in brain of mouse model following administration of HSCs transduced with GFP encoding vector**



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.

Table of Contents

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,

Table of Contents

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

Table of Contents

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.

Table of Contents

- **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.

Table of Contents

- **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.

Table of Contents

***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

Table of Contents

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.

Table of Contents

- 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.

Table of Contents

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.

Table of Contents

## 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 underwriting discount and estimated offering expenses payable by us, to be approximately $119.9 million based on the public offering price of $14.25 per ADS. 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." |

Table of Contents

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.

Table of Contents

# 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;

Table of Contents

- 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 the public offering price of $14.25 per ADS, you will experience immediate dilution of $9.96 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,

Table of Contents

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."

Table of Contents

***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.

Table of Contents

***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.

Table of Contents

# 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;

Table of Contents

- 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.

Table of Contents

# Use of proceeds

We estimate that the net proceeds to us in this offering will be $119.9 million, after deducting the underwriting discount and estimated offering expenses payable by us, based on the public offering price of $14.25 per ADS. 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 $138.0 million, after deducting the underwriting discount and estimated offering expenses payable by us.

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.

Table of Contents

# 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.

Table of Contents

# 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 are based on the public offering price of $14.25 per ADS, after deducting the underwriting discount 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 | $ 415,312 |
| 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; 94,867,028 issued and outstanding, as adjusted | 10,924 | 12,094 |
| Additional paid-in capital | 591,316 | 710,051 |
| Accumulated other comprehensive (loss) income | 6,214 | 6,214 |
| Accumulated deficit | (320,978) | (320,978) |
| Total shareholders' equity | 287,476 | 407,381 |
| Total capitalization | $ 287,476 | $ 407,381 |

(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 the public offering price of $14.25 per share, after deducting the underwriting discount and estimated offering expenses payable by us.

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.

Table of Contents

# 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 the public offering price of $14.25 per ADS, and after deducting the underwriting discount and estimated offering expenses payable by us, our as adjusted net tangible book value at March 31, 2019 would have been $4.29 per ordinary share, or $4.29 per ADS. This represents an immediate increase in as adjusted net tangible book value, of $0.94 per ADS to new investors and immediate dilution of $9.96 per ADS to new investors. The following table illustrates this dilution to new investors purchasing ADSs in this offering:

| | | |
|---|---|---|
| Public offering price per ADS | | $14.25 |
| 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) | 0.94 | |
| As adjusted net tangible book value per ADS as of March 31, 2019 | | 4.29 |
| Dilution per share to new investors purchasing ADSs in this offering | | $ 9.96 |

(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 $4.42, the increase in net tangible book value per ADS to existing shareholders would be $1.07 and the immediate dilution in net tangible book value per ADS to new investors in this offering would be $9.83.

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.

Table of Contents

# 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

Table of Contents

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.

Table of Contents

# 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.

Table of Contents

# 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.

Table of Contents

### 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.

Table of Contents

### 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.

Table of Contents

## 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.

Table of Contents

# 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.

| | Number of shares beneficially owned | Percentage of shares beneficially owned | |
|---|---|---|---|
| **Name of beneficial owner** | | **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% |

Table of Contents

| Name of beneficial owner | Number of shares beneficially owned | Percentage of shares beneficially owned: Before offering | Percentage of shares beneficially owned: 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.

Table of Contents

(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.

Table of Contents

# 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

Table of Contents

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.

Table of Contents

***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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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

Table of Contents

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

Table of Contents

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

Table of Contents

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.

Table of Contents

## 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 |

Table of Contents

| | 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.<br><br>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. |

Table of Contents

| | 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 |

Table of Contents

| | 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:<br>• any breach of the director's duty of loyalty to the corporation or its stockholders;<br>• acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;<br>• intentional or negligent payment of unlawful dividends or stock purchases or redemptions; or<br>• any transaction from which the director derives an improper personal benefit. |

Table of Contents

| | 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.<br><br>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. |

Table of Contents

| | 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:<br>• 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<br>• 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:<br>• the approval of the board of directors; and<br>• 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:<br>• 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;<br>• 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;<br>• 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.<br>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 |

Table of Contents

| | England and Wales | Delaware |
|---|---|---|
| | • to exercise independent judgment;<br>• to exercise reasonable care, skill and diligence;<br>• 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<br>• 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.<br><br>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:<br>• state that the plaintiff was a stockholder at the time of the transaction of which the plaintiff complains or that the plaintiffs |

Table of Contents

| | 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<br>• 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<br>• state the reasons for not making the effort.<br>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.

Table of Contents

# 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

Table of Contents

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.

Table of Contents

## 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.

Table of Contents

***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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

### 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.

Table of Contents

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;

Table of Contents

- 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

Table of Contents

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.

Table of Contents

### 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.

Table of Contents

- 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.

Table of Contents

### 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.

Table of Contents

# 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

Table of Contents

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.”

Table of Contents

# 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.

Table of Contents

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

Table of Contents

- 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

Table of Contents

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

Table of Contents

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

Table of Contents

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.

Table of Contents

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

Table of Contents

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.

Table of Contents

*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

Table of Contents

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

Table of Contents

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.

Table of Contents

# 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 discount 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 | 2,767,500 |
| Goldman Sachs & Co. LLC | 2,362,500 |
| Cowen and Company, LLC | 1,822,500 |
| Barclays Capital Inc. | 1,057,500 |
| Guggenheim Securities, LLC | 540,000 |
| Wedbush Securities Inc. | 450,000 |
| **Total** | **9,000,000** |

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 $0.513 per ADS. 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 1,350,000 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 $0.8550 per ADS. The following table

Table of Contents

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 | $ 0.844 | $ 0.855 |
| **Total** | **$ 7,695,000** | **$ 8,849,250** |

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 discount, 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

Table of Contents

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

Table of Contents

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.

Table of Contents

## 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

Table of Contents

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,

Table of Contents

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).

Table of Contents

***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.

Table of 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.

Table of Contents

# 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 | 29,547 |
| Printing expenses | 65,000 |
| Legal fees and expenses | 350,000 |
| Accounting fees and expenses | 170,000 |
| Miscellaneous costs | 11,982 |
| **Total** | **$ 650,000** |

Table of Contents

# 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 is Davis Polk & Wardwell LLP.

Table of Contents

# 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.

Table of Contents

# 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

Table of Contents

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.

Table of Contents

# 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 (File Number 333-231916) 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.

Table of Contents

# 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***


# PROSPECTUS

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

June 5, 2019