

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**
Washington, D.C. 20549
FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933
ORCHARD THERAPEUTICS PLC
(Exact name of registrant as specified in its charter)

England and Wales
(State or other jurisdiction of
incorporation or organization)

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

245 Hammersmith Road
London W6 8PW
United Kingdom
Tel: +44 (0) 203 808 8286
(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

Cogency Global Inc.
122 East 42nd Street, 18th Floor
New York, New York 10168
+1 212 947 7200
(Name, Address, Including Zip Code, and Telephone Number, Including Area Code, of Agent for Service)
Copies of all communications, including communications sent to agent for service, should be sent to:

Michael H. Bison
Benjamin K. Marsh
Catherine Magazu
Goodwin Procter LLP
100 Northern Avenue
Boston, MA 02210
(617) 570-1000

Andrew Harrow
Goodwin Procter (UK) LLP
100 Cheapside
London EC2V 6DY
United Kingdom
+44 20 7447 4200

Approximate date of commencement of proposed sale to the public: From time to time after this registration statement becomes effective.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box.

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

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

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

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

Large accelerated filer
Non-accelerated filer

Accelerated filer
Smaller reporting company
Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

THE REGISTRANT HEREBY AMENDS THIS REGISTRATION STATEMENT ON SUCH DATE OR DATES AS MAY BE NECESSARY TO DELAY ITS EFFECTIVE DATE UNTIL THE REGISTRANT SHALL FILE A FURTHER AMENDMENT WHICH SPECIFICALLY STATES THAT THIS REGISTRATION STATEMENT SHALL THEREAFTER BECOME EFFECTIVE IN ACCORDANCE WITH SECTION 8(a) OF THE SECURITIES ACT OF 1933, AS AMENDED, OR UNTIL THE REGISTRATION STATEMENT SHALL BECOME EFFECTIVE ON SUCH DATE AS THE COMMISSION ACTING PURSUANT TO SAID SECTION 8(a), MAY DETERMINE.

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

SUBJECT TO COMPLETION, DATED AUGUST 10, 2023

PROSPECTUS



20,825,049 American Depositary Shares
Representing 208,250,490 Ordinary Shares
Offered by the Selling Securityholders

This prospectus relates to the proposed resale or other disposition by the selling securityholders identified herein of (i) up to 99,166,900 of our ordinary shares, nominal value £0.10 per share, or Ordinary Shares, represented by 9,916,690 American Depositary Shares, or ADSs, of which 53,461,574 Ordinary Shares are presently issued and 45,705,326 are issuable upon the redesignation of 45,705,326 non-voting ordinary shares, nominal value £0.10 per share, or Non-Voting Ordinary Shares, and (ii) up to 109,083,590 Ordinary Shares issuable upon the exercise of outstanding warrants to purchase Ordinary Shares held by the selling securityholders (or upon the redesignation of Non-Voting Ordinary Shares that are issuable to holders of warrants upon exercise of such warrants for Non-Voting Ordinary Shares in lieu of Ordinary Shares).

The Ordinary Shares represented by ADSs being offered were issued and sold to qualified institutional buyers or accredited investors in a private placement, or the Private Placement, which consisted of two closings. The initial closing occurred on March 10, 2023 and the second closing occurred on June 22, 2023. We are not selling any ADSs under this prospectus and will not receive any of the proceeds from the sale or other disposition of ADSs by the selling securityholders.

The selling securityholders may sell the ADSs on Nasdaq or any other national securities exchange or quotation service on which the ADSs may be listed at the time of sale, in the over-the-counter market, through ordinary brokerage trades, pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods or through underwriters or broker-dealers, through agents and/or directly to one or more purchasers, or by any other legally available means. These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, or at negotiated prices. See "Plan of Distribution" beginning on page 51 for more information about how the selling securityholders may sell or dispose of their ADSs.

The selling securityholders (which term as used herein includes their respective donees, pledgees, transferees or other successors in interest) may offer and sell or otherwise dispose of any or all of the ADSs described in this prospectus from time to time. The selling securityholders may sell any, all or none of the securities offered by this prospectus and we do not know when or in what amount the selling securityholders may sell their ADSs hereunder.

All expenses of registration incurred in connection with this offering are being borne by us. All selling and other expenses incurred by the selling securityholders will be borne by the selling securityholders.

Our ADSs trade on the Nasdaq Capital Market under the symbol "ORTX". On August 9, 2023, the last reported sale price for our ADSs on the Nasdaq Capital Market was \$5.06 per share.

INVESTING IN THESE SECURITIES INVOLVES CERTAIN RISKS. PLEASE READ THE INFORMATION UNDER THE HEADING "[RISK FACTORS](#)" ON PAGE 7 OF THIS PROSPECTUS AND IN THE DOCUMENTS INCORPORATED BY REFERENCE IN THIS PROSPECTUS FOR A DISCUSSION OF THE FACTORS YOU SHOULD CAREFULLY CONSIDER BEFORE DECIDING TO PURCHASE THESE SECURITIES.

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

The date of this prospectus is _____, 2023

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, utilizing a “shelf” registration process. Under this shelf registration process, certain selling securityholders may from time to time sell any combination of the securities described in this prospectus in one or more offerings.

Neither we nor the selling securityholders have authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus. Neither we nor the selling securityholders take responsibility for, and can provide no assurance as to the reliability of, any other information others may give you. The selling securityholders are offering to sell, and seeking offers to buy, our securities only in jurisdictions where it is lawful to do so. This prospectus does not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor does this prospectus constitute an offer to sell or the solicitation of an offer to buy shares in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained in this prospectus is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus is delivered or shares are sold on a later date. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

Unless the context otherwise indicates, references in this prospectus to “Orchard,” “we,” “our,” “us” and “the Company” refer, collectively, to Orchard Therapeutics plc, a public limited company registered under the laws of England and Wales, and its consolidated subsidiaries.

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.

FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference into it contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Forward-looking statements relate to future events or our future financial performance. Without limiting the foregoing, we generally identify forward-looking statements by terminology such as “may,” “would,” “should,” “expects,” “plans,” “anticipates,” “could,” “intends,” “target,” “projects,” “contemplates,” “believes,” “estimates,” “predicts,” “assume,” “intend,” “potential,” “continue” or other similar words or the negative of these terms. These statements are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. The outcome of the events described in these forward-looking statements is subject to risks, uncertainties and other factors, including those contained in or incorporated by reference into this prospectus and in the sections entitled “Risk Factors” in our most recent Annual Report on Form 10-K, Quarterly Reports on Form 10-Q or Current Reports on Form 8-K. Accordingly, you should not place undue reliance upon these forward-looking statements. We cannot assure you that the events and circumstances reflected in the forward-looking statements will be achieved or occur, and the timing of events and circumstances and actual results could differ materially from those projected in the forward looking statements. Forward-looking statements contained in this prospectus include, but are not limited to, express or implied statements about:

- the timing, progress and results of clinical trials and pre-clinical studies for our programs and product candidates, including statements regarding the timing of initiation and completion of trials or studies and related preparatory work and the period during which the results of the trials or studies will become available;
- the timing, scope and likelihood of regulatory submissions, filings and approvals, including with respect to our biologics license application, or BLA, for OTL-200;
- our ability to develop and advance product candidates into, and successfully complete, clinical trials;
- our expectations regarding the market opportunity for and size of the patient populations for Libmeldy (OTL-200) and our product candidates, if approved for commercial use;
- the implementation of our business model and our strategic plans for our business, commercial products, product candidates and technology;
- our plans and ability to build out our commercial infrastructure and successfully identify eligible patients for Libmeldy in Europe and our product candidates, if approved for commercial use;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the pricing and reimbursement of Libmeldy and any of our product candidates, if approved, including reimbursement for patients treated in a country where they are not a resident;
- the adequacy, scalability and commercial viability of our manufacturing capacity, methods and processes, including those of our manufacturing partners, and our plans for future development;
- the rate and degree of market acceptance and clinical utility of our commercial products and product candidates and gene therapy in general;
- our ability to establish or maintain collaborations or strategic relationships or obtain additional funding;
- our competitive position;
- the scope of protection we and our licensors are able to establish and maintain for intellectual property rights covering our commercial products and product candidates;
- developments and projections relating to our competitors and our industry;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- the impact of laws and regulations;
- our ability to attract and retain qualified employees and key personnel;
- our ability to contract with third-party suppliers, clinical sites and manufacturers and their ability to perform adequately;
- our projected financial condition, including the sufficiency of our cash, cash equivalents and investments to fund operations in future periods and future liquidity, working capital and capital requirements; and

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- other risks and uncertainties, including those listed under the caption “Item 1A. Risk Factors” of our most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q.

The forward-looking statements made or incorporated by reference in this prospectus relate only to events as of the date on which the statements are made. We have included important factors in the cautionary statements included in this prospectus and incorporated herein by reference, including under the caption entitled “Risk Factors” that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make. Except as required by law, we do not assume any intent to update any forward-looking statements after the date on which the statement is made, whether as a result of new information, future events or circumstances or otherwise.

ABOUT ORCHARD THERAPEUTICS PLC

Company Overview

We are a global gene therapy company dedicated to ending the devastation caused by genetic and other severe diseases. We aim to do this by discovering, developing and commercializing new treatments using the curative potential of hematopoietic stem cell, or HSC, gene therapy. Our *ex vivo* autologous HSC gene therapy approach harnesses the power of genetically modified blood stem cells and seeks to correct the underlying cause of disease in a single administration. We seek to achieve this outcome by utilizing a lentiviral vector to introduce a functional copy of a missing or faulty gene into the patient's own, or autologous, HSCs through an *ex vivo* process, resulting in a gene-modified cellular drug product that can then be administered to the patient at the bedside.

To date, over 170 patients have been treated with our current and former product candidates across seven different diseases, with follow-up periods of more than 11 years following a single administration. We believe the data observed across these development programs, in combination with our expertise in the development, manufacturing and commercialization of gene and cell therapies, position us to provide potentially curative therapies to people suffering from a broad range of diseases.

We are currently focusing our *ex vivo* autologous HSC gene therapy approach on severe neurometabolic diseases and early research programs. Our lead program is OTL-200, which was approved in the European Union, the United Kingdom, Iceland, Liechtenstein and Norway under the brand name Libmeldy for eligible patients with early-onset metachromatic leukodystrophy, or MLD. In August 2023 we announced that we completed a rolling BLA for OTL-200.

Our portfolio includes a commercial-stage product and research and development-stage product candidates. 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 drive the migration of gene-corrected cells into multiple physiological systems and organs, including the central nervous system, immune system, red blood cell and platelet lineage, as well as the intestine, lung, bone, and liver. This enables the delivery of therapeutic enzymes and proteins locally to potentially correct multiple severe genetic 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.

Private Placement

In connection with the Private Placement, on March 6, 2023, we entered into a Securities Purchase Agreement, or the Purchase Agreement, with the purchasers named therein, or the Purchasers, pursuant to which we agreed to sell to the Purchasers, up to an aggregate of (i) 99,166,900 shares, consisting of a combination of Ordinary Shares and Non-Voting Ordinary Shares and (ii) accompanying warrants to purchase an aggregate of 109,083,590 Ordinary Shares or Non-Voting Ordinary Shares.

The Private Placement consisted of two closings. On March 10, 2023 we sold in the initial closing of the Private Placement (i) 40,053,500 Ordinary Shares, (ii) 16,613,400 Non-Voting Ordinary Shares and (iii) warrants to purchase an aggregate of 62,333,590 Ordinary Shares or Non-Voting Ordinary Shares, at a purchase price of \$6.00 per ten (10) shares and accompanying warrant to purchase eleven (11) Ordinary Shares or Non-Voting Ordinary Shares. On June 22, 2023, we sold in the second closing of the Private Placement an aggregate of (i) 13,408,074 Ordinary Shares, (ii) 29,091,926 Non-Voting Ordinary Shares and (iii) warrants to purchase an aggregate of 46,750,000 Ordinary Shares or Non-Voting Ordinary Shares, at a purchase price of \$8.00 per ten (10) shares and accompanying warrant to purchase eleven (11) Ordinary Shares or Non-Voting Ordinary Shares.

Purchasers of Non-Voting Ordinary Shares do not have the right to redesignate any Non-Voting Ordinary Shares into Ordinary Shares if such Purchaser, together with its affiliates, would beneficially own in excess of 9.99% of the number of voting Ordinary Shares (including Ordinary Shares that may be represented by ADSs) outstanding

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after giving effect to such redesignation; *provided, however*, that each holder of Non-Voting Ordinary Shares may increase or decrease such percentage by giving us sixty-one (61) days' notice, but not to any percentage in excess of 19.99%.

The warrants will be exercisable during the thirty (30) days following our announcement of receipt of marketing approval of our BLA with respect to OTL-200 for the treatment of MLD in the United States, or the Vesting Event. Each warrant has an exercise price equal to \$1.10 per share in the event the Vesting Event occurs on or prior to December 31, 2024 and \$0.95 per share in the event the Vesting Event occurs after December 31, 2024. The warrants will expire on March 10, 2026, even if approval of our BLA is not received by that date.

The warrants provide that a holder of warrants will not have the right to exercise any portion of its warrants for Ordinary Shares if such holder, together with its affiliates, would beneficially own in excess of 4.99% or 9.99% (at the election of such holder) of the number of voting Ordinary Shares (including Ordinary Shares that may be represented by ADSs) outstanding immediately after giving effect to such exercise; *provided, however*, that each holder may increase or decrease such percentage by giving us sixty-one (61) days' notice, but not to any percentage in excess of 19.99%. If the holder is not permitted to exercise a warrant for Ordinary Shares due to the foregoing limitation, then the holder may exercise the warrant for an equivalent number of Non-Voting Ordinary Shares. If there is no effective registration statement at the time of exercise, the warrants may be exercised on a cashless basis.

The Ordinary Shares and Non-Voting Ordinary Shares issued to the Purchasers, and the Ordinary Shares and Non-Voting Ordinary Shares issuable upon exercise of the warrants, as applicable, were not initially registered under the Securities Act or any state securities laws. We have relied on the exemption from the registration requirements pursuant to Section 4(a)(2) of the Securities Act and Regulation D promulgated thereunder, as a transaction by an issuer not involving a public offering. In connection with their execution of the Purchase Agreement, each of the Purchasers represented that securities purchased by such Purchaser were being acquired for investment only and not with a view to or for resale or distribution thereof.

Pursuant to the Purchase Agreement, we agreed to file a resale registration statement with the SEC within sixty (60) days following the second closing of the Private Placement to register (i) the Ordinary Shares issued and sold in the Private Placement, which may be represented by ADSs, including the Ordinary Shares into which the Non-Voting Ordinary Shares may be redesignated and (ii) the Ordinary Shares issuable upon exercise of the warrants issued and sold in the Private Placement, which may be represented by ADSs, including the Ordinary Shares into which the Non-Voting Ordinary Shares may be redesignated. We also agreed, among other things, to indemnify the Purchasers, their partners, members, officers and directors, and each person who controls such Purchasers, from certain liabilities and to pay certain expenses incurred by us in connection with such registration.

The registration statement of which this prospectus is a part relates to the offer and resale of the ADSs representing the Ordinary Shares issued to the Purchasers pursuant to the Purchase Agreement, including the Ordinary Shares issuable upon exercise of the warrants and redesignation of Non-Voting Ordinary Shares.

Company 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 (Europe) Limited (previously known as Orchard Therapeutics 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 (Europe) Limited was originally incorporated under the laws of England and Wales in September 2015 as Newincco 1387 Limited and subsequently changed its name to Orchard Therapeutics Limited in November 2015 and to Orchard Therapeutics (Europe) Limited in October 2018.

Our registered office is located at 245 Hammersmith Road, London W6 8PW, United Kingdom, and our telephone number is +44 (0) 203 808 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.

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THE OFFERING

ADSs Offered by the Selling Securityholders	Up to 20,825,049 ADSs, each representing ten Ordinary Shares.
Use of Proceeds	We will not receive any proceeds from the sale of the ADSs covered by this prospectus, except with respect to amounts received by us due to the exercise of warrants.
Nasdaq Capital Market Symbol	ORTX
Offering Price	The selling securityholders may offer the ADSs offered by this prospectus at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, or at negotiated prices.
Risk Factors	You should read the “Risk Factors” section of this prospectus for a discussion of factors to consider carefully before deciding to invest in our ADSs.

RISK FACTORS

Investment in any securities offered pursuant to this prospectus involves risks. You should carefully consider the risk factors described below and incorporated by reference to our most recent Annual Report on Form 10-K, Quarterly Reports on Form 10-Q or Current Reports on Form 8-K, and all other information contained or incorporated by reference into this prospectus, as updated by our subsequent filings under the Exchange Act, before acquiring any of such securities. Our business, financial condition or results of operations could be materially adversely affected by the materialization of any of these risks. The trading price of our securities could decline due to the materialization of any of these risks, and you may lose all or part of your investment. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations.

Risks Related to this Offering

The number of shares being registered for sale is significant in relation to the number of our outstanding Ordinary Shares.

We have filed a registration statement of which this prospectus is a part to register the shares offered hereunder for sale into the public market by the selling securityholders. Upon registration of the ADSs representing Ordinary Shares hereunder, 9,916,690 ADSs, representing 99,166,900 Ordinary Shares, registered hereunder may be resold in the public market immediately without restriction. Upon exercise of the warrants, an additional 10,908,359 ADSs, representing 109,083,590 Ordinary Shares, registered hereunder may be resold in the public market without restriction. These shares represent a large number of our Ordinary Shares, and if sold in the market all at once or at about the same time, could depress the market price of our ADSs during the period the registration statement remains effective and could also affect our ability to raise equity capital.

The warrants issued pursuant to the Purchase Agreement may not be exercised.

The warrant holders are not obligated to exercise the warrants, so we may not receive any additional proceeds under the Purchase Agreement. The warrants become exercisable during the 30 days following the Company's announcement of receipt of marketing approval of its BLA with respect to OTL-200. If the Company does not receive marketing approval of its BLA, the warrants will expire on March 10, 2026. In addition, the exercise price of the warrants is lower if OTL-200 is approved by the FDA after 2024, so any proceeds the Company receives from their exercise could be lower than the total amount possible under the Purchase Agreement. If the warrants are not exercised, only a portion of the warrants are exercised, or if the exercise price of the warrants is lower due to a delay in OTL-200 BLA approval, we may need to obtain additional funding to continue operations. Adequate additional financing may not be available to us on acceptable terms or at all.

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 245 Hammersmith Road, London W6 8PW, United Kingdom.

Certain resolutions were passed by our shareholders at our 2021 annual general shareholder meeting. These include resolutions for the:

- general authorization of our directors for purposes of Section 551 of the U.K. 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 from the date of the meeting; and
- empowering of our directors pursuant to Section 570 of the U.K. 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 U.K. Companies Act 2006 did not apply to such allotments.

Certain resolutions were also passed by our shareholders at our 2023 annual general shareholder meeting. These include resolutions for the:

- general authorization of our directors for purposes of Section 551 of the U.K. Companies Act 2006 to issue shares in the Company or to grant rights to subscribe for or convert any securities into shares in the Company up to a maximum aggregate nominal amount of £18,398,450 for a period of five years from the date of the meeting;
- general authorization of our directors for purposes of Section 551 of the U.K. Companies Act 2006 to allot non-voting ordinary shares of the Company and voting ordinary shares of the Company and/or to grant rights to subscribe for or to convert any security into ordinary shares up to a maximum nominal amount of £15,158,359, pursuant to the securities purchase agreement between us and the purchasers named therein, dated March 6, 2023 (including, upon exercise of any warrants granted in accordance with such securities purchase agreement, the allotment and issue of any resulting ordinary shares); and
- empowering of our directors pursuant to Section 570 of the U.K. Companies Act 2006 to allot equity securities for cash pursuant to the Section 551 authority referred to in both cases above as if the statutory preemption rights under Section 561(1) of the U.K. Companies Act 2006 did not apply to such allotments.

This authority to allot shares on a non-pre-emptive basis approved by shareholders at the 2023 annual general meeting is in addition to all subsisting authorities conferred on the directors (including, without limitation, the authority conferred at the 2021 annual general meeting of the Company's shareholders).

Issued Share Capital

As of June 30, 2023, our issued share capital was 181,510,373 ordinary shares with a nominal value of £0.10 per share and 45,705,326 non-voting ordinary shares with a nominal value of £0.10 per share.

We also have in issue one (1) deferred share with a nominal value of £4.89687.

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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 our 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.

Non-Voting Ordinary Shares

In accordance with their terms of issue, our non-voting ordinary shares have the same rights and restrictions as ordinary shares and shall otherwise rank pari passu in all respects, except that:

- each holder of our non-voting ordinary shares is not entitled to receive notice of, or attend or vote at, any general meeting of shareholders (save in relation to variation of class rights attaching to the non-voting ordinary shares);
- the non-voting ordinary shares shall be non-transferable; and
- Subject to the terms of issue, the non-voting ordinary shares may be redesignated as ordinary shares by our board of directors, or a duly authorised representative thereof, only upon receipt of a redesignation notice from the holder of the non-voting ordinary shares.

Deferred Shares

In accordance with our Articles of Association, the following summarizes the main rights of holders of our deferred shares:

- deferred shares shall confer no rights to dividends or to participate in our profits;
- on a return of assets on liquidation, the deferred shares shall confer on the holders thereof an entitlement to receive out of the assets of the Company available for distribution amongst the members (subject to the rights of any new class of shares with preferred rights) the amount credited as paid up on the deferred shares held by them respectively after (but only after) payment shall have been made to the holders of the ordinary shares of the amounts paid up or credited as paid up on such shares and the sum of £1,000,000 in respect of each ordinary share held by them respectively. The deferred shares shall confer on the holders thereof no further right to participate in the assets of the Company;
- the holders of the deferred shares shall not be entitled in their capacity as holders of such shares to receive notice of, attend, speak, form part of the quorum of, or vote at our general meetings;
- any reduction of capital involving the cancellation of the deferred shares for no consideration shall not be deemed to be a variation, modification or abrogation of the rights or privileges attaching to them and the Company shall be authorized at any time to reduce its capital (in accordance with the Companies Act 2006) without obtaining the consent of the holders of the deferred shares;
- any special rights conferred upon the holders of the deferred shares shall be deemed to not be modified, varied or abrogated by the creation or issue of further shares ranking pari passu with or in priority to the deferred shares;

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- no transfer of any deferred shares shall be permitted except as provided below;
- the Company shall have irrevocable authority at any time, without making payment to the holders of the deferred shares, to transfer on behalf of the holders to such person as the Company may determine, to cancel and/or to acquire any of the deferred shares (in accordance with the provisions of the Companies Act 2006); and
- subject to the Companies Act 2006, the Company shall be entitled to purchase any deferred shares in issue at any time for no consideration and the Company shall be entitled to cancel all or any of the deferred shares so acquired by the Company.

Registered Shares

We are required by the U.K. Companies Act 2006 to keep a register of our shareholders. Under English law, the shares are deemed to be issued when the name of the shareholder is entered in our share register. The share register therefore is prima facie evidence of the identity of our shareholders, and the shares that they hold. The share register generally provides limited, or no, information regarding the ultimate beneficial owners of our 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 hold the shares underlying our ADSs. Holders of our ADSs have a right to receive the ordinary shares underlying their ADSs. For a discussion of our ADSs and ADS holder rights, see “Description of American Depositary Shares” in this prospectus.

Under the U.K. 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 are also required by the U.K. 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). At our annual general meetings in June 2021 and June 2023, our shareholders approved the exclusion of preemptive rights for a period of five years from the respective dates of approval, which exclusions 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).

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Registration Rights

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

Demand Registration Rights

Certain holders 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.

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

The 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 with respect to such holder on the earliest of (i) a deemed liquidation event, as defined in our Articles of Association, (ii) the fifth anniversary of the completion of our initial public offering in November 2018 and (iii) such time as SEC Rule 144 under the Securities Act or another similar exemption under the Securities Act is available for the sale of all of such holder's shares without limitation during a three-month period without registration.

Articles of Association

Our current Articles of Association, or the Articles, were adopted by our shareholders at our 2020 annual general shareholder meeting and have been publicly filed with the SEC. A summary of certain key provisions of the Articles, and the relevant provisions of applicable English law, is set out below. The summary below does not purport to be complete and is qualified in its entirety by reference to applicable English law.

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

Share Capital

As of the date of this prospectus, our share capital consists of ordinary shares, non-voting ordinary shares and one deferred share. We may in accordance with section 551 of the Companies Act 2006, be authorized by our shareholders to generally and unconditionally allot shares or grant rights to subscribe for or to convert any security into shares by way of an ordinary resolution. We may issue these shares with such rights or restrictions as may be determined by the ordinary resolution, or if no ordinary resolution is passed or so far as the resolution does not make specific provision, as our board of directors may determine, including shares which are to be redeemed, or are liable to be redeemed at our option or the option of the holder of such shares.

Voting

The holders of ordinary shares 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. The holders of non-voting ordinary shares do not have the right to receive notice of, and to vote at, our general meetings.

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 not less than three-quarters in nominal value of the issued shares of that class or with the authority 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 U.K. 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 U.K. 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 the Company. No dividend or other monies 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.

Our board of directors 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;

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- (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 U.K. 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 U.K. Companies Act 2006, the board of directors may be generally and unconditionally authorized to exercise for each prescribed period of up to five (5) years all the powers of the Company to allot shares or grant rights to subscribe for or to convert any security into 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 ordinary resolutions passed in June 2021 and June 2023 and remain in force at the date of this prospectus.

The provisions of section 561 of the U.K. 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 they are disapplied by the Articles of Association or by shareholders at a general meeting representing at least 75% of ordinary shares present (in person or by proxy) and eligible to vote at that general meeting. Such a disapplication of preemption rights may be for a maximum period of up to five (5) years from the date of the shareholder special resolution. Such preemption rights have been disapplied pursuant to the special resolutions passed at our annual general meetings in June 2021 and June 2023.

Alteration of Share Capital

We may, in accordance with the Companies Act 2006, by ordinary resolution consolidate all or any of our share capital into a smaller number of shares of a larger nominal value than our 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 our share capital by the amount of shares so cancelled, or sub-divide the shares, or any of them, into shares of a smaller nominal amount than our existing shares.

We may, in accordance with the U.K. Companies Act 2006, reduce or cancel our 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.

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Board of Directors

Appointment of Directors

Unless otherwise determined by us 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 U.K. Companies Act 2006, we 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, designated as “Class I”, “Class II” and “Class III”, each of which will consist, as nearly as possible, of one-third of the total number of directors constituting the entire board of directors 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. Directors of the class retiring at the annual general meeting shall be eligible for re-appointment by ordinary resolution at such annual general meeting.

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.

Proceedings of Directors

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 fewer 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 chairperson will have a second or casting vote (unless the chairperson is not entitled to vote on the resolution in question).

Directors' Compensation

Directors shall be entitled to receive such remuneration as the board of directors shall determine for their services to the Company as directors, and for any other service which they undertake for us provided that the aggregate fees payable to the directors must not exceed £250,000 per annum or such higher amount as may from time to time be decided by ordinary resolution of the Company. 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 us.

Conflicts of Interest

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 U.K. Companies Act 2006, to avoid conflicts of interests.

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A director seeking authorization in respect of such conflict shall declare to the board of directors the nature and extent of his interest in a conflict as soon as is reasonably practicable. The director shall provide the board with such details of the matter as are necessary for the board to decide how to address the conflict together with such additional information as may be requested by the board of directors.

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

- (i) to the extent permitted by the U.K. 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.

Permitted Interests

Under our Articles, certain transactions which would otherwise give rise to a conflict are considered to be permitted interests of our directors. In the event that these permitted interests arise, the director in question will still count towards the quorum requirements of the relevant meeting and be entitled to vote on resolutions relating to such permitted interests, including but not limited to the following matters:

- (i) the giving by such director of any security, guarantee or indemnity for any money or any liability which such director, or any other person, has lent or obligations such director or any other person has undertaken at the request, or for the benefit, of us or any of our subsidiary undertakings;
- (ii) the giving of any security, guarantee or indemnity to any other person for a debt or obligation which is owed by us or any of our subsidiary undertakings, to that other person if such director has taken responsibility for some or all of that debt or obligation. Such director can take this responsibility by giving a guarantee, indemnity or security;
- (iii) a proposal or contract relating to an offer of any shares or debentures or other securities for subscription or purchase by us or any of our subsidiary undertakings, if such director takes part because such director is a holder of shares, debentures or other securities, or if such director takes part in the underwriting or sub-underwriting of the offer;
- (iv) any arrangement for the benefit of our employees or the employees of any of our subsidiary undertakings which only gives such director benefits which are also generally given to employees to whom the arrangement relates;
- (v) any arrangement involving any other company if such director (together with any person connected with such director) has an interest of any kind in that company (including an interest by holding any position in that company or by being a shareholder of that company). This does not apply if such director knows that that such director has a relevant interest in a company. A company shall be deemed to be one in which such director has a relevant interest if and so long as (but only if and so long as) such director is to their knowledge (either directly or indirectly) the holder of or beneficially interested in one percent or more of any class of the equity share capital of that company (calculated exclusive of any shares of that class in that company held as treasury shares) or of the voting rights available to shareholders of that company;
- (vi) a contract relating to insurance which we can buy or renew for the benefit of our directors or a group of people which includes our directors; and
- (vii) a contract relating to a pension, superannuation or similar scheme or a retirement, death, disability benefits scheme or employees' share scheme which gives such director benefits which are also generally given to the employees to whom the scheme relates.

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A director is not permitted to vote (or count towards the quorum) on a resolution relating to their own appointment or the settlement or variation of the terms of their appointment to an office or place of profit with us, or any other company in which we have an interest.

Directors' Indemnity

Subject to the provisions of the Companies Act 2006, all of the directors, secretaries or other officers (other than an auditor) shall be indemnified against any loss or liability incurred by them in connection with their duties or powers in relation to us or any of our subsidiaries or any pension fund or employees' share scheme of ours or any of our subsidiaries or in relation to our activities as trustee of any occupational pension scheme which is operated by us from time to time. This indemnity includes any liability incurred by a director in defending any civil or criminal proceedings in which judgment is given in that director's favor or the director is acquitted or the proceedings are otherwise disposed of without any finding or admission of any material breach of duty on his or her part and we may provide the director with funds to meet expenditure incurred in connection with the proceedings set out above

General Meetings

We must convene and hold general meetings in accordance with the U.K. Companies Act 2006. Under the U.K. Companies Act 2006, an annual general meeting must be called by notice of at least 21 clear days and a general meeting must be called by notice of at least 14 clear 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 chairperson of the meeting, which shall not be treated as part of the business of the meeting. Save as otherwise provided by the Articles, shareholders holding thirty-three and one-third percent (33 1/3%) of our issued shares (excluding any shares held as treasury shares) present in person or by proxy (or in the case of a corporation, by a representative) and entitled to vote shall be a quorum for all purposes.

Borrowing Powers

Subject to the Articles and the U.K. 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 all or any part of the undertaking, property and assets (present and future) and uncalled capital of the Company;
- (d) create and issue debentures and other securities; and
- (e) give security either outright or as collateral security for any debt, liability or obligation of the company or of any third party.

Capitalization of Profits

The directors may, if they are so authorized by an ordinary resolution of the shareholders, decide to capitalize any undivided profits of the Company (whether or not they are available for distribution), or any sum standing to the credit of the Company's share premium account or capital redemption reserve. The directors may also, subject to the aforementioned ordinary resolution, appropriate any sum which they so decide to capitalize to the persons who would have been entitled to it if it were distributed by way of dividend and in the same proportions.

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Limitation on Owning Securities

Neither English nor our Articles restrict in any way the ownership or voting of our shares by non-residents.

Uncertificated Shares

Subject to the U.K. 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.

We 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 uncertificated share or otherwise to enforce a lien in respect of it.

Other Relevant UK Laws and Regulations

Mandatory Bid

We believe that, as of the date of this prospectus, our place of central management and control is not in the UK (or the Channel Islands or the Isle of Man) for the purposes of the jurisdictional criteria of the Takeover Code. Accordingly, we believe that we are not currently subject to the Takeover Code and, as a result, our shareholders are not currently entitled to the benefit of certain takeover offer protections provided under the Takeover Code, including the rules regarding mandatory takeover bids (a summary of which is set out below). In the event that this changes, or if the interpretation and application of the Takeover Code by the Takeover Panel changes (including changes to the way in which the Takeover Panel assesses the application of the Takeover Code to English companies whose shares are listed outside of the UK), the Takeover Code may apply to us in the future.

Squeeze-out

(i) Under Sections 979 to 982 of the Companies Act 2006, where a takeover offer has been made for us and the offeror has acquired, or unconditionally contracted to acquire, not less than 90% in value of the shares to which the offer relates and not less than 90% of the voting rights carried by those shares, it could then compulsorily acquire the remaining 10%. It would do so by sending a notice to the 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

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all the ordinary shares of the company is made and the offeror has acquired or unconditionally agreed to acquire not less than 90% in value of the voting shares and not less than 90% of the voting rights carried by those shares, at any time before the end of the period within which the offer could be accepted, 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.

Disclosure of Interest in Shares

Pursuant to Part 22 of the Companies Act 2006, a company incorporated in England and Wales is empowered by notice in writing to require any person whom the company knows to be, or has reasonable cause to believe to be, interested in the company's shares or at any time during the three years immediately preceding the date on which the notice is issued to have been so interested, within a reasonable time to disclose to the company details of that person's interest and (so far as is within such person's knowledge) details of any other interest that subsists or subsisted in those shares.

Under our Articles, if a shareholder defaults in supplying us with the required details in relation to the shares in question, or the Default Shares, within the prescribed period of 14 days, the shareholder shall not be entitled to vote or exercise any other right conferred by membership in relation to general meetings. Where the Default Shares represent 0.25% or more in nominal value of the issued shares of the class in question (calculated exclusive of any shares held as treasury shares), the directors may direct that:

- any dividend or other money payable in respect of the Default Shares shall be retained by us without any liability to pay interest on it when such dividend or other money is finally paid to the shareholder; and/or
- no transfer by the relevant shareholder of shares (other than a transfer permitted in accordance with the provisions of our Articles) may be registered (unless such shareholder is not in default and the transfer does not relate to Default Shares).

Purchase of Own Shares

English law permits a public limited company to purchase its own shares out of the distributable profits of the company or the proceeds of a fresh issue of shares made for the purpose of financing the purchase, subject to complying with procedural requirements under the Companies Act 2006 and provided that its articles of association do not prohibit it from doing so. Our Articles, a summary of which is provided above, do not prohibit us from purchasing our own shares. A public limited company must not purchase its own shares if, as a result of the purchase, there would no longer be any issued shares of the company other than redeemable shares or shares held as treasury shares. Shares must be fully paid in order to be repurchased.

Any such purchase will be either a "market purchase" or "off-market purchase," each as defined in the Companies Act 2006. A "market purchase" is a purchase made on a "recognized investment exchange" (other than an overseas exchange) as defined in the UK Financial Services and Markets Act 2000, as amended, or FSMA. An "off-market purchase" is a purchase that is not made on a "recognized investment exchange." Both "market purchases" and "off-market purchases" require prior shareholder approval by way of an ordinary resolution. In the case of an "off-market purchase," a company's shareholders, other than the shareholders from whom the company is purchasing shares, must approve the terms of the contract to purchase shares and in the case of a "market purchase," the shareholders must approve the maximum number of shares that can be purchased and the maximum and minimum prices to be paid by the company. Both resolutions authorizing "market purchases" and "off-market purchases" must specify a date, not later than five years after the passing of the resolution, on which the authority to purchase is to expire.

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Nasdaq is an “overseas exchange” for the purposes of the Companies Act 2006 and does not fall within the definition of a “recognized investment exchange” for the purposes of FSMA and any purchase made by us would need to comply with the procedural requirements under the Companies Act 2006 that regulate “off-market purchases.”

A buy-back by a company of its shares will generally give rise to UK stamp duty at the rate of 0.5% of the amount or value of the consideration payable by the company (rounded up to the next £5.00).

Our Articles do not have conditions governing changes to our capital which are more stringent than those required by law.

Distributions and Dividends

Under the Companies Act 2006, before a company can lawfully make a distribution or dividend, it must ensure that it has sufficient distributable reserves, as determined on a non-consolidated basis. The basic rule is that a company’s profits available for the purpose of making a distribution are its accumulated, realized profits, so far as not previously utilized by distribution or capitalization, less its accumulated, realized losses, so far as not previously written off in a reduction or reorganization of capital duly made. The requirement to have sufficient distributable reserves before a distribution or dividend can be paid applies to us and to each of our subsidiaries that has been incorporated under English law.

As a public company, it is also not sufficient that we have made a distributable profit for the purpose of making a distribution. An additional capital maintenance requirement is imposed on us to ensure that our net worth is at least equal to the amount of our capital. A public company can only make a distribution:

- if, at the time that the distribution is made, the amount of its net assets (that is, the total excess of assets over liabilities) is not less than the total of its called up share capital and undistributable reserves; and
- if, and to the extent that, the distribution itself, at the time that it is made, does not reduce the amount of the net assets to less than that total.

Shareholder Rights

Certain rights granted under the Companies Act 2006, including the right to requisition a general meeting or require a resolution to be put to shareholders at the annual general meeting, are only available to our shareholders. For English law purposes, our shareholders are the persons who are registered as the owners of the legal title to the shares and whose names are recorded in our share register. If a person who holds their ADSs in DTC wishes to exercise certain of the rights granted under the Companies Act 2006, they may be required to first take steps to withdraw their ADSs from the settlement system operated by DTC and become the registered holder of the shares in our share register. A withdrawal of shares from DTC may have tax implications. For additional information on the potential tax implications of withdrawing your shares from the settlement system operated by DTC, see “Material Income Tax Considerations - UK Taxation.”

Exchange Controls

There are no governmental laws, decrees, regulations or other legislation in the UK that may affect the import or export of capital, including the availability of cash and cash equivalents for use by us, or that may affect the remittance of dividends, interest, or other payments by us to non-resident holders of our ordinary shares or ADSs, other than, on current law, withholding tax requirements that may apply in respect of interest. There is no limitation imposed by English law or in our Articles on the right of non-residents to hold or vote shares.

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.

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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, resolutions appointing each director must be voted on individually.	Under Delaware law, vacancies and newly created directorships may be filled by a majority of the directors then in office (even though less than a quorum) or by a sole remaining director unless (i) otherwise provided in the certificate of incorporation or bylaws of the 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.

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England and Wales

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General Meeting	<p>Under the Companies Act 2006, a general meeting of the shareholders of a public limited company may be called by the directors.</p> <p>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.</p>	<p>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.</p>
Notice of General Meetings	<p>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 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.</p>	<p>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.</p>
Quorum	<p>Subject to the provisions of a company's articles of association, the Companies Act 2006 provides that two shareholders present at a meeting (in person, by proxy or authorized representative under the Companies Act 2006) shall constitute a quorum for companies with more than one shareholder.</p>	<p>The certificate of incorporation or bylaws may specify the number of shares, the holders of which shall be present or represented by proxy at any meeting in order to constitute a quorum, but in no event shall a quorum consist of less than one third of the shares entitled to vote at the meeting. In the absence of such specification in the certificate of incorporation or bylaws, a majority of the shares entitled to vote, present in person or represented by proxy, shall constitute a quorum at a meeting of stockholders.</p>

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England and Wales

Delaware

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. See "Description of Share Capital and Articles of Association—Preemptive Rights" in this prospectus.	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 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.	Under Delaware law, if the corporation's charter or certificate of incorporation so provides, the board of directors has the power to authorize the issuance of stock. 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.

England and Wales

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 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.

Delaware

Under Delaware law, a corporation's certificate of incorporation may include a provision eliminating or limiting the personal liability of a director to the corporation and its stockholders for damages arising from a breach of fiduciary duty as a director. However, no provision can limit the liability of a director for:

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

England and Wales

Delaware

Voting Rights

Under English law, unless a poll is demanded by the shareholders of a company or is required by the chairman of the meeting or the company's articles of association, shareholders shall vote on all resolutions on a show of hands. Under the Companies Act, a poll may be demanded by (i) not fewer than five shareholders having the right to vote on the resolution; (ii) any shareholder(s) representing not less than 10% of the total voting rights of all the shareholders having the right to vote on the resolution (excluding any voting rights attaching to treasury shares); or (iii) any shareholder(s) holding shares in the company conferring a right to vote on the resolution (excluding any voting rights attaching to treasury shares) being shares on which an aggregate sum has been paid up equal to not less than 10% of the total sum paid up on all the shares conferring that right. A company's articles of association may provide more extensive rights for shareholders to call a poll. Under English law, an ordinary resolution is passed on a show of hands if it is approved by a simple majority (more than 50%) of the votes cast by shareholders present (in person or by proxy) and entitled to vote. If a poll is demanded, an ordinary resolution is passed if it is approved by holders representing a simple majority of the total voting rights of shareholders 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.

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.

Shareholder Vote on Certain Transactions

The Companies Act 2006 provides for schemes of arrangement, which are arrangements or compromises between a company and any class of shareholders or creditors and used in certain types of reconstructions, amalgamations, capital reorganizations or takeovers.

These arrangements require:

- the approval at a shareholders' or creditors' meeting convened by order of the court, of a majority in number representing 75% in value of the shareholders or creditors or class thereof present and voting, either in person or by proxy; and
- the approval of the court.

Generally, under Delaware law, unless the certificate of incorporation provides for the vote of a larger portion of the stock, completion of a merger, consolidation, sale, lease or exchange of all or substantially all of a corporation's assets or dissolution requires:

- the approval of the board of directors; and
- the approval by the vote of the holders of a majority of the outstanding stock or, if the certificate of incorporation provides for more or less than one vote per share, a majority of the votes of the outstanding stock of the corporation entitled to vote on the matter.

England and Wales

Standard of Conduct for Directors

Under English law, a director owes various statutory and fiduciary duties to the company, including:

- to act in the way he considers, in good faith, would be most likely to promote the success of the company for the benefit of its members as a whole, and in doing so have regard (amongst other matters) to: (i) the likely consequences of any decision in the long-term, (ii) the interests of the company's employees, (iii) the need to foster the company's business relationships with suppliers, customers and others, (iv) the impact of the company's operations on the community and the environment, (v) the desirability to maintain a reputation for high standards of business conduct, and (vi) the need to act fairly as between members of the company;
- to avoid a situation in which he has, or can have, a direct or indirect interest that conflicts, or possibly conflicts, with the interests of the company;
- to act in accordance with the company's constitution and only exercise his powers for the purposes for which they are conferred;
- to exercise independent judgment;
- to exercise reasonable care, skill and diligence;
- not to accept benefits from a third party conferred by reason of his being a director or doing, or not doing, anything as a director; and
- to declare any interest that he has, whether directly or indirectly, in a proposed or existing transaction or arrangement with the company.

Delaware

Delaware law does not contain specific provisions setting forth the standard of conduct of a director. The scope of the fiduciary duties of directors is generally determined by the courts of the State of Delaware. In general, directors have a duty to act without self-interest, on a well-informed basis and in a manner they reasonably believe to be in the best interest of the stockholders.

Directors of a Delaware corporation owe fiduciary duties of care and loyalty to the corporation and to its shareholders. The duty of care generally requires that a director act in good faith, with the care that an ordinarily prudent person would exercise under similar circumstances. Under this duty, a director must inform himself of all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director act in a manner he reasonably believes to be in the best interests of the corporation. He must not use his corporate position for personal gain or advantage. In general, but subject to certain exceptions, actions of a director are presumed to have been made on an informed basis, in good faith and in the honest belief that the action taken was in the best interests of the corporation. However, this presumption may be rebutted by evidence of a breach of one of the fiduciary duties. Delaware courts have also imposed a heightened standard of conduct upon directors of a Delaware corporation who take any action designed to defeat a threatened change in control of the corporation. In addition, under Delaware law, when the board of directors of a Delaware corporation approves the sale or break-up of a corporation, the board of directors may, in certain circumstances, have a duty to obtain the highest value reasonably available to the shareholders.

England and Wales

Shareholder 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 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.

Delaware

Under Delaware law, a stockholder may initiate a derivative action to enforce a right of a corporation if the corporation fails to enforce the right itself. The complaint must:

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

Stock Exchange Listing

Our ADSs are listed on the Nasdaq Capital Market under the symbol "ORTX".

Transfer Agent and Registrar of Shares

Our share register is maintained by Equiniti Limited. The share register is prima facie evidence of the identity of our shareholders, and the shares that they hold. 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 ten ordinary shares underlying each of their ADSs. For a discussion of the Company's ADSs and ADS holder rights, see "Description of American Depositary Shares" in this prospectus.

DESCRIPTION OF AMERICAN DEPOSITARY SHARES

Citibank, N.A., or Citibank, is the depository for the ADSs. Citibank's depository offices are located at, 388 Greenwich Street, New York, New York 10013. ADSs represent ownership interests in securities that are on deposit with the depository. ADSs may be represented by certificates that are commonly known as American Depositary Receipts, or ADRs. The depository 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 depository 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. A copy of the deposit agreement may be obtained from the SEC's website (www.sec.gov). Please refer to registration number 333-227905 when retrieving such copy.

The following is a summary description of the material terms of the ADSs and of the material rights of owners 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, ten ordinary shares that is on deposit with the depository and/or custodian. An ADS also represents the right to receive, and to exercise the beneficial interests in, any other property received by the depository 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 depository may agree to change the ADS-to-ordinary share ratio by amending the deposit agreement. This amendment may give rise to, or change, the depository fees payable by ADS owners. The custodian, the depository 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 depository, 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 depository, 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 depository, and the depository (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.

Owners of our ADSs 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 such ADSs. The deposit agreement and the ADR specify our rights and obligations as well as the rights and obligations of owners of ADSs and those of the depository. ADS holders appoint the depository to act on their behalf in certain circumstances. The deposit agreement and the ADRs are governed by New York law. However, our obligations to the holders of ordinary shares will continue to be governed by the laws of England and Wales, which may be different from the laws of the United States.

In addition, applicable laws and regulations may require holders of ADSs to satisfy reporting requirements and obtain regulatory approvals in certain circumstances. Holders of ADSs are solely responsible for complying with such reporting requirements and obtaining such approvals. Neither the depository, the custodian, us or any of their or our respective agents or affiliates shall be required to take any actions whatsoever on behalf of holders of ADSs to satisfy such reporting requirements or obtain such regulatory approvals under applicable laws and regulations.

Owners of ADSs will not be treated as one of our shareholders and will not have direct shareholder rights. The depository will hold on the ADS holders' behalf the shareholder rights attached to the ordinary shares underlying such ADSs. Owners of ADSs will be able to exercise the shareholders rights for the ordinary shares represented

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by such ADSs through the depository only to the extent contemplated in the deposit agreement. To exercise any shareholder rights not contemplated in the deposit agreement a holder of ADSs will, as an ADS owner, need to arrange for the cancellation of such ADSs and become a direct shareholder.

The manner in which ADSs are owned (e.g., in a brokerage account vs. as registered holder, or as holder of certificated vs. uncertificated ADSs) may affect the rights and obligations, and the manner in which, and extent to which, the depository's services are made available to the holder of ADSs. Owners of ADSs may hold their ADSs either by means of an ADR registered in their name, through a brokerage or safekeeping account, or through an account established by the depository in their name reflecting the registration of uncertificated ADSs directly on the books of the depository (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 depository. Under the direct registration system, ownership of ADSs is evidenced by periodic statements issued by the depository to the holders of the ADSs. The direct registration system includes automated transfers between the depository and The Depository Trust Company, or DTC, the central book-entry clearing and settlement system for equity securities in the United States. If an ADS owner decides to hold their ADSs through their brokerage or safekeeping account, such holder must rely on the procedures of their broker or bank to assert their 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 such holder's ability to exercise their rights as an owner of ADSs. ADS owners should consult with their broker or bank if they 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 holders of ADSs have opted to own the ADSs directly by means of an ADS registered in their name and, as such, refers to the owner as the "holder." This summary also assumes holders will own ADSs at the relevant time.

The registration of the ordinary shares in the name of the depository or the custodian shall, to the maximum extent permitted by applicable law, vest in the depository 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 depository or the custodian shall at all times be entitled to exercise the beneficial ownership rights in all deposited property, in each case only on behalf of the holders and beneficial owners of the ADSs representing the deposited property.

Dividends and Other Distributions

Holders of ADSs generally have the right to receive the distributions we make on the securities deposited with the custodian. Receipt of these distributions by an ADS holder 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 depository 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 depository 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 depository 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

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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 held will represent rights and interests in the additional ordinary shares so deposited. Only whole new ADSs will be distributed. Fractional entitlements will be sold and the proceeds of such sale will be distributed as in the case of a cash distribution.

The distribution of new ADSs or the modification of the ADS-to-ordinary share ratio upon a distribution of ordinary shares will be made net of the fees, expenses, taxes, and governmental charges payable by holders under the terms of the deposit agreement. In order to pay such taxes or governmental charges, the depositary may sell all or a portion of the new ordinary shares so distributed.

No such distribution of new ADSs will be made if it would violate a law (e.g., the U.S. securities laws) or if it is not operationally practicable. If the depositary does not distribute new ADSs as described above, it may sell the ordinary shares received upon the terms described in the deposit agreement and will distribute the proceeds of the sale as in the case of a distribution of cash.

Distributions of Rights

Whenever we intend to distribute rights to purchase additional ordinary shares, we will give prior notice to the depositary and 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). Holders of ADSs may have to pay fees, expenses, taxes and other governmental charges to subscribe for the new ADSs upon the exercise of their 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 an ADS holder if:

- we do not timely request that the rights be distributed to such holders or we request that the rights not be distributed to such holders;
- 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 ADS holders. In such case, we will assist the depositary in determining whether such distribution is lawful and reasonably practicable.

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The depositary will make the election available to ADS holders 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 ADS holders 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 ADS holders, ADS holders 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 ADS holders. 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 ADS holders and if we provide all of the documentation contemplated in the deposit agreement, the depositary will distribute the property to the holders in a manner it deems practicable.

The distribution will be made net of fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. In order to pay such taxes and governmental charges, the depositary may sell all or a portion of the property received.

The depositary will *not* distribute the property to holders of ADSs and will sell the property if:

- we do not request that the property be distributed to holders of ADSs or if we ask that the property not be distributed to holders of ADSs; or
- we do not deliver satisfactory documents to the depositary; or
- the depositary determines that all or a portion of the distribution to holders of ADSs 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. ADS holders may have to pay fees, expenses, taxes and other governmental charges upon the redemption of their 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 ADSs may change from time to time. For example, there may be a change in nominal or par value, split-up, cancellation, consolidation, or any other reclassification of such ordinary shares or a recapitalization, reorganization, merger, consolidation, or sale of assets of the Company.

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If any such change were to occur, the 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 the holders, amend the deposit agreement, the ADRs and the applicable Registration Statement(s) on Form F-6, call for the exchange of 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 the holders of ADSs, the depositary may sell such property and distribute the net proceeds to such holders as in the case of a cash distribution.

Issuance of ADSs upon Deposit of Ordinary Shares

The depositary may create ADSs on behalf of a holder if such holder or their broker deposits ordinary shares with the custodian. The depositary will deliver these ADSs to the person such holder indicates only after such holder pays any applicable issuance fees and any charges and taxes payable for the transfer of the ordinary shares to the custodian. The ability for a holder 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 a holder makes a deposit of ordinary shares, such holder will be responsible for transferring good and valid title to the depositary. As such, the holder 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;
- the holder is 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 the holder’s cost and expense, take any and all actions necessary to correct the consequences of the misrepresentations.

Transfer, Combination and Split up of ADRs

ADR holders will be entitled to transfer, combine or split up their ADRs and the ADSs evidenced thereby. For transfers of ADRs, a holder 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.

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To have ADRs either combined or split up, a holder must surrender the ADRs in question to the depository with their request to have them combined or split up, and such holder must pay all applicable fees, charges and expenses payable by ADR holders, pursuant to the terms of the deposit agreement, upon a combination or split up of ADRs.

Withdrawal of Ordinary Shares upon Cancellation of ADSs

Holders are entitled to present their ADSs to the depository for cancellation and then receive the corresponding number of underlying ordinary shares at the custodian's offices. The ability of a holder 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 ADSs, a holder will be required to pay to the depository the fees for cancellation of ADSs and any charges and taxes payable upon the transfer of the ordinary shares. Holders 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.

The depository may ask holders who hold ADSs registered in their name to provide proof of identity and genuineness of any signature and such other documents as the depository may deem appropriate before it will cancel such holders' ADSs. The withdrawal of the ordinary shares represented by ADSs may be delayed until the depository receives satisfactory evidence of compliance with all applicable laws and regulations. The depository will only accept ADSs for cancellation that represent a whole number of securities on deposit.

ADS holders have the right to withdraw the securities represented by their 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 ADS holders' right to withdraw the ordinary shares represented by their ADSs except to comply with mandatory provisions of law.

Voting Rights

ADS holders generally have the right under the deposit agreement to instruct the depository to exercise the voting rights for the ordinary shares represented by their 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 depository will distribute to ADS holders any notice of shareholders' meeting received from us together with information explaining how to instruct the depository to exercise the voting rights of the ordinary shares represented by ADSs. In lieu of distributing such materials, the depository bank may distribute to holders of ADSs instructions on how to retrieve such materials upon request.

If the depository 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 depository 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.

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- *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.

If the depositary does not receive voting instructions from a holder of ADSs as of the applicable ADS record date on or before the date established by the depositary for such purpose, such holder will be deemed, and the depositary will deem such holder, to have instructed the depositary to give a discretionary proxy to a person designated by us to vote the securities represented by ADSs; provided, however, that no such discretionary proxy will be given by the depositary with respect to any matter to be voted upon as to which we inform the depositary that (a) we do not wish such proxy to be given, (b) substantial opposition exists or (c) the rights of holders of securities represented by ADSs may be adversely affected.

Securities for which no voting instructions have been received will not be voted (except as otherwise contemplated in the deposit agreement). 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 ADS holders that they will receive voting materials in time to enable them to return voting instructions to the depositary in a timely manner.

Fees and Charges

ADS holders are required to pay the following fees under the terms of the deposit agreement:

Service	Fees
• 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

ADS holders are also be responsible to pay certain charges such as:

- taxes (including applicable interest and penalties) and other governmental charges;
- the registration fees as may from time to time be in effect for the registration of ordinary shares on the share register and applicable to transfers of ordinary shares to or from the name of the custodian, the depositary, or any nominees upon the making of deposits and withdrawals, respectively;
- certain cable, telex and facsimile transmission and delivery expenses;
- the expenses and charges incurred by the depositary in the conversion of foreign currency;

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- the fees and expenses incurred by the depository 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 depository, 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 depository 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 depository fees, the depository may, under the terms of the deposit agreement, refuse the requested service until payment is received or may set off the amount of the depository fees from any distribution to be made to the ADS holder. Certain depository 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 an ADS holder may be required to pay may vary over time and may be changed by us and by the depository. ADS holders will receive prior notice of such changes. The depository 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 depository agree from time to time.

Amendments and Termination

We may agree with the depository to modify the deposit agreement at any time without the consent of ADS holders. We undertake to give holders 30 days' prior notice of any modifications that would materially prejudice any of their substantial rights under the deposit agreement. We will not consider to be materially prejudicial to ADS holders' 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 ADS holders are required to pay. In addition, we may not be able to provide ADS holders with prior notice of any modifications or supplements that are required to accommodate compliance with applicable provisions of law.

ADS holders are bound by the modifications to the deposit agreement if such holder continues to hold their ADSs after the modifications to the deposit agreement become effective. The deposit agreement cannot be amended to prevent ADS holders from withdrawing the ordinary shares represented by their ADSs (except as permitted by law).

We have the right to direct the depository to terminate the deposit agreement. Similarly, the depository may in certain circumstances on its own initiative terminate the deposit agreement. In either case, the depository must give notice to the holders at least 30 days before termination. Until termination, the rights of ADS holders under the deposit agreement will be unaffected.

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Termination

After termination, the depositary will continue to collect distributions received (but will not distribute any such property until an ADS holder requests the cancellation of their 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. ADS holders may inspect such records at such office during regular business hours but solely for the purpose of communicating with other holders in the interest of business matters relating to the ADSs and the deposit agreement.

The depositary will maintain in New York facilities to record and process the issuance, cancellation, combination, split-up and transfer of ADSs. These facilities may be closed from time to time, to the extent not prohibited by law.

Transmission of Notices, Reports and Proxy Soliciting Material

The depositary will make available for ADS holders' 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 ADS holders copies of those communications or otherwise make those communications available to ADS holders if we ask it to.

Limitations on Obligations and Liabilities

The deposit agreement limits our obligations and the depositary's obligations to holders of our ADSs. 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 a holder of ADSs 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.

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- 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 us or the depositary 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 holders of ADSs.
- 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 any 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

ADS holders are 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. ADS holders are 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 behalf of the ADS holders. However, holders of ADSs 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. Holders of ADSs are required to indemnify us, the depositary and the custodian for any claims with respect to taxes based on any tax benefit obtained for such holder.

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. Holders of ADSs may have to pay fees and expenses incurred in converting foreign currency, such as fees and expenses incurred in complying with currency exchange controls and other governmental requirements.

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

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

Governing Law/Waiver of Jury Trial

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

AS A PARTY TO THE DEPOSIT AGREEMENT, HOLDERS OF ADSs IRREVOCABLY WAIVE, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, THEIR RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING ARISING OUT OF THE DEPOSIT AGREEMENT, THE ADRs AND ADSs AGAINST THE COMPANY 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, holders of ADSs 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.

USE OF PROCEEDS

We are registering these securities pursuant to registration rights granted to the selling securityholders. We are not selling any securities under this prospectus and will not receive any of the proceeds from the sale of the ADSs in this offering, except with respect to amounts received by us due to the exercise of the warrants. The selling securityholders will receive all of the proceeds from this offering, except with respect to amounts received by us due to the exercise of the warrants.

SELLING SECURITYHOLDERS

This prospectus covers the sale or other disposition from time to time by the selling securityholders of up to the total number of Ordinary Shares represented by ADSs that were issued to the selling securityholders pursuant to the Purchase Agreement (including upon the redesignation of Non-Voting Ordinary Shares), plus the total number of Ordinary Shares represented by ADSs issuable upon exercise of the warrants issued to the selling securityholders pursuant to the Purchase Agreement (including upon the redesignation of Non-Voting Ordinary Shares that are issuable to holders of warrants upon exercise of such warrants for Non-Voting Ordinary Shares in lieu of Ordinary Shares), without giving effect to the beneficial ownership limitations described under “Company Overview—Private Placement.”

We are registering the above-referenced ADSs to permit each of the selling securityholders and their pledgees, donees, transferees or other successors-in interest that receive their shares after the date of this prospectus to resell or otherwise dispose of the ADSs representing the Ordinary Shares in the manner contemplated under “Plan of Distribution” below.

The following table sets forth the name of each selling securityholder, the number of Ordinary Shares owned by each of the respective selling securityholders (which Ordinary Shares may be represented by ADSs), subject to the beneficial ownership limitations described under “Company Overview—Private Placement,” the number of ADSs that may be offered under this prospectus and the number of our Ordinary Shares owned by the selling securityholders (which Ordinary Shares may be represented by ADSs) assuming all of the ADSs covered hereby are sold. The percentages of shares owned before and after the offering are based on 181,524,753 Ordinary Shares outstanding as of July 31, 2023, which includes ADSs representing the outstanding Ordinary Shares offered by this prospectus but does not include any ADSs representing Ordinary Shares offered by this prospectus that are issuable upon redesignation of the outstanding Non-Voting Ordinary Shares or issuable pursuant to the warrants. In computing the number of shares of Ordinary Shares beneficially owned by a selling securityholder and the percentage ownership of such selling securityholder, we deemed outstanding any Ordinary Shares issuable upon the redesignation of Non-Voting Ordinary Shares held by that selling securityholder within 60 days of July 31, 2023. We did not deem these shares outstanding, however, for the purpose of computing the percentage ownership of any other selling securityholder.

The information set forth below is based upon information obtained from the selling securityholders and upon information in our possession regarding the issuance of Ordinary Shares, Non-Voting Ordinary Shares and warrants to the selling securityholders in connection with the Private Placement. The number of ADSs in the column “Maximum Number of ADSs that may be Offered Pursuant to this Prospectus” represents all of the ADSs that a selling securityholder may offer under this prospectus, assuming the redesignation of all Non-Voting Ordinary Shares and the exercise of all warrants. The selling securityholders may sell some, all or none of their ADSs. We do not know how long the selling securityholders will hold the shares before selling them, and we currently have no agreements, arrangements or understandings with the selling securityholders regarding the sale or other disposition of any of the shares. The ADSs covered hereby may be offered from time to time by the selling securityholders.

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None of the selling securityholders has, or within the past three years has had, any position, office or other material relationship with us.

Name of Selling Securityholders	Ordinary Shares Beneficially Owned Prior to Offering(1)(3)		As-Converted to ADSs Beneficially Owned Prior to Offering(2)	Maximum Number of ADSs that may be Offered Pursuant to this Prospectus	Ordinary Shares Beneficially Owned After Offering(1)(3)	
	Number	Percent			Number	Percent
Entities affiliated with RA Capital Management	18,291,295(4)	9.99%	1,829,129	12,250,014	—	—
Deep Track Biotechnology Master Fund, Ltd.	18,157,618(5)	9.99%	1,815,761	4,287,507	—	—
Entities affiliated with CHI Advisors LLC	18,157,618(6)	9.99%	1,815,761	2,450,007	7,557,380	3.89%
Woodline Master Fund LP	5,933,400(7)	3.27%	593,340	1,225,014	100,000	*
Entities Affiliated with Zentree Investments Limited	20,154,980(8)	11.10%	2,015,498	459,375	17,967,480	9.77%
Albemarle Life Sciences LLP	855,633(9)	*	85,563	153,132	126,433	*

* Less than one percent

- (1) “Beneficial ownership” is a term broadly defined by the SEC in Rule 13d-3 under the Exchange Act, and includes more than the typical form of share ownership, that is, shares held in the person’s name. The term also includes what is referred to as “indirect ownership,” meaning ownership of shares as to which a person has or shares investment power. For purposes of this table, a person or group of persons is deemed to have “beneficial ownership” of any shares underlying options and other purchase rights that are currently exercisable or exercisable within 60 days of July 31, 2023.
- (2) Selling securityholders may hold Ordinary Shares, ADSs or a combination of both. This column shows each holder’s beneficial ownership assuming all shares were held in ADS form, which is not the case. Our ADSs are listed on The Nasdaq Capital Market under the trading symbol “ORTX.” Ordinary Shares are convertible to American Depositary Shares at a ten to one ratio. The Company does not issue fractional shares, so for purposes of these illustrative figures each figure has been rounded down to the nearest whole number.
- (3) Assumes that all ADSs being registered in this prospectus are resold to third parties and that with respect to a particular selling securityholder, such selling securityholder sells all securities registered under this prospectus held by such selling securityholder.
- (4) Consists of (i) 16,720,000 Ordinary Shares held by RA Capital Healthcare Fund, L.P. (the “Fund”) and (ii) 1,571,295 Ordinary Shares currently issuable upon the redesignation of Non-Voting Ordinary Shares held by the Fund within 60 days of July 31, 2023. These amounts exclude 40,042,105 Non-Voting Ordinary Shares held by the Fund which may not be redesignated into Ordinary Shares if such redesignation would result in beneficial ownership of more than 9.99%. The Fund may increase or decrease such beneficial ownership limitation percentage not in excess of 19.99% by providing us with at least 61 days’ prior notice. These amounts also exclude warrants issued in the Private Placement to the Fund through which it will have the right, once exercisable, to acquire 64,166,740 Ordinary Shares, subject to certain beneficial ownership limitations. RA Capital Healthcare Fund GP, LLC is the general partner of the Fund. The general partner of RA Capital Management L.P. (“RA Capital”) is RA Capital Management GP, LLC, of which Peter Kolchinsky and Rajeev Shah are the controlling persons. RA Capital serves as investment adviser for the Fund and may be deemed a beneficial owner, for purposes of Section 13(d) of the Securities Exchange Act of 1934 (“Section 13(d)”), of any of the securities held by the Fund. The Fund has delegated to RA Capital the sole power to vote and the sole power to dispose of all securities held in the Fund’s portfolio, including the securities described herein. Because the Fund has divested voting and investment power over the reported securities it holds and may not revoke that delegation on less than 61 days’ notice, the Fund disclaims beneficial ownership of the securities it holds for purposes of Section 13(d) and therefore disclaims any obligation to report ownership of the reported securities under Section 13(d).

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As managers of RA Capital, Dr. Kolchinsky and Mr. Shah may be deemed beneficial owners, for purposes of Section 13(d), of any of our securities beneficially owned by RA Capital. RA Capital, Dr. Kolchinsky and Mr. Shah disclaim beneficial ownership of such securities other than for the purpose of determining their obligations under Section 13(d). The address of RA Fund is 200 Berkeley Street, 18th Floor, Boston MA 02116.

- (5) Consists of (i) 17,924,427 Ordinary Shares held by Deep Track Biotechnology Master Fund, Ltd. (“Deep Track Biotech”) and (ii) 233,191 Ordinary Shares currently issuable upon the redesignation of Non-Voting Ordinary Shares held by Deep Track Biotech within 60 days of July 31, 2023. These amounts exclude 2,259,082 Non-Voting Ordinary Shares held by Deep Track Biotech which may not be redesignated into Ordinary Shares if such redesignation would result in beneficial ownership of more than 9.99%. Deep Track Biotech may increase or decrease such beneficial ownership limitation percentage not in excess of 19.99% by providing us with at least 61 days’ prior notice. This amount excludes warrants issued in the Private Placement to Deep Track Biotech through which it will have the right, once exercisable, to acquire 22,458,370 Ordinary Shares, subject to certain beneficial ownership limitations. Deep Track Capital, LP (“Deep Track Capital”) and David Kroin have shared voting power and shared dispositive power over the shares held by the Deep Track Biotech. David Kroin may be considered a control person for Deep Track Capital. The address of Deep Track Capital and David Kroin is 200 Greenwich Ave, 3rd Floor, Greenwich, CT 06830, and the address for Deep Track Biotech is 190 Elgin Avenue, George Town, KY1-9001, Cayman Islands.
- (6) Consists of (i) ADSs beneficially owned by CHI Advisors LLC (“CHI Advisors”), which if all held in Ordinary Share form would equal 2,731,170 shares, (ii) Ordinary Shares and ADSs held by CHI IV Public Investments LP (“CHI IV Public Investments”), which if all held in Ordinary Share form would equal 15,193,257 shares, and (iii) 233,191 Ordinary Shares currently issuable upon the redesignation of Non-Voting Ordinary Shares held by CHI IV Public Investments within 60 days of July 31, 2023. These amounts exclude 1,366,462 Non-Voting Ordinary Shares held by CHI IV Public Investments which may not be redesignated into Ordinary Shares if such redesignation would result in beneficial ownership of more than 9.99%. CHI IV Public Investments may increase or decrease such beneficial ownership limitation percentage not in excess of 19.99% by providing us with at least 61 days’ prior notice. These amounts exclude warrants issued in the Private Placement to CHI IV Public Investments through which it will have the right, once exercisable, to acquire 12,833,370 Ordinary Shares, subject to certain beneficial ownership limitations. CHI Advisors is the investment manager of CHI IV Public Investments LP and has sole voting control and investment discretion over securities owned by CHI IV Public Investments LP. The address of CHI Advisors and CHI IV Public Investments LP is 599 Lexington Avenue, 19th Floor, New York, NY 10022.
- (7) Consists of Ordinary Shares and ADSs beneficially owned by Woodline Master Fund LP (the “Fund”), which if all held in Ordinary Share form would equal 5,933,400 shares. This amount excludes warrants issued in the Private Placement to the Fund through which it will have the right, once exercisable, to acquire 6,416,740 Ordinary Shares, subject to certain beneficial ownership limitations. Woodline Partners LP serves as the investment manager of the Fund and may be deemed to be the beneficial owner of the shares. Woodline Partners LP disclaims any beneficial ownership of these shares. The address of the Fund is 4 Embarcadero Center, Suite 3450, San Francisco, CA 94111.
- (8) Consists of (i) Ordinary Shares and ADSs held by Zentree Investments Limited (“Zentree”), which if all held in Ordinary Share form would equal 8,160,450 shares and (ii) Ordinary Shares and ADSs held by Richard Magides, which if all held in ordinary share form would equal 11,994,530 shares. These amounts exclude (i) warrants issued in the Private Placement to Zentree through which it will have the right, once exercisable, to acquire 1,201,325 Ordinary Shares, subject to certain beneficial ownership limitations and (ii) warrants issued in the Private Placement to Mr. Magides through which he will have the right, once exercisable, to acquire 1,201,325 Ordinary Shares, subject to certain beneficial ownership limitations. Mr. Magides is the director of Zentree and may be deemed to have shared voting control and investment discretion over securities owned by Zentree. The address of Zentree and Mr. Magides is 18 Robinson Road, Level 15-01, Singapore 048547.
- (9) Consists of Ordinary Shares and ADSs held by Albemarle Life Sciences LLP (“Albemarle”), which if all held in ordinary share form would equal 855,633 shares. This amount excludes warrants issued in the Private Placement to Albemarle through which it will have the right, once exercisable, to acquire 802,102 Ordinary Shares, subject to certain beneficial ownership limitations. Albemarle’s address is 49 St. James’s Street, 2nd Floor, London, SW1A 1JT.

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 holds our Ordinary Shares or ADSs as a capital asset for tax purposes (generally, property held for investment). In addition, it does not describe all of the tax consequences that may be relevant in light of a U.S. Holder's particular circumstances, including state and local tax consequences, estate tax consequences, alternative minimum tax consequences, the potential application of the Medicare contribution tax, and tax consequences applicable to U.S. Holders subject to special rules, such as:

- banks, insurance companies, and certain other financial institutions;
- U.S. expatriates and certain former citizens or long-term residents of the United States;
- dealers or traders in securities who use a mark-to-market method of tax accounting;
- persons holding Ordinary Shares or ADSs as part of a hedging transaction, "straddle," wash sale, conversion transaction or integrated transaction or persons entering into a constructive sale with respect to Ordinary Shares or ADSs;
- persons whose "functional currency" for U.S. federal income tax purposes is not the U.S. dollar;
- brokers, dealers or traders in securities, commodities or currencies;
- tax-exempt entities or government organizations;
- S corporations, partnerships, or other entities or arrangements classified as partnerships for U.S. federal income tax purposes;
- regulated investment companies or real estate investment trusts;
- persons who acquired our Ordinary Shares or ADSs pursuant to the exercise of any employee stock option or otherwise as compensation; and
- persons holding our Ordinary Shares or ADSs in connection with a trade or business, permanent establishment, or fixed base outside the United States.

If an entity that is classified as a partnership for U.S. federal income tax purposes holds Ordinary Shares or ADSs, the U.S. federal income tax treatment of a partner will generally depend on the status of the partner and the activities of the partnership. Partnerships holding Ordinary Shares or ADSs and partners in such partnerships are encouraged to consult their tax advisers as to the particular U.S. federal income tax consequences of holding and disposing of Ordinary Shares or ADSs.

The discussion is based on Internal Revenue Code of 1986, as amended, or the Code, administrative pronouncements, judicial decisions, final, temporary and proposed Treasury Regulations, and the income tax treaty between the United Kingdom and the United States, or the Treaty, all as of the date hereof, changes to any of which may affect the tax consequences described herein—possibly with retroactive effect.

A "U.S. Holder" is a holder who, for U.S. federal income tax purposes, is a beneficial owner of Ordinary Shares or ADSs 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;

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- (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.

Passive Foreign Investment Company Rules

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

A non-U.S. corporation will be classified as a PFIC for any taxable year in which, after applying certain look-through rules, either:

- at least 75% of its gross income is passive income (such as interest income); or
- at least 50% of its gross assets (determined on the basis of a quarterly average) is attributable to assets that produce passive income or are held for the production of passive income.

We will be treated as owning our proportionate share of the assets and earning our proportionate share of the income of any other corporation, the equity of which we own, directly or indirectly, 25% or more (by value).

Based on the current and expected composition of our income and assets and the value of our assets, we believe that we were a PFIC for U.S. federal income tax purposes for our taxable year ended December 31, 2022. 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.

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If we are classified as a PFIC in any year with respect to which a U.S. Holder owns the Ordinary Shares or ADSs, we will continue to be treated as a PFIC with respect to such U.S. Holder in all succeeding years during which the U.S. Holder owns the Ordinary Shares or ADSs, regardless of whether we continue to meet the tests described above unless (i) we cease to be a PFIC and the U.S. Holder has made a “deemed sale” election under the PFIC rules, or (ii) the U.S. Holder makes a Qualified Electing Fund Election, or QEF Election, with respect to all taxable years during such U.S. Holders holding period in which we are a PFIC. If the “deemed sale” election is made, a U.S. Holder will be deemed to have sold the Ordinary Shares or ADSs the U.S. Holder holds at their fair market value and any gain from such deemed sale would be subject to the rules described below. After the deemed sale election, so long as we do not become a PFIC in a subsequent taxable year, the U.S. Holder’s Ordinary Shares or ADSs with respect to which such election was made will not be treated as shares in a PFIC and the U.S. Holder will not be subject to the rules described below with respect to any “excess distribution” the U.S. Holder receives from us or any gain from an actual sale or other disposition of the Ordinary Shares or ADSs. U.S. Holders should consult their tax advisors as to the possibility and consequences of making a deemed sale election if we cease to be a PFIC and such election becomes available.

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

- the excess distribution or gain will be allocated ratably over a U.S. Holder’s holding period for the Ordinary Shares or ADSs;
- the amount allocated to the current taxable year, and any taxable year prior to the first taxable year in which we became a PFIC, will be treated as ordinary income; and
- the amount allocated to each other year will be subject to the highest tax rate in effect for that year and the interest charge generally applicable to underpayments of tax will be imposed on the resulting tax attributable to each such year.

The tax liability for amounts allocated to years prior to the year of disposition or “excess distribution” cannot be offset by any net operating losses for such years, and gains (but not losses) realized on the sale of the Ordinary Shares or ADSs cannot be treated as capital, even if a U.S. Holder holds the Ordinary Shares or ADSs as capital assets.

Because it was possible that we were a PFIC for the 2022 taxable year, we have provided the information necessary for U.S. holders to make a QEF Election on our website (www.orchard-tx.com). 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

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on Nasdaq, which is a qualified exchange for these purposes. Consequently, if our ADSs remain listed on Nasdaq and are regularly traded, we expect the mark-to-market election would be available to U.S. Holders if we are a PFIC. Each U.S. Holder should consult its tax advisor as to the whether a mark-to-market election is available or advisable with respect to the Ordinary Shares or ADSs.

A U.S. Holder that makes a mark-to-market election must include in ordinary income for each year an amount equal to the excess, if any, of the fair market value of the Ordinary Shares or ADSs at the close of the taxable year over the U.S. Holder's adjusted tax basis in the Ordinary Shares or ADSs. An electing holder may also claim an ordinary loss deduction for the excess, if any, of the U.S. Holder's adjusted basis in the Ordinary Shares or ADSs over the fair market value of the Ordinary Shares or ADSs at the close of the taxable year, but this deduction is allowable only to the extent of any net mark-to-market gains for prior years. Gains from an actual sale or other disposition of the Ordinary Shares or ADSs will be treated as ordinary income, and any losses incurred on a sale or other disposition of the shares will be treated as an ordinary loss to the extent of any net mark-to-market gains for prior years. Once made, the election cannot be revoked without the consent of the Internal Revenue Service, or the IRS, unless the Ordinary Shares or ADSs cease to be marketable.

However, a mark-to-market election generally cannot be made for equity interests in any lower-tier PFICs that we own, unless shares of such lower-tier PFIC are themselves "marketable." As a result, even if a U.S. Holder validly makes a mark-to-market election with respect to our Ordinary Shares or ADSs, the U.S. Holder may continue to be subject to the PFIC rules (described above) with respect to its indirect interest in any of our investments that are treated as an equity interest in a PFIC for U.S. federal income tax purposes. U.S. Holders should consult their tax advisors to determine whether any of these elections would be available and if so, what the consequences of the alternative treatments would be in their particular circumstances.

Unless otherwise provided by the U.S. Treasury, each U.S. shareholder of a PFIC is required to file an annual report containing such information as the U.S. Treasury may require. A U.S. Holder's failure to file the annual report will cause the statute of limitations for such U.S. Holder's U.S. federal income tax return to remain open with regard to the items required to be included in such report until three years after the U.S. Holder files the annual report, and, unless such failure is due to reasonable cause and not willful neglect, the statute of limitations for the U.S. Holder's entire U.S. federal income tax return will remain open during such period. U.S. Holders should consult their tax advisors regarding the requirements of filing such information returns under these rules.

WE STRONGLY URGE YOU TO CONSULT YOUR TAX ADVISOR REGARDING THE IMPACT OF OUR PFIC STATUS ON YOUR INVESTMENT IN THE ORDINARY SHARES OR ADSs AS WELL AS THE APPLICATION OF THE PFIC RULES TO YOUR INVESTMENT IN THE ORDINARY SHARES OR ADSs.

Controlled foreign corporation considerations

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

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We believe that we were not a CFC in the 2022 taxable year, though we have not made a determination regarding our CFC status in the current taxable year, and we may become a CFC in a subsequent taxable year. The determination of CFC status is complex and includes attribution rules, the application of which is not entirely certain. In addition, recent changes to the attribution rules relating to the determination of CFC status may make it difficult to determine our CFC status for any taxable year. It is possible that, following this offering, a shareholder treated as a U.S. person for U.S. federal income tax purposes will acquire, directly or indirectly, enough shares to be treated as a Ten Percent Shareholder. We also believe that immediately following this offering we may have certain shareholders that are Ten Percent Shareholders for U.S. federal income tax purposes. U.S. Holders should consult their own tax advisors with respect to the potential adverse U.S. tax consequences of becoming a Ten Percent Shareholder in a CFC. If we are classified as both a CFC and a PFIC, we generally will not be treated as a PFIC with respect to those U.S. Holders that meet the definition of a Ten Percent Shareholder during the period in which we are a CFC.

Taxation of distributions

Subject to the discussion above under “Passive Foreign Investment Company Rules,” distributions paid on Ordinary Shares or ADSs, other than certain pro rata distributions of Ordinary Shares or ADSs, will generally be treated as dividends to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). Because we 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 “Passive Foreign Investment Company Rules,” gain or loss realized on the sale or other taxable disposition of Ordinary Shares or ADSs will be capital gain or loss, and will be long-term capital gain or loss if the U.S. Holder held the Ordinary Shares or ADSs for more than one year. The amount of the gain or loss will equal the difference between the U.S. Holder’s tax basis in the Ordinary Shares or ADSs disposed of and the amount realized on the disposition, in each case as determined in U.S. dollars. This gain or loss will generally be U.S.-source gain or loss for foreign tax credit purposes. The deductibility of capital losses is subject to limitations.

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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 HM Revenue and Customs, or HMRC, published practice (which is not binding) applying as at the date of this prospectus (both of which are subject to change at any time, possibly with retrospective effect) relating to the holding of ADSs. It does not constitute legal or tax advice and does not purport to be a complete analysis of all U.K. tax considerations relating to the holding of ADSs, or all of the circumstances in which holders of ADSs may benefit from an exemption or relief from U.K. taxation. It is written on the basis that the company is not (and will not) directly or indirectly at any time derive 75% or more of our qualifying asset value from U.K. land, and that it 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

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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 that 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 or to whom split year treatment applies.

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 OR PERSONS SUBJECT TO TAXATION IN ANY JURISDICTION OTHER THAN THE UK ARE ADVISED TO CONSIDER THE POTENTIAL IMPACT OF ANY RELEVANT DOUBLE TAXATION AGREEMENTS.

Dividends

Withholding Tax

Dividends paid by the company will not be subject to any withholding or deduction for or on account of U.K. tax.

Income Tax

An individual U.K. Holder may, depending on his or her particular circumstances, be subject to U.K. tax on dividends received from the company. An individual holder of ADSs who is not resident for tax purposes in the United Kingdom should not be chargeable to U.K. income tax on dividends received from the company unless he or she carries on (whether solely or in partnership) a trade, profession or vocation in the U.K. through a permanent establishment, branch or agency to which the ADSs are attributable. There are certain exceptions for trading in the U.K. through independent agent, such as some brokers and investment managers.

Dividend income is treated as the top slice of the total income chargeable to U.K. income tax for an individual U.K. Holder. An individual U.K. Holder who receives a dividend in the 2023/2024 tax year will be entitled to a tax-free allowance of £1,000. Income within the dividend allowance counts towards an individual's basic or higher rate limits and may, therefore, affect the level of personal allowance to which they are entitled. Dividend income in excess of this tax-free allowance will (subject to the availability of any income tax personal allowance) be charged at 8.75% to the extent the excess amount falls within the basic rate band, 33.75% to the extent the excess amount falls within the higher rate band, and 39.35% to the extent the excess amount falls within the additional rate band. The U.K. government has announced that the dividend tax-free allowance of £1,000 will be reduced to £500 with effect from April 2024 for the tax year 2024/2025 and thereafter.

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

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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. It should be noted that the exemptions, whilst of wide application, are not comprehensive and are subject to anti-avoidance rules in relation to a dividend. If the conditions for the exemption are not satisfied or such anti-avoidance provisions apply, 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 25% in the tax year 2023/2024 for companies with profits of more than £250,000, whilst a rate of 19% will apply to companies with profits not exceeding £50,000 with a tapered rate applying to profits between £50,000 and £250,000).

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% (for the tax year 2023/2024). 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% (for the tax year 2023/2024), save to the extent that any capital gains when aggregated with the U.K. Holder's other taxable income and gains in the relevant tax year exceed the unused basic rate tax band. In that case, the rate applicable to the excess would be 20% (for the tax year 2023/2024).

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 would apply (currently 25% for the tax year 2023/2024 for companies with profits of more than £50,000, whilst a rate of 19% will apply to companies with profits not exceeding £250,000 with a tapered rate applying to profits between £50,000 and £250,000).

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 U.K. through a branch or agency (or, in the case of a corporate holder of ADSs, through a permanent establishment) to which the ADSs are attributable. However, an individual holder of ADSs who has ceased to be resident for tax purposes in the U.K. for a period of less than five years and who disposes of ADSs during that period of temporary non-residence may be liable on his or her return to the U.K. (or upon ceasing to be regarded as resident outside the U.K. for the purposes of double taxation treaty) 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

As a general rule, no U.K. stamp duty or stamp duty reserve tax (or SDRT) is payable on the issue of underlying Ordinary Shares in the company.

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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.

Clearance Services and Depositary Receipts

Under current U.K. legislation, an issue or transfer of Ordinary Shares or an unconditional agreement to transfer Ordinary Shares to a clearance service or a depositary receipt system (including, 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, in the case of transfers, 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.

However, based on current published HMRC practice following European Union 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 in respect of such an issue of Ordinary Shares and no SDRT or stamp duty is generally payable in respect of such a transfer of Ordinary Shares where such transfer is an integral part of an issue of share capital. This position was reaffirmed by HMRC in their January 2021 Newsletter where they confirmed that the SDRT 1.5% charge on issues (or transfers integral to capital raising) remained disappplied under the terms of the European Union (Withdrawal) Act 2018 following the end of the transition period and that this would remain the position unless stamp taxes on shares legislation was amended.

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 transferors or participants in the clearance service or depositary receipt system. Specific professional advice should be sought before incurring or reimbursing the costs of a 1.5% charge.

Transfers of ADSs

No U.K. SDRT or stamp duty is required to be paid in respect of the issue of or an agreement to transfer ADSs (including by way of a paperless transfer of ADSs through the facilities of DTC).

PLAN OF DISTRIBUTION

The selling securityholders and their pledgees, donees, transferees or other successors in interest may offer and sell the Ordinary Shares represented by ADSs from time to time on Nasdaq or any other national securities exchange or quotation service on which the ADSs may be listed at the time of sale, in the over-the-counter market, through ordinary brokerage trades, pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods or through underwriters or broker-dealers, through agents and/or directly to one or more purchasers, or by any other legally available means. The ADSs may be distributed from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

The selling securityholders may also sell shares under Rule 144 under the Securities Act, if available, or Section 4(a)(1) under the Securities Act rather than under this prospectus, provided that they meet the criteria and conform to the requirements of those provisions.

If the selling securityholders effect such transactions by selling shares to or through underwriters, broker-dealers or agents, such underwriters, broker-dealers or agents engaged by the selling securityholders may arrange for other broker-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling securityholders (or, if any broker-dealer acts as agent for the purchaser of shares, from the purchaser) in amounts to be negotiated.

The selling securityholders may, from time to time, pledge or grant a security interest in some or all of the shares owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares from time to time under this prospectus, or under a supplement or amendment to this prospectus amending, if necessary, the list of selling securityholders to include the pledgee, transferee or other successors in interest as selling securityholders under this prospectus.

The selling securityholders have informed us that, except as set forth below, none of them has any agreement or understanding, directly or indirectly, with any person to distribute the Ordinary Shares. If any selling securityholder notifies us that a material arrangement has been entered into with a broker-dealer for the sale of shares through a block trade, special offering or secondary distribution or a purchase by a broker or dealer, we may be required to file a prospectus supplement pursuant to the applicable rules promulgated under the Securities Act. Certain selling securityholders who are entities rather than natural persons may distribute shares to their partners, shareholders or other owners in normal course, who may in turn sell the shares in the manner listed above. The selling securityholders also may transfer the Ordinary Shares in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

In connection with the sale of the Ordinary Shares or interests in Ordinary Shares, the selling securityholders may enter into hedging transactions after the effective date of the registration statement of which this prospectus is a part with broker-dealers or other financial institutions, which may in turn engage in short sales of the shares in the course of hedging the positions they assume. The selling securityholders may also sell shares short after the effective date of the registration statement of which this prospectus is a part and deliver these shares to close out their short positions, or loan or pledge the shares to broker-dealers that in turn may sell these shares. The selling securityholders may also enter into option or other transactions after the effective date of the registration statement of which this prospectus is a part with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction). The selling securityholders

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and any broker-dealers or agents that are involved in selling the shares may be deemed to be “underwriters” within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. Any selling securityholder who is an “underwriter” within the meaning of the Securities Act will be subject to the prospectus delivery requirements of the Securities Act and the provisions of the Exchange Act and the rules thereunder relating to stock manipulation. We have advised the selling securityholders that they are required to comply with Regulation M promulgated under the Exchange Act during such time as they may be engaged in a distribution of the shares. The foregoing may affect the marketability of the shares.

The aggregate proceeds to the selling securityholders from the sale of the ADSs offered by them will be the purchase price of the shares less discounts or commissions, if any. Each of the selling securityholders reserves the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of shares to be made directly or through agents. We will not receive any of the proceeds from this offering.

We will pay all expenses of the registration of the ADSs representing the Ordinary Shares, including, without limitation, SEC filing fees. We have agreed with the selling securityholders to keep the registration statement of which this prospectus supplement constitutes a part effective until such time as the ADSs offered by the selling securityholders have been disposed of in accordance with such registration statement, the ADSs offered by the selling securityholders have been disposed of pursuant to Rule 144 under the Securities Act or the ADSs offered by the selling securityholders may be resold pursuant to Rule 144 without restriction or limitation (including without any limitation as to volume of sales and without the selling securityholder complying with any method of sale requirements or notice requirements under Rule 144).

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC’s website at <http://www.sec.gov>. Copies of certain information filed by us with the SEC are also available on our website at www.orchard-tx.com. The information on our website is not incorporated by reference into this prospectus and should not be considered to be a part of this prospectus. Our website address is included in this prospectus as an inactive technical reference only.

This prospectus is part of a registration statement we filed with the SEC. The registration statement contains more information than this prospectus regarding us and our securities, including certain exhibits and schedules. With respect to the statements contained in this prospectus regarding the contents of any agreement or any other document, in each instance, the statement is qualified in all respects by the complete text of the agreement or document, a copy of which has been filed as an exhibit to the registration statement. You can obtain a copy of the registration statement from the SEC’s website.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded.

This prospectus incorporates by reference the documents listed below (File No. 001-38722) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (in each case, other than

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those documents or the portions of those documents not deemed to be filed) until the offering of the securities under the registration statement is terminated or completed:

- Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2022, filed with the SEC on March 14, 2023;
- the information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2022 from our definitive proxy statement on [Schedule 14A](#) (other than information furnished rather than filed), which was filed with the SEC on April 27, 2023;
- Our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2023 and June 30, 2023, filed with the SEC on [May 15, 2023](#) and [August 10, 2023](#);
- Current Reports on Form 8-K filed with the SEC on [January 5, 2023](#), [February 10, 2023](#), [February 24, 2023](#), [February 27, 2023](#), [March 6, 2023](#), [March 27, 2023](#), and [May 23, 2023](#), [June 14, 2023](#) and [June 26, 2023](#) (in each case, except for information contained therein which is furnished rather than filed); and
- The description of our Ordinary Shares and ADSs contained in our [Registration Statement](#), as filed with the SEC under Section 12(b) of the Exchange Act on October 29, 2018 (File No. 001-38722), including any amendment or report filed for the purpose of updating such description.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address and phone number:

Orchard Therapeutics plc
Attention: Investor Relations
245 Hammersmith Road
London W6 8PW
United Kingdom
+44 (0) 203 808 8286

LEGAL MATTERS

Certain legal matters of English law and U.S. federal law will be passed upon for us by Goodwin Procter (UK) LLP and Goodwin Procter LLP, respectively.

EXPERTS

The financial statements incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2022 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.



**20,825,049 American Depositary Shares
Representing 208,250,490 Ordinary Shares
Offered by the Selling Securityholders
PROSPECTUS**

, 2023

PART II.
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution.

Set forth below is an estimate (except in the case of the registration fee) of the amount of fees and expenses to be incurred in connection with the issuance and distribution of the offered securities, other than underwriting discounts and commissions. All fees and expenses including the amounts set forth below, other than underwriting discounts and commissions and the legal fees of counsel for any party other than us, incurred in connection with the sale of the offered securities will be borne by us.

SEC registration fee	\$ 11,531.98
Legal fees and expenses	\$ 100,000
Accounting fees and expenses	\$ 25,000
Total	<u>\$ 136,531.98</u>

Item 15. Indemnification of Directors and Officers.

Subject to the U.K. Companies Act 2006, members of the Registrant's board of directors and its officers have the benefit of the following indemnification provisions in the registrant's Articles of Association:

Current and former members of the Registrant's board of directors or officers shall be reimbursed for:

- (i) all costs, charges, losses, expenses and liabilities sustained or incurred in relation to his or her actual or purported execution of his or her duties in relation to the Registrant, including any liability incurred in defending any criminal or civil proceedings; and
- (ii) expenses incurred or to be incurred in defending any criminal or civil proceedings, in an investigation by a regulatory authority or against a proposed action to be taken by a regulatory authority, or in connection with any application for relief under the statutes of the United Kingdom and any other statutes that concern and affect the Registrant as a company (collectively, the "Statutes") arising in relation to the Registrant or an associated company, by virtue of the actual or purported execution of the duties of his or her office or the exercise of his or her powers.

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

In addition, members of the Registrant's board of directors and its officers who have received payment from the Registrant under these indemnification provisions must repay the amount they received in accordance with the Statutes or in any other circumstances that the Registrant may prescribe or where the Registrant has reserved the right to require repayment.

In addition, the Registrant has entered or intends to enter into a deed of indemnity with each of its directors and officers. In addition to such indemnification, the Registrant provides its directors and officers with directors' and officers' liability insurance.

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Item 16. Exhibits.

Exhibit No.	Description
3.1	<u>Articles of Association of Orchard Therapeutics plc (filed as Exhibit 3.1 to Registrant's Current Report on Form 8-K (File No. 001-38722), filed with the Securities and Exchange Commission on June 19, 2020 and incorporated herein by reference)</u>
4.1	<u>Deposit Agreement (filed as Exhibit 2.1 to the Registrant's Annual Report on Form 20-F (File No. 001-38722), filed with the Securities and Exchange Commission on March 22, 2019 and incorporated herein by reference)</u>
4.2	<u>Amendment No. 1 to Deposit Agreement (filed as Exhibit 4.2 to the Registrant's Annual Report on Form 10-K (File No. 001-38722), filed with the Securities and Exchange Commission on March 14, 2023 and incorporated herein by reference)</u>
4.3	<u>Form of American Depositary Receipt (filed as Exhibit 2.1 to the Registrant's Annual Report on Form 20-F (File No. 001-38722), filed with the Securities and Exchange Commission on March 22, 2019 and incorporated herein by reference)</u>
4.4	<u>Investment and shareholders' agreement by and between the Registrant and the shareholders named therein, dated August 2, 2018, as amended (filed as Exhibit 10.1 to the Registrant's Registration Statement on Form F-1 (File No. 333-231916), filed with the Securities and Exchange Commission on June 3, 2019 and incorporated herein by reference)</u>
4.5	<u>Securities Purchase Agreement, by and among the Registrant and the investors listed in Exhibit A thereto, dated March 6, 2023 (filed as Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-38722), filed with the Securities and Exchange Commission on March 6, 2023 and incorporated herein by reference)</u>
5.1#	<u>Opinion of Goodwin Procter (UK) LLP</u>
23.1#	<u>Consent of PricewaterhouseCoopers LLP, an Independent Registered Public Accounting Firm</u>
23.2#	<u>Consent of Goodwin Procter (UK) LLP (included in Exhibit 5.1)</u>
24.1#	<u>Powers of Attorney (included in the signature pages to the Registration Statement)</u>
107#	<u>Filing Fee Table</u>

Filed herewith.

Item 17. Undertakings.

The undersigned Registrant hereby undertakes:

- (1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:
 - (i) to include any prospectus required by Section 10(a)(3) of the Securities Act of 1933, as amended, or the Securities Act of 1933;
 - (ii) to reflect in the prospectus any facts or events arising after the effective date of this registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in this registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

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- (iii) to include any material information with respect to the plan of distribution not previously disclosed in this registration statement or any material change to such information in this registration statement; provided, however, that paragraphs (1)(i), (1)(ii) and (1)(iii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the Registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), that are incorporated by reference in this registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of this registration statement.
- (2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at the time shall be deemed to be the initial bona fide offering thereof.
- (3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
- (4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:
 - (i) each prospectus filed by the Registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and
 - (ii) each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii) or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

- (5) That, for the purpose of determining liability of the Registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned Registrant undertakes that in a primary offering of securities of such undersigned Registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, such undersigned Registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:
 - (i) any preliminary prospectus or prospectus of such undersigned Registrant relating to the offering required to be filed pursuant to Rule 424;
 - (ii) any free writing prospectus relating to the offering prepared by or on behalf of such undersigned Registrant or used or referred to by such undersigned Registrant;
 - (iii) the portion of any other free writing prospectus relating to the offering containing material information about such undersigned Registrant or its securities provided by or on behalf of such undersigned Registrant; and
 - (iv) any other communication that is an offer in the offering made by such undersigned Registrant to the purchaser.
- (6) That, for purposes of determining any liability under the Securities Act of 1933, each filing of the Registrant's annual report pursuant to Section 13(a) or 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) that

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is incorporated by reference in this registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the Registrant pursuant to the indemnification provisions described herein, or otherwise, the Registrant has been advised that in the opinion of the Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of London, United Kingdom, on this 10th day of August, 2023.

ORCHARD THERAPEUTICS PLC

By: /s/ Bobby Gaspar
Name: Bobby Gaspar
Title: Chief Executive Officer

SIGNATURES AND POWER OF ATTORNEY

We, the undersigned officers and directors of Orchard Therapeutics plc, hereby severally constitute and appoint Bobby Gaspar and Frank E. Thomas, and each of them singly (with full power to each of them to act alone), our true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution in each of them for him or her and in his or her name, place and stead, and in any and all capacities, to sign for us and in our names in the capacities indicated below the Registration Statement on Form S-3 filed herewith and any and all amendments (including post-effective amendments) to said Registration Statement (or any other registration statement for the same offering that is to be effective upon filing pursuant to Rule 462 under the Securities Act of 1933, as amended) and generally to do all such things in our name and behalf in our capacities as officers and directors to enable Orchard Therapeutics plc to comply with the provisions of the Securities Act of 1933, as amended, and all requirements of the Securities and Exchange Commission, hereby ratifying and confirming our signatures as they may be signed by our said attorneys, or any of them, to said Registration Statement and any and all amendments (including post-effective amendments) thereto.

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
<u>/s/ Bobby Gaspar</u> Bobby Gaspar	Chief Executive Officer and Director (Principal Executive Officer)	August 10, 2023
<u>/s/ Frank E. Thomas</u> Frank E. Thomas	President and Chief Operating Officer (Principal Financial Officer and Principal Accounting Officer)	August 10, 2023
<u>/s/ James A. Geraghty</u> James A. Geraghty	Chairman of the Board of Directors	August 10, 2023
<u>/s/ Steven M. Altschuler</u> Steven M. Altschuler, M.D.	Director	August 10, 2023
<u>/s/ Joanne T. Beck</u> Joanne T. Beck, Ph.D.	Director	August 10, 2023
<u>/s/ John Curnutte</u> John Curnutte, M.D., Ph.D.	Director	August 10, 2023
<u>/s/ Marc Dunoyer</u> Marc Dunoyer	Director	August 10, 2023

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Signature	Title	Date
<u>/s/ Charles A. Rowland, Jr.</u> Charles A. Rowland, Jr.	Director	August 10, 2023
<u>/s/ Alicia Secor</u> Alicia Secor	Director	August 10, 2023
Cogency Global Inc. By: <u>/s/ Colleen A. De Vries</u> Name: Colleen A. De Vries Title: Senior Vice-President on behalf of Cogency Global Inc.	Authorized Representative in the United States	August 10, 2023



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

goodwinlaw.com
+44 (0) 20 7447 4200

10 August 2023

Orchard Therapeutics plc
245 Hammersmith Road
3rd Floor
London
W6 8PW
England

Ladies and Gentlemen:

Orchard Therapeutics plc – Registration Statement on Form S-3 – Exhibit 5.1

We have acted as English legal advisers to Orchard Therapeutics plc, a public limited company incorporated in England and Wales (the “**Company**”) in connection with the preparation and filing on the date hereof with the U.S. Securities and Exchange Commission (the “**SEC**”) of a registration statement on Form S-3 to which this letter is attached as an exhibit (the “**Registration Statement**”) including a prospectus (the “**Prospectus**”) pursuant to the U.S. Securities Act of 1933, as amended (the “**Securities Act**”). The Registration Statement covers the resale by certain selling securityholders of up to 20,825,049 American Depositary Shares of the Company (“**ADSs**”) representing 208,250,490 of the Company’s ordinary shares, nominal value £0.10 per share (“**Ordinary Shares**”), consisting of (i) 99,166,900 Ordinary Shares represented by 9,916,690 ADSs, of which 53,461,574 Ordinary Shares are presently issued and 45,705,326 are issuable upon the redesignation of 45,705,326 non-voting ordinary shares, nominal value £0.10 per share (“**Non-Voting Ordinary Shares**” and together with the Ordinary Shares, the “**Shares**”), and (ii) up to 109,083,590 Ordinary Shares issuable upon the exercise of outstanding warrants (the “**Warrants**”) to purchase Ordinary Shares held by the selling securityholders (or upon the redesignation of Non-Voting Ordinary Shares that are issuable to holders of the Warrants upon exercise of such Warrants for Non-Voting Ordinary Shares in lieu of Ordinary Shares) and represented by up to 10,908,359 ADSs (the “**Warrant Shares**”).

The filing of the Registration Statement is in connection with the private placement of the Shares and the Warrants pursuant to a securities purchase agreement dated 6 March 2023 (the “**Purchase Agreement**”) by and among the Company and the Purchasers (as defined in the Purchase Agreement) set out therein. The Purchase Agreement provides for the registration of (i) the Ordinary Shares issued and sold under the Purchase Agreement, which may be represented by ADSs, (ii) the Ordinary Shares resulting from the redesignation of Non-Voting Ordinary Shares issued and sold under the Purchase Agreement, which may be represented by ADSs and (iii) the Warrant Shares (collectively, the “**Registrable Shares**”) and, in particular, includes the terms of issue attaching to the Non-Voting Ordinary Shares attached thereto at Exhibit B (the “**Terms of Issue**”).

The Company’s ADSs are listed on The Nasdaq Capital Market under the symbol “ORTX”.

We understand that the existing issued Ordinary Shares are not, and are not intended to be, admitted to trading on any market or exchange, or otherwise listed, in the United Kingdom.

1. INTRODUCTION

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

1.1 Purpose

In connection with the preparation and filing of a registration statement on Form S-3, we have been asked to provide opinions on certain matters, as set out below. We have taken instruction in this regard solely from the Company.

1.2 Defined terms and headings

In this letter:

- (a) capitalised terms used without definition in this letter or the schedules hereto have the meanings assigned to them in the Registration Statement unless a contrary indication appears; and
- (b) headings are for ease of reference only and shall not affect interpretation.

1.3 Legal review

For the purpose of issuing this letter, we have examined such questions of law as we have considered appropriate. We have reviewed the following documents and conducted only the following enquiries and searches:

- (a) an online search at Companies House in respect of information available for inspection on the Company's file conducted on 10 August 2023 at 10.00 a.m. (London time);
- (b) an enquiry of the Central Index of Winding Up Petitions, London on 10 August 2023 at 10.00 a.m. (London time) ((a) and (b) together, the "**Searches**");
- (c) a certificate dated 10 August 2023 signed by the President and Chief Operating Officer of the Company (the "**Certificate**") relating to certain factual matters as at the date of the Certificate and having annexed thereto copies (certified by the President and Chief Operating Officer of the Company as being true, complete, accurate and up-to-date in each case) of the following documents:
 - i. PDF executed copies of resolutions of the board of directors of the Company (the "**Board**") dated 5 March 2023 and the transaction committee constituted by certain members of the Board (the "**Transaction Committee**") dated 5 March 2023 authorising the Company, *inter alia*, to issue for sale the Shares and the Warrants in accordance with the offer terms set out in the Purchase Agreement and the Warrants;
 - ii. PDF executed copies of the resolutions passed by the shareholders of the Company at (a) the general meeting of the Company held on 16 June 2021 and (b) the general meeting of the Company held on 14 June 2023, at both of which it was resolved, *inter alia*, to grant authorities to the Board for the purposes of sections 551 and 570 of the Companies Act 2006, as amended to allot shares or grant rights to subscribe for shares (the "**Shareholder Resolutions**");
 - iii. a PDF copy of the current articles of association of the Company adopted on 17 June 2020 (the "**Articles**");

- iv. PDF copies of (a) the certificate of incorporation of the Company dated 1 August 2018 and (b) the certificate of incorporation on re-registration of the Company as a public limited company dated 29 October 2018; and
 - v. a PDF copy of the Terms of Issue in relation to the Non-Voting Ordinary Shares issued pursuant to the Purchase Agreement,
- (d) a PDF copy of the duly executed Purchase Agreement dated 6 March 2023 which for the avoidance of doubt includes the Terms of Issue (referred to above);
- (e) PDF executed copies of the Warrants issued to each Purchaser by the Company at each Closing (as defined in the Purchase Agreement) pursuant to which the Company granted each Purchaser the right to subscribe for and purchase a certain number of Warrant Shares in the Company (in accordance with the terms of the Purchase Agreement); and
- (f) a draft copy of the Registration Statement (which for the avoidance of doubt includes the Prospectus) to be filed with the SEC on 10 August 2023.

1.4 **Applicable law**

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

- (a) we have not investigated the laws of any country other than England and we express no opinion in this letter on the laws of any jurisdiction other than England and we assume that no foreign law affects any of the opinions given below. It is assumed that no foreign law which may apply to the matters contemplated by the Prospectus Supplement, the Company, any document or any other matter contemplated by any document would or might affect this letter and/or the opinions given in it;
- (b) we do not undertake or accept any obligation to update this letter and/or the opinions given in it to reflect subsequent changes in English law or factual matters; and
- (c) we express no opinion in this letter on the laws of any jurisdiction other than England. It is assumed that no foreign law which may apply to the matters contemplated by the Registration Statement, the Company, any document or any other matter contemplated by any document would or might affect this letter and/or the opinions given in it.

1.5 Assumptions and reservations

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

2. OPINIONS

Subject to paragraph 1 (*Introduction*) and the other matters set out in this letter and its schedules, we are of the opinion that as at today's date:

- (a) the Company is a public limited company duly incorporated under English law, noting the Searches revealed no order or resolution for the winding-up of the Company and no notice of the appointment of a receiver or administrator in respect of it or any of its assets;
- (b) the Ordinary Shares represented by ADSs, when issued and sold as contemplated in the Registration Statement, the Prospectus and any related Prospectus supplement(s) and in accordance with the Purchase Agreement, will be duly and validly authorised and issued, fully paid or credited as fully paid and will not be subject to any call for payment of further capital; and
- (c) the Warrant Shares represented by ADSs, when issued against payment therefore in accordance with the terms of the Warrants and sold as contemplated in the Registration Statement, the Prospectus and any related Prospectus supplement(s), will be duly and validly authorised and issued, fully paid or credited as fully paid and will not be subject to any call for payment of further capital.

3. EXTENT OF OPINIONS

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

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

4. DISCLOSURE AND RELIANCE

This letter is addressed to you in connection with the Registration Statement. We consent to the filing of this letter as an exhibit to the Registration Statement. In giving such consent, we do not thereby admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations thereunder.

Orchard Therapeutics plc
10 August 2023
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Other than for the purpose set out in the prior paragraph, this letter may not be relied upon, or assigned, for any purpose, without our prior written consent, which may be granted or withheld in our discretion.

Yours faithfully

/s/ Goodwin Procter (UK) LLP

Goodwin Procter (UK) LLP

SCHEDULE 1

ASSUMPTIONS

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

- (a) the genuineness of all signatures, stamps and seals on all documents, the authenticity and completeness of all documents submitted to us as originals, and the conformity to original documents of all documents submitted to us as copies;
- (b) that each of the individuals who signs as, or otherwise claims to be, an officer of the Company is the individual whom they claim to be and holds the office they claim to hold;
- (c) the accuracy as to factual matters of each document we have reviewed;
- (d) that, where a document has been examined by us in draft or specimen form, it will be or has been duly executed in the form of that draft or specimen, and that each of the signed documents examined by us has been duly executed and, where applicable, delivered on behalf of the Company;
- (e) that the Articles remain in full force and effect and no alteration has been made or will be made to such articles of association, in each case prior to the date of allotment and issue of any of the Registrable Shares (the “**Allotment Date**”);
- (f) that all documents, forms and notices which should have been delivered to the Registrar of Companies in respect of the Company have been so delivered, that information revealed by the Searches was complete and accurate in all respects and has not, since the time of the Searches, been altered and that the results of the Searches will remain complete and accurate as at the date of the Registration Statement;
- (g) that the Registration Statement (including the Prospectus), as finally amended, has become effective under the Securities Act;
- (h) that the contents of the Certificate were true and not misleading when given and remain true and not misleading as at the date of this letter and there is no fact or matter not referred to in the Certificate which could make any of the information in the Certificate inaccurate or misleading;
- (i) the Registrable Shares are not, and are not intended to be, admitted to trading on any market or exchange, or otherwise listed, in the United Kingdom;
- (j) that all documents, forms and notices which should have been delivered to the Registrar of Companies in respect of the Company have been so delivered, that information revealed by the Searches was complete and accurate in all respects and has not, since the time of the Searches, been altered and that the results of the Searches will remain complete and accurate as at the date of the Registration Statement;

- (k) an appropriate prospectus supplement with respect to the Registrable Shares has been prepared, delivered and filed in compliance with the Securities Act and the rules and regulations thereunder;
- (l) that the resolutions of the Board and the Transaction Committee provided to us in connection with the giving of this opinion were duly and validly passed in accordance with the requirements of the Companies Act 2006 and have not been rescinded or amended and each remains in full force and effect and that any provisions contained in the Companies Act 2006 or the Articles relating to the declaration of directors' interests of the power of interested directors to vote were duly observed;
- (m) in respect of the resolutions of the Board and the Transaction Committee provided to us in connection with the giving of this opinion, (i) in passing such resolutions the directors of the Company were acting in good faith, (ii) the transactions and other matters referred to in the resolutions were or are to be entered into and effected by the Company for the purpose of carrying on its business, (iii) at the time such transactions or matters were or (as the case may be) are to be entered into or effected the directors of the Company had or (as the case may be) will have reasonable grounds for believing that the transactions or matters would or (as the case may be) will promote the success of such company for the benefit of its members as a whole and (iv) the directors of the Company exercise their powers in connection with the transactions or matters in accordance with all applicable laws and the memorandum and articles of association of the Company;
- (n) that the Shareholder Resolutions provided to us in connection with the giving of this opinion are a true record of the resolutions of the Company' shareholders, were duly and validly passed in accordance with the requirements of the Companies Act 2006 and, as at the Allotment Date, have not been rescinded or amended and remain in full force and effect;
- (o) that, as at the Allotment Date, the directors have not issued shares, or granted rights to subscribe for, or to convert, any security into, shares which would, when aggregated with the allotment of Registrable Shares, result in the directors exceeding the limited prescribed by the Shareholder Resolutions;
- (p) that in relation to the allotment and issue of the Registrable Shares, the directors of the Company have acted and will act in the manner required by section 172 of the Companies Act (Duty to promote the success of the Company), and there has not been and will not be any bad faith, breach of trust, fraud, coercion, duress or undue influence on the part of any of the directors of the Company;
- (q) the Shares and the Warrants have been sold and issued in accordance with the Purchase Agreement, or similar agreement duly authorised, executed and delivered as may be required from time to time;
- (r) the Warrant Shares will be issued in accordance with the Warrants, if and when such Warrants are exercised in accordance with their terms;

- (s) that the issue of the Shares and the Warrants was accurately and properly completed, duly authorised, executed and delivered on behalf of the Company and authenticated, issued and paid for and, in the case of the Shares, registered in the register of holders of shares maintained for this purpose, in accordance with the then operative Articles and all applicable laws (for the avoidance of doubt, as in force at all relevant times);
- (t) that the Warrant Shares when issued will be accurately and properly completed, duly authorised, executed and delivered on behalf of the Company and authenticated, issued and paid for and registered in the register of holders of shares maintained for this purpose, in accordance with the then operative Articles and all applicable laws (for the avoidance of doubt, as in force at all relevant times);
- (u) the directors of the Company, including the Transaction Committee or other appropriate committee appointed thereby, and appropriate officers of the Company have taken all necessary corporate action to approve the allotment and issue of the Registrable Shares and related matters;
- (v) that the directors of the Company acted or will act in accordance with sections 171 to 174 of the UK Companies Act 2006 in approving the board resolutions and that all actions to be carried out by the Company are or will be in its commercial interests;
- (w) that there are no facts or circumstances (and no documents, agreements, instruments or correspondence) which are not apparent from the face of the documents listed in paragraph 1.3 or which have not been disclosed to us that may affect the validity or enforceability of the documents listed in paragraph 1.3 or any obligation therein or otherwise affect the opinions expressed in this letter;
- (x) that no Registrable Shares shall be allotted or issued, or are or shall be committed to be allotted or issued, at a discount to their nominal value (whether in dollars or equivalent in any other currency);
- (y) that no Registrable Shares or rights to subscribe for Registrable Shares have been or shall be offered to the public in the United Kingdom in breach of the Financial Services and Markets Act 2000 (“**FSMA**”) or of any other United Kingdom laws or regulations concerning offers of securities to the public, and no communication has been or shall be made in relation to the Registrable Shares in breach of section 21 of the FSMA or any other United Kingdom laws or regulations relating to offers or invitations to subscribe for, or to acquire rights to subscribe for or otherwise acquire, shares or other securities;
- (z) that the Company has not taken any corporate or other action nor have any steps been taken or legal proceedings been started against the Company for the liquidation, winding up, dissolution, reorganisation or bankruptcy of, or for the appointment of a liquidator, receiver, trustee, administrator, administrative receiver or similar officer of, the Company or all or any of its assets (or any analogous proceedings in any jurisdiction) and the Company is not unable to pay its debts as they fall due within the meaning of section 123 of the Insolvency Act 1986 and will not become unable to pay its debts within the meaning of that section as a result of any of the transactions contemplated herein, is not insolvent and has not been dissolved or declared bankrupt (although the Searches gave no indication that any winding-up, dissolution or administration order or appointment of a receiver, administrator, administrative receiver or similar officer has been made with respect to the Company); and

- (aa) the Company is not, nor will be, engaging in criminal, misleading, deceptive or unconscionable conduct or seeking to conduct any relevant transaction or any associated activity in a manner or for a purpose which might render any transaction contemplated under any corporate approvals or any associated activity illegal, void or voidable.

SCHEDULE 2

RESERVATIONS

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

- (a) the Searches are not capable of revealing conclusively whether or not a winding-up or administration petition or order has been presented or made, a receiver appointed, a company voluntary arrangement proposed or approved or any other insolvency proceeding commenced, and the available records may not be complete or up-to-date. In particular, the Central Registry of Winding-Up Petitions in England may not contain details of administration applications filed, or appointments recorded in or orders made by, district registries and county courts outside London. Searches at Companies House and at the Central Registry of Winding Up Petitions in England are not capable of revealing whether or not a winding up petition or a petition for the making of an administration order has been presented and, further, notice of a winding up order or resolution, notice of an administration order and notice of the appointment of a receiver may not be filed at Companies House immediately and there may be a delay in the relevant notice appearing on the file of the company concerned. Further, not all security interests are registrable, such security interests have not in fact been registered or such security interests have been created by an individual or an entity which is not registered in England. We have not made enquiries of any District Registry or County Court in England;
- (b) the opinions set out in this letter are subject to: (i) any limitations arising from applicable laws relating to insolvency, bankruptcy, administration, reorganisation, liquidation, moratoria, schemes or analogous circumstances; and (ii) an English court exercising its discretion under section 426 of the Insolvency Act 1986 (*co-operation between courts exercising jurisdiction in relation to insolvency*) to assist the courts having the corresponding jurisdiction in any part of the United Kingdom or any relevant country or territory;
- (c) we express no opinion as to matters of fact;
- (d) save for the matters set out in the Certificate, we have made no enquiries of any individual connected with the Company and have relied entirely on the facts, statements and confirmations contained in the Certificate and we have not undertaken any independent investigation or verification of the matters referred to in the Certificate;
- (e) a certificate, documentation, notification, opinion or the like might be held by the English courts not to be conclusive if it can be shown to have an unreasonable or arbitrary basis or in the event of a manifest error; and
- (f) it should be understood that we have not been responsible for investigating or verifying (i) the accuracy of the facts, including statements of foreign law, or the reasonableness of any statements of opinion, contained in the Registration Statement; or (ii) that no material facts have been omitted from it.

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in this Registration Statement on Form S-3 of Orchard Therapeutics plc of our report dated March 14, 2023 relating to the financial statements, which appears in Orchard Therapeutics plc's Annual Report on Form 10-K for the year ended December 31, 2022. We also consent to the reference to us under the heading "Experts" in such Registration Statement.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
August 10, 2023

Calculation of Filing Fee Tables

Form S-3
(Form Type)

Orchard Therapeutics plc
(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered Securities

	Security Type	Security Class Title	Fee Calculation Rule	Amount Registered(1)(2)	Proposed Maximum Offering Price Per Share(3)	Maximum Aggregate Offering Price(3)	Fee Rate	Amount of Registration Fee
Fees to Be Paid	Equity	Ordinary Shares, nominal value £0.10 per share (1)	457(c)	208,250,490	\$0.5135	\$106,936,626.62	0.00011020	\$11,784.42
		Total Offering Amounts						\$11,784.42
		Total Fees Previously Paid						—
		Total Fee Offsets						—
		Net Fee Due						\$11,784.42

- (1) Consists of (a) 53,461,574 ordinary shares represented by American Depositary Shares, or ADSs, each representing ten ordinary shares, (b) 45,705,326 ordinary shares issuable upon the redesignation of 45,705,326 non-voting ordinary shares, nominal value £0.10 per share, and represented by ADSs, and (c) 109,083,590 ordinary shares issuable upon the exercise of outstanding warrants to purchase ordinary shares (or upon the redesignation of non-voting ordinary shares that are issuable to holders of warrants upon exercise of such warrants for non-voting ordinary shares in lieu of ordinary shares), and represented by ADSs. Pursuant to Rule 416(a) of the Securities Act of 1933, as amended, this Registration Statement shall also cover any additional ordinary shares of the Registrant that become issuable by reason of any stock dividend, stock split, recapitalization or other similar transaction effected without receipt of consideration that increases the number of the Registrant's outstanding ordinary shares. The ADSs issuable upon deposit of the ordinary shares registered hereby have been registered under a separate registration statement on Form F-6 (File No. 333-227905), as amended.
- (2) The ordinary shares represented by ADSs will be offered for resale by the selling securityholders pursuant to the prospectus contained herein.
- (3) Estimated in accordance with Rule 457(c) solely for purposes of calculating the registration fee on the basis of the average of the high and low prices of the Registrant's ADSs as reported on the Nasdaq Capital Market on August 8, 2023. One ADS represents ten ordinary shares.