
**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549**

**Post-Effective Amendment No. 2
to
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 No.)

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United Kingdom
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(Address, including zip code, and telephone number, including area code, for principal executive offices)

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(Name, address, including zip code, and telephone number, including area code, of agent for service)

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Approximate date of commencement of proposed sale to the public: From time to time after the effective date of this Registration Statement.

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, 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 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	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
		Emerging growth company	<input type="checkbox"/>

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 Securities Act.

EXPLANATORY NOTE

This Post-Effective Amendment No. 2 to the Registration Statement on Form S-3, Registration No. 333-234439 (the “Registration Statement”) of Orchard Therapeutics plc (the “Registrant”) is being filed because the Registrant expects that it will no longer be a well-known seasoned issuer (as such term is defined in Rule 405 of the Securities Act of 1933, as amended) when it files its Annual Report on Form 10-K for the fiscal year ended December 31, 2021. This Post-Effective Amendment No. 2 adds disclosure to the Registration Statement required for a registrant other than a well-known seasoned issuer and makes certain other amendments.

PROSPECTUS



\$200,000,000

Ordinary Shares
American Depositary Shares representing Ordinary Shares
Debt Securities
Warrants
Units

We may offer and sell from time to time up to \$200,000,000 in the aggregate of our: ordinary shares, each of which may be represented by one American Depositary Share; senior or subordinated debt securities; warrants to purchase any securities that may be sold under this prospectus; units or any combination of these securities as described in this prospectus. We will describe in a prospectus supplement the securities we are offering and selling, as well as the specific terms of the securities. We may also authorize one or more free writing prospectuses to be provided to you in connection with each offering of the securities. Any prospectus supplement and related free writing prospectuses may also add, update or change information contained in this prospectus. For more detailed information, see "Plan of Distribution" on page 52.

We may offer these securities in amounts, at prices and on terms determined at the time of offering. We may sell the securities directly to you, through agents, or through underwriters and dealers on or off the Nasdaq Global Select Market. If we use agents, underwriters or dealers to sell the securities, we will name them and describe their compensation in a prospectus supplement. You should read this prospectus and the accompanying prospectus supplement and any free writing prospectus, as well as documents incorporated by reference into this prospectus, carefully before you invest.

Our American Depositary Shares representing ordinary shares are traded on The Nasdaq Global Select Market under the symbol "ORTX". A separate Registration Statement on Form F-6 for the registration of American Depositary Shares issuable upon deposit of the ordinary shares was previously filed with the Securities and Exchange Commission and was effective on October 30, 2018 (Registration No. 333-227905). If we decide to list any of these other securities on a national securities exchange upon issuance, the applicable prospectus supplement to this prospectus will identify the exchange and the date when we expect trading to begin. On March 28, 2022, the closing price of our American Depositary Shares on The Nasdaq Global Select Market was \$0.75 per share.

Investing in our securities involves certain risks. See "Risk Factors" beginning on page 5 of this prospectus and in the applicable prospectus supplement and any related free writing prospectus and in the documents that are incorporated by reference into this prospectus or the applicable prospectus supplement for certain risks you should consider. You should read the entire prospectus carefully before you make your investment decision.

Neither the Securities and Exchange Commission nor any state or other securities commission or other regulatory body has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is March 30, 2022

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement, as amended, that we filed with the U.S. Securities and Exchange Commission, or SEC, under the Securities Act of 1933, as amended. Under this shelf registration process, we may offer the securities described in this prospectus from time to time in one or more offerings for an aggregate offering amount of up to \$200,000,000, at prices and on terms to be determined by market conditions at the time of offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities.

Registration of the securities covered by this prospectus does not mean that these securities will necessarily be offered or sold. As of the date of filing this registration statement, we have no specific plans for selling the securities registered hereunder.

A prospectus supplement may include a discussion of risks or other special considerations applicable to us or the offered securities. A prospectus supplement or any free writing prospectus may also add, update or change information in this prospectus. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement, you must rely on the information in the prospectus supplement. Please carefully read both this prospectus, including the information incorporated by reference into this prospectus, and the applicable prospectus supplement or any free writing prospectus together with additional information described under the heading “Where You Can Find More Information.” This prospectus may not be used to offer or sell any securities unless accompanied by a prospectus supplement.

The registration statement containing this prospectus, including exhibits to the registration statement, provides additional information about us and the securities offered under this prospectus. The registration statement can be read at the SEC website mentioned under the heading “Where You Can Find More Information.”

We may sell the securities directly to or through underwriters, dealers or agents. We and our underwriters or agents, reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities through underwriters or agents, we will include in the applicable prospectus supplement:

- the names of those underwriters or agents;
- applicable fees, discounts and commissions to be paid to them;
- details regarding over-allotment options, if any; and
- the net proceeds to us.

We have not authorized any broker-dealer, salesperson or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus and the accompanying supplement to this prospectus. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus or the accompanying prospectus supplement. This prospectus and the accompanying supplement to this prospectus and any free writing prospectus do not constitute an offer to sell or the solicitation of an offer to buy securities, nor do this prospectus and the accompanying supplement to this prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation. The information contained in this prospectus and the accompanying prospectus supplement speaks only as of their respective dates and may not reflect subsequent changes in our business, financial condition, results of operations and prospects even though this prospectus and any accompanying prospectus supplement is delivered or securities are sold on a later date.

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

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appearing in this prospectus are the property of their respective holders. Solely for convenience, the trademarks and trade names in this prospectus may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend to use or display other companies' trademarks and trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

PRESENTATION OF FINANCIAL INFORMATION

Although we are a UK company, the functional currency of our reporting entity is the U.S. Dollar and we prepare our consolidated financial statements in accordance with generally accepted accounting principles in the United States, or U.S. GAAP, as issued by the Financial Accounting Standards Board. All references included or incorporated by reference in this prospectus to “\$” are to U.S. Dollars and all references to “£” are to pounds sterling.

We have made rounding adjustments to some of the figures included or incorporated by reference in this prospectus. Accordingly, numerical figures shown as totals in some tables may not be an arithmetic aggregation of the figures that preceded them. We have historically conducted our business through Orchard Therapeutics (Europe) Limited (formerly Orchard Therapeutics Limited) and our U.S. subsidiary, and therefore our historical consolidated financial statements previously presented the consolidated results of operations of Orchard Therapeutics (Europe) Limited. Following our reorganization that we completed in connection with our initial public offering, our consolidated financial statements present the consolidated results of operations of Orchard Therapeutics plc.

PROSPECTUS SUMMARY

This summary only highlights the more detailed information appearing elsewhere in this prospectus or incorporated by reference in this prospectus. It may not contain all of the information that is important to you. You should carefully read the entire prospectus and the documents incorporated by reference in this prospectus before deciding whether to invest in our securities.

Unless otherwise indicated or the context requires otherwise, in this prospectus and any prospectus supplement hereto, references to “Orchard Therapeutics,” “our company,” “we,” “us” and “our” mean Orchard Therapeutics plc, a public limited company incorporated under the laws of England and Wales.

We are a global gene therapy company dedicated to transforming the lives of people affected by rare diseases through the development of innovative, potentially curative gene therapies. Our *ex vivo* autologous hematopoietic stem cell, or 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 160 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. Three eligible patients have been treated in a commercial setting to date. Our planned BLA submission timeline for OTL-200 with the U.S. Food and Drug Administration is late 2022 to early 2023.

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

Corporate Information

We were originally incorporated under the laws of England and Wales in August 2018 as Orchard Rx Limited (now known as Orchard Therapeutics plc) to become a holding company for Orchard Therapeutics (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 108 Cannon Street, London EC4N 6EU, 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.

RISK FACTORS

Before making an investment decision, you should carefully consider the risks described under “Risk Factors” in the applicable prospectus supplement, together with all of the other information appearing in this prospectus or incorporated by reference into this prospectus and any applicable prospectus supplement, including (i) our annual report on Form 10-K for the fiscal year ended December 31, 2020, which is on file with the SEC and is incorporated herein by reference, (ii) our quarterly reports on Form 10-Q for the quarters ended March 31, 2021, June 30, 2021 and September 30, 2021, which are on file with the SEC and incorporated herein by reference, and (iii) other documents we file with the SEC that are deemed incorporated by reference into this prospectus. Our business, financial condition or results of operations could be materially adversely affected by any of these risks. The trading price of our securities could decline due to any of these risks, and you may lose all or part of your investment. This prospectus and the incorporated documents also contain forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks mentioned elsewhere in this prospectus.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference into it contain forward-looking statements. Forward-looking statements relate to future events or our future financial performance. 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 referenced under in “Risk Factors” in this prospectus and described in any prospectus supplement and our periodic filings with the SEC incorporated by reference in this prospectus or any prospectus supplement. 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, 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, statements about:

- the timing, progress and results of clinical trials and preclinical studies for our programs and product candidates, including statements regarding the timing of initiation and completion of trials or studies and related preparatory work 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;
- 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;
- the impact of the COVID-19 global pandemic on our business operations;
- 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;

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- 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
- other risks and uncertainties, including those listed under the caption “Risk factors” in this prospectus as well as those risk factors that are incorporated by reference in this prospectus.

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.

CAPITALIZATION

We intend to include information about our capitalization and indebtedness in prospectus supplements, as applicable.

SECURITIES WE MAY OFFER

We may offer our ordinary shares, each of which may be represented by one ADS, various series of senior or subordinated debt securities, warrants to purchase any such securities, units, or any combination of these securities in an amount up to \$200,000,000 from time to time under this prospectus at prices and on terms to be determined by market conditions at the time of offering. Each time we offer a type or series of securities, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities.

DESCRIPTION OF SHARE CAPITAL AND ARTICLES OF ASSOCIATION

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

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

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

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

- general authorization of our directors for purposes of Section 551 of the Companies Act 2006 to allot shares in the company or 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 2021 annual general meeting; and
- empowering of our directors pursuant to Section 570 of Companies Act 2006 to allot equity securities for cash pursuant to the Section 551 authority referred to above as if the statutory preemption rights under Section 561(1) of the Companies Act 2006 did not apply to such allotments.

Issued share capital

As of December 31, 2021, our issued share capital was 125,674,095 ordinary shares with a nominal value of £0.10 per share.

Ordinary shares

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

- each holder of our ordinary shares is entitled to one vote per ordinary share on all matters to be voted on by shareholders generally;
- the holders of the ordinary shares are entitled to receive notice of, attend, speak and vote at our general meetings; and
- the holders of our ordinary shares are entitled to receive such dividends as are recommended by our directors and declared by our shareholders.

Registered shares

We are required by the Companies Act 2006 to keep a register of our shareholders. Under English law, the ordinary shares are deemed to be issued when the name of the shareholder is entered in our share register. The share register therefore is prima facie evidence of the identity of our shareholders, and the shares that they hold. The share register generally provides limited, or no, information regarding the ultimate beneficial owners of our ordinary shares. Our share register is maintained by our registrar. Holders of our ADSs are not treated as shareholders and their names are therefore not entered in our share register. The depositary, the custodian or their

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nominees is the holder of the shares underlying our ADSs. Holders of our ADSs have a right to receive the ordinary shares underlying their ADSs. For a discussion of our ADSs and ADS holder rights, see “Description of American depositary shares” in this prospectus.

Under the Companies Act 2006, we must enter an allotment of shares in our share register as soon as practicable and in any event within two months of the allotment. We will perform all procedures necessary to update the share register to reflect the ordinary shares being sold in any offering, including updating the share register with the number of ordinary shares to be issued to the depositary upon the closing of any offering. We are also required by the Companies Act 2006 to register a transfer of shares (or, if applicable, 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 persons 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 meeting in June 2021 our shareholders approved the exclusion of preemptive rights for a period of five years from the date of approval, which exclusion will need to be renewed upon expiration (i.e., at least every five years) to remain effective, but may be sought more frequently for additional five-year terms (or any shorter period).

Registration rights

The holders of up to 8,611,375 shares of our ordinary shares are entitled to rights with respect to the registration of these securities under the Securities Act. These rights are provided under the terms of an investment and shareholders’ agreement between us and holders of our convertible preferred shares, which were subsequently converted into ordinary shares in connection with our initial public offering in November 2018. The investment and shareholders’ agreement includes demand registration rights, short-form registration rights and piggyback registration rights.

Demand registration rights

The holders of up to 8,611,375 shares of our ordinary shares are entitled to demand registration rights. Under the terms of the investment and shareholders’ agreement, we will be required, upon the written request of holders of a majority of these securities to file a registration statement and use best efforts to effect the registration of all or a portion of these shares for public resale.

Short-form registration rights

Pursuant to the investment and shareholders’ agreement, for so long as 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

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

Piggyback registration rights

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

Indemnification

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

Expiration of registration rights

The registration rights granted under the investment and shareholders' agreement will terminate 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. A summary of the terms of the Articles is set out below. The summary below is not a complete copy of the terms of the Articles.

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

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

Share capital

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

Voting

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

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Variation of rights

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

Dividends

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

Any dividend unclaimed after a period of 12 years from the date such dividend was declared or became payable shall, if the board of directors resolve, be forfeited and cease to remain owing by us. 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.

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

- (i) it is for a share which is fully paid up;
- (ii) it is for a share upon which the company has no lien;
- (iii) it is only for one class of share;
- (iv) it is in favor of a single transferee or no more than four joint transferees;
- (v) it is duly stamped or is duly certificated or otherwise shown to the satisfaction of the board of directors to be exempt from stamp duty; and
- (vi) it is delivered for registration to the registered office of the company (or such other place as the board of directors may determine), accompanied (except in the case of a transfer by a person to whom the company is not required by law to issue a certificate and to whom a certificate has not been issued or in the case of a renunciation) by the certificate for the shares to which it relates and such other evidence as the board of directors may reasonably require to prove the title of the transferor (or person renouncing) and the due execution of the transfer or renunciation by him or, if the transfer or renunciation is executed by some other person on his behalf, the authority of that person to do so.

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

Allotment of shares and preemption rights

Subject to the Companies Act 2006 and to any rights attached to existing shares, any share may be issued with or have attached to it such rights and restrictions as the company may by ordinary resolution determine, or if no

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ordinary resolution has been passed or so far as the resolution does not make specific provision, as the board of directors may determine (including shares which are to be redeemed, or are liable to be redeemed at the option of the company or the holder of such shares).

In accordance with section 551 of the Companies Act 2006, the board of directors may be generally and unconditionally authorized to exercise all the powers of the company to allot shares up to an aggregate nominal amount equal to the amount stated in the relevant ordinary resolution authorizing such allotment. The authorities referred to above were included in the special resolution passed in June 2021 and remain in force at the date of this prospectus.

The provisions of section 561 of the Companies Act 2006 (which confer on shareholders rights of preemption in respect of the allotment of equity securities which are paid up in cash) apply to the company except to the extent disapplied by special resolution of the company. Such preemption rights have been disapplied pursuant to the special resolution passed at our annual general meeting in June 2021.

Alteration of share capital

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

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

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

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

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

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

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Questions and matters requiring resolution arising at a meeting shall be decided by a majority of votes of the participating directors, with each director having one vote. In the case of an equality of votes, the chairman will have a casting vote or second vote, unless he is not entitled to vote on the resolution in question.

Directors shall be entitled to receive such remuneration as the board shall determine for their services to us 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. 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.

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

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

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

- (i) to the extent permitted by the Companies Act 2006, the matter in question shall have been proposed by any director for consideration in the same way that any other matter may be proposed to the directors under the provisions of the Articles;
- (ii) any requirement as to the quorum for consideration of the relevant matter is met without counting the conflicted director and any other conflicted director; and
- (iii) the matter is agreed to without the conflicted director voting or would be agreed to if the conflicted director's and any other interested director's vote is not counted.

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

General meetings

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

No business shall be transacted at any general meeting unless a quorum is present when the meeting proceeds to business, but the absence of a quorum shall not preclude the choice or appointment of a chairman of the meeting which shall not be treated as part of the business of the meeting. One or more qualifying persons present at a meeting and between them holding (or being the proxy or corporate representative of the holders of) at least 33 1/3 percent in number of the issued shares (excluding any shares held as treasury shares) entitled to attend and vote on the business to be transacted shall constitute a quorum.

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Borrowing Powers

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

- (a) borrow money;
- (b) indemnify and guarantee;
- (c) mortgage or charge;
- (d) create and issue debentures and other securities; and
- (e) give security either outright or as collateral security for any debt, liability or obligation of the company or of any third party.

Capitalization of profits

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

Uncertificated shares

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

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

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.

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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.

	<u>England and Wales</u>	<u>Delaware</u>
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.

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	<u>England and Wales</u>	<u>Delaware</u>
Annual General Meeting	<p>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.</p>	<p>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.</p>
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>

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	<u>England and Wales</u>	<u>Delaware</u>
Proxy	<p>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.</p>	<p>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.</p>
Preemptive Rights	<p>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.</p>	<p>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.</p>
Authority to Allot	<p>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.</p>	<p>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.</p>

	<u>England and Wales</u>	<u>Delaware</u>
Liability of Directors and Officers	<p>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.</p>	<p>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:</p> <ul style="list-style-type: none">• any breach of the director’s duty of loyalty to the corporation or its stockholders;• acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;• intentional or negligent payment of unlawful dividends or stock purchases or redemptions; or• any transaction from which the director derives an improper personal benefit.
Voting Rights	<p>Under English law, unless a poll is demanded by the shareholders of a company or is required by the chairman of the meeting or the company’s articles of association, shareholders shall vote on all resolutions on a show of hands. Under the Companies Act, a poll may be demanded by (i) not fewer than five</p>	<p>Delaware law provides that, unless otherwise provided in the certificate of incorporation, each stockholder is entitled to one vote for each share of capital stock held by such stockholder.</p>

	<u>England and Wales</u>	<u>Delaware</u>
	<p>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.</p> <p>Under English law, an ordinary resolution is passed on a show of hands if it is approved by a simple majority (more than 50%) of the votes cast by shareholders present (in person or by proxy) and entitled to vote. If a poll is demanded, an ordinary resolution is passed if it is approved by holders representing a simple majority of the total voting rights of shareholders present, in person or by proxy, who, being entitled to vote 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.</p>	
Shareholder Vote on Certain Transactions	<p>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:</p> <ul style="list-style-type: none">• the approval at a shareholders' or creditors' meeting convened by order of the court, of a majority in number representing 75% in value of the shareholders or creditors or	<p>Generally, under Delaware law, unless the certificate of incorporation provides for the vote of a larger portion of the stock, completion of a merger, consolidation, sale, lease or exchange of all or substantially all of a corporation's assets or dissolution requires:</p> <ul style="list-style-type: none">• the approval of the board of directors; and• 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

	<u>England and Wales</u>	<u>Delaware</u>
	class thereof present and voting, either in person or by proxy; and	vote per share, a majority of the votes of the outstanding stock of the corporation entitled to vote on the matter.
	<ul style="list-style-type: none">• the approval of the court.	
Standard of Conduct for Directors	<p>Under English law, a director owes various statutory and fiduciary duties to the company, including:</p> <ul style="list-style-type: none">• to act in the way he considers, in good faith, would be most likely to promote the success of the company for the benefit of its members as a whole;• to avoid a situation in which he has, or can have, a direct or indirect interest that conflicts, or possibly conflicts, with the interests of the company;• to act in accordance with the company's constitution and only exercise his powers for the purposes for which they are conferred;• 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.	<p>Delaware law does not contain specific provisions setting forth the standard of conduct of a director. The scope of the fiduciary duties of directors is generally determined by the courts of the State of Delaware. In general, directors have a duty to act without self-interest, on a well-informed basis and in a manner they reasonably believe to be in the best interest of the stockholders.</p> <p>Directors of a Delaware corporation owe fiduciary duties of care and loyalty to the corporation and to its shareholders. The duty of care generally requires that a director act in good faith, with the care that an ordinarily prudent person would exercise under similar circumstances. Under this duty, a director must inform himself of all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director act in a manner he reasonably believes to be in the best interests of the corporation. He must not use his corporate position for personal gain or advantage. In general, but subject to certain exceptions, actions of a director are presumed to have been made on an informed basis, in good faith and in the honest belief that the action taken was in the best interests of the corporation. However, this presumption may be rebutted by evidence of a breach of one of the fiduciary duties. Delaware courts have also imposed a heightened standard of conduct upon directors of a Delaware corporation who take any action designed to defeat a threatened change in control of the corporation.</p> <p>In addition, under Delaware law, when the board of directors of a Delaware corporation approves the sale or</p>

	<u>England and Wales</u>	<u>Delaware</u>
Shareholder Suits	<p>Under English law, generally, the company, rather than its shareholders, is the proper claimant in an action in respect of a wrong done to the company or where there is an irregularity in the company's internal management. Notwithstanding this general position, the Companies Act 2006 provides that (i) a court may allow a shareholder to bring a derivative claim (that is, an action in respect of and on behalf of the company) in respect of a cause of action arising from a director's negligence, default, breach of duty or breach of trust and (ii) a shareholder may bring a claim for a court order where the company's affairs have been or are being conducted in a manner that is unfairly prejudicial to some of its shareholders.</p>	<p>break-up of a corporation, the board of directors may, in certain circumstances, have a duty to obtain the highest value reasonably available to the shareholders.</p> <p>Under Delaware law, a stockholder may initiate a derivative action to enforce a right of a corporation if the corporation fails to enforce the right itself. The complaint must:</p> <ul style="list-style-type: none">• state that the plaintiff was a stockholder at the time of the transaction of which the plaintiff complains or that the 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. <p>Additionally, the plaintiff must remain a stockholder through the duration of the derivative suit. The action will not be dismissed or compromised without the approval of the Delaware Court of Chancery.</p>

Stock exchange listing

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

Transfer agent and registrar of shares

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

DESCRIPTION OF AMERICAN DEPOSITARY SHARES

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. You may obtain a copy of the deposit agreement from the SEC's website (www.sec.gov). Please refer to Registration No. 333-227905 when retrieving such copy.

We are providing you with a summary description of the material terms of the ADSs and of your material rights as an owner of ADSs. Summaries by their nature lack the precision of the information summarized and that the rights and obligations of an owner of ADSs will be determined by reference to the terms of the deposit agreement and not by this summary. We urge you to review the deposit agreement in its entirety. The portions of this summary description that are italicized describe matters that may be relevant to the ownership of ADSs but that may not be contained in the deposit agreement.

Each ADS represents the right to receive, and to exercise the beneficial ownership interests in, one ordinary share 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.

If you become an owner of ADSs, you will become a party to the deposit agreement and therefore will be bound to its terms and to the terms of any ADR that represents your ADSs. The deposit agreement and the ADR specify our rights and obligations as well as your rights and obligations as owner of ADSs and those of the depository. As an ADS holder you appoint the depository to act on your behalf in certain circumstances. The deposit agreement and the ADRs are governed by New York law. However, our obligations to the holders of ordinary shares will continue to be governed by the laws of England and Wales, which may be different from the laws of the United States.

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

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As an owner of ADSs, we will not treat you as one of our shareholders and you will not have direct shareholder rights. The depositary will hold on your behalf the shareholder rights attached to the ordinary shares underlying your ADSs. As an owner of ADSs, you will be able to exercise the shareholders rights for the ordinary shares represented by your ADSs through the depositary only to the extent contemplated in the deposit agreement. To exercise any shareholder rights not contemplated in the deposit agreement you will, as an ADS owner, need to arrange for the cancellation of your ADSs and become a direct shareholder.

The manner in which you own the ADSs (e.g., in a brokerage account vs. as registered holder, or as holder of certificated vs. uncertificated ADSs) may affect your rights and obligations, and the manner in which, and extent to which, the depositary's services are made available to you. As an owner of ADSs, you may hold your ADSs either by means of an ADR registered in your name, through a brokerage or safekeeping account, or through an account established by the depositary in your name reflecting the registration of uncertificated ADSs directly on the books of the depositary (commonly referred to as the direct registration system or DRS). The direct registration system reflects the uncertificated (book-entry) registration of ownership of ADSs by the depositary. Under the direct registration system, ownership of ADSs is evidenced by periodic statements issued by the depositary to the holders of the ADSs. The direct registration system includes automated transfers between the depositary and The Depository Trust Company, or DTC, the central book-entry clearing and settlement system for equity securities in the United States. If you decide to hold your ADSs through your brokerage or safekeeping account, you must rely on the procedures of your broker or bank to assert your rights as ADS owner. Banks and brokers typically hold securities such as the ADSs through clearing and settlement systems such as DTC. The procedures of such clearing and settlement systems may limit your ability to exercise your rights as an owner of ADSs. Please consult with your broker or bank if you have any questions concerning these limitations and procedures. All ADSs held through DTC will be registered in the name of a nominee of DTC. This summary description assumes you have opted to own the ADSs directly by means of an ADS registered in your name and, as such, we will refer to you as the "holder." When we refer to "you," we assume the reader owns ADSs and will own ADSs at the relevant time.

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

Dividends and Distributions

As a holder of ADSs, you generally have the right to receive the distributions we make on the securities deposited with the custodian. Your receipt of these distributions may be limited, however, by practical considerations and legal limitations. Holders of ADSs will receive such distributions under the terms of the deposit agreement in proportion to the number of ADSs held as of the specified record date, after deduction the applicable fees, taxes and expenses.

Distributions of Cash

Whenever we make a cash distribution for the securities on deposit with the custodian, we will deposit the funds with the custodian. Upon receipt of confirmation of the deposit of the requisite funds, the depositary will arrange for the funds received in a currency other than U.S. Dollars to be converted into U.S. Dollars and for the distribution of the U.S. Dollars to the holders, subject to the laws and regulations of England and Wales.

The conversion into U.S. Dollars will take place only if practicable and if the U.S. Dollars are transferable to the United States. The depositary will apply the same method for distributing the proceeds of the sale of any property (such as undistributed rights) held by the custodian in respect of securities on deposit.

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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 ADSs until the distribution can be effected or the funds that the depository 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 depository will either distribute to holders new ADSs representing the ordinary shares deposited or modify the ADS-to-ordinary shares ratio, in which case each ADS you hold will represent rights and interests in the additional ordinary shares so deposited. Only whole new ADSs will be distributed. Fractional entitlements will be sold and the proceeds of such sale will be distributed as in the case of a cash distribution.

The distribution of new ADSs or the modification of the ADS-to-ordinary share ratio upon a distribution of ordinary shares will be made net of the fees, expenses, taxes, and governmental charges payable by holders under the terms of the deposit agreement. In order to pay such taxes or governmental charges, the depository 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 depository 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 subscribe for additional ordinary shares, we will give prior notice to the depository and we will assist the depository in determining whether it is lawful and reasonably practicable to distribute rights to subscribe for additional ADSs to holders.

The depository will establish procedures to distribute rights to subscribe for additional ADSs to holders and to enable such holders to exercise such rights if it is lawful and reasonably practicable to make the rights available to holders of ADSs, and if we provide all of the documentation contemplated in the deposit agreement (such as opinions to address the lawfulness of the transaction). You may have to pay fees, expenses, taxes and other governmental charges to subscribe for the new ADSs upon the exercise of your rights. The depository is not obligated to establish procedures to facilitate the distribution and exercise by holders of rights to subscribe for new ordinary shares other than in the form of ADSs.

The depository will *not* distribute the rights to you if:

- we do not timely request that the rights be distributed to you or we request that the rights not be distributed to you;
- we fail to deliver satisfactory documents to the depository; or
- it is not reasonably practicable to distribute the rights.

The depository 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 depository 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 depository and will indicate whether we wish the elective

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distribution to be made available to you. In such case, we will assist the depositary in determining whether such distribution is lawful and reasonably practicable.

The depositary will make the election available to you only if it is reasonably practicable and if we have provided all of the documentation contemplated in the deposit agreement. In such case, the depositary will establish procedures to enable you to elect to receive either cash or additional ADSs, in each case as described in the deposit agreement.

If the election is not made available to you, you will receive either cash or additional ADSs, depending on what a shareholder in England and Wales would receive upon failing to make an election, as more fully described in the deposit agreement.

Other Distributions

Whenever we intend to distribute property other than cash, ordinary shares or rights to purchase additional ordinary shares, we will notify the depositary in advance and will indicate whether we wish such distribution to be made to you. If so, we will assist the depositary in determining whether such distribution to holders is lawful and reasonably practicable.

If it is reasonably practicable to distribute such property to you and if we provide all of the documentation contemplated in the deposit agreement, the depositary will distribute the property to the holders in a manner it deems practicable.

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

The depositary will *not* distribute the property to you and will sell the property if:

- we do not request that the property be distributed to you or if we ask that the property not be distributed to you; or
- we do not deliver satisfactory documents to the depositary; or
- the depositary determines that all or a portion of the distribution to you is not reasonably practicable.

The proceeds of such a sale will be distributed to holders as in the case of a cash distribution.

Redemption

Whenever we decide to redeem any of the ordinary shares on deposit with the custodian, we will notify the depositary in advance. If it is practicable and if we provide all of the documentation contemplated in the deposit agreement, the depositary will provide notice of the redemption to the holders.

The custodian will be instructed to surrender the ordinary shares being redeemed against payment of the applicable redemption price. The depositary will convert the redemption funds received in a currency other than U.S. Dollars into U.S. Dollars upon the terms of the deposit agreement and will establish procedures to enable holders to receive the net proceeds from the redemption upon surrender of their ADSs to the depositary. You may have to pay fees, expenses, taxes and other governmental charges upon the redemption of your ADSs. If less than all ADSs are being redeemed, the ADSs to be retired will be selected by lot or on a pro rata basis, as the depositary may determine.

Changes Affecting Ordinary Shares

The ordinary shares held on deposit for your ADSs may change from time to time. For example, there may be a change in nominal or par value, split-up, cancellation, consolidation, or any other reclassification of such ordinary shares or a recapitalization, reorganization, merger, consolidation, or sale of assets of our company.

If any such change were to occur, your ADSs would, to the extent permitted by law and the deposit agreement, represent the right to receive the property received or exchanged in respect of the ordinary shares held on deposit. The depositary may in such circumstances deliver new ADSs to you, amend the deposit agreement, the ADRs and the applicable Registration Statement(s) on Form F-6, call for the exchange of your existing ADSs for new ADSs and take any other actions that are appropriate to reflect as to the ADSs the change affecting the ordinary shares. If the depositary may not lawfully distribute such property to you, the depositary may sell such property and distribute the net proceeds to you as in the case of a cash distribution.

Issuance of ADSs upon Deposit of Ordinary Shares

Any ordinary shares sold pursuant to this prospectus or any accompanying prospectus supplement will be deposited by us with the custodian. Upon receipt of confirmation of such deposit, the depositary will issue ADSs to the underwriters named in this prospectus.

After the closing of any offering, the depositary may create ADSs on your behalf if you or your broker deposit ordinary shares with the custodian. The depositary will deliver these ADSs to the person you indicate only after you pay any applicable issuance fees and any charges and taxes payable for the transfer of the ordinary shares to the custodian. Your ability to deposit ordinary shares and receive ADSs may be limited by the legal considerations in the United States and England and Wales applicable at the time of deposit.

The issuance of ADSs may be delayed until the depositary or the custodian receives confirmation that all required approvals have been given and that the ordinary shares have been duly transferred to the custodian. The depositary will only issue ADSs in whole numbers.

When you make a deposit of ordinary shares, you will be responsible for transferring good and valid title to the depositary. As such, you will be deemed to represent and warrant that:

- the ordinary shares are duly authorized, validly issued, fully paid, non-assessable, and legally obtained;
- all preemptive (and similar) rights, if any, with respect to such ordinary shares have been validly waived or exercised;
- you are duly authorized to deposit the ordinary shares;
- the ordinary shares presented for deposit are free and clear of any lien, encumbrance, security interest, charge, mortgage, or adverse claim, and are not, and the ADSs issuable upon such deposit will not be, “restricted securities” (as defined in the deposit agreement);
- the ordinary shares presented for deposit have not been stripped of any rights or entitlements; and
- the deposit of shares does not violate any applicable provision of English law.

If any of the representations or warranties are incorrect in any way, we and the depositary may, at your cost and expense, take any and all actions necessary to correct the consequences of the misrepresentations.

Transfer, Combination and Split Up of ADRs

As an ADR holder, you will be entitled to transfer, combine or split up your ADRs and the ADSs evidenced thereby. For transfers of ADRs, you will have to surrender the ADRs to be transferred to the depositary and also must:

- ensure that the surrendered ADR is properly endorsed or otherwise in proper form for transfer;

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- provide such proof of identity and genuineness of signatures as the depository deems appropriate;
- provide any transfer stamps required by the State of New York or the United States; and
- pay all applicable fees, charges, expenses, taxes, and other government charges payable by ADR holders pursuant to the terms of the deposit agreement, upon the transfer of ADRs.

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

Withdrawal of Ordinary Shares upon Cancellation of ADSs

As a holder, you will be entitled to present your ADSs to the depository for cancellation and then receive the corresponding number of underlying ordinary shares at the custodian's offices. Your ability to withdraw the ordinary shares held in respect of the ADSs may be limited by the legal consideration in the United States and England and Wales applicable at the time of withdrawal. In order to withdraw the ordinary shares represented by your ADSs, you will be required to pay to the depository the fees for cancellation of ADSs and any charges and taxes payable upon the transfer of the ordinary shares. You assume the risk for delivery of all funds and securities upon withdrawal. Once canceled, the ADSs will not have any rights under the deposit agreement.

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

You will have the right to withdraw the securities represented by your ADSs at any time except as a result of:

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

The deposit agreement may not be modified to impair your right to withdraw the ordinary shares represented by your ADSs except to comply with mandatory provisions of law.

Voting rights

As a holder, you generally have the right under the deposit agreement to instruct the depository to exercise the voting rights for the ordinary shares represented by your ADSs. The voting rights of holders of ordinary shares are described in "Description of share capital and articles of association—Articles of association" in this prospectus.

At our request, the depository will distribute to you 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.

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If the depositary timely receives voting instructions from a holder of ADSs, it will endeavor to vote (or cause the custodian to vote) the securities (in person or by proxy) represented by the holder's ADSs as follows:

- *In the event of voting by show of hands*, the depositary will vote (or cause the custodian to vote) all ordinary shares represented by ADSs in accordance with the voting instructions received from a majority of holders of ADSs who provide timely voting instructions.
- *In the event of voting by poll*, the depositary will vote (or cause the custodian to vote) the ordinary shares represented by ADSs in accordance with the voting instructions received from the holders of ADSs.

Securities for which no voting instructions have been received will not be voted (except as otherwise contemplated in the deposit agreement). Please note that the ability of the depositary to carry out voting instructions may be limited by practical and legal limitations and the terms of the securities on deposit. We cannot assure you that you will receive voting materials in time to enable you to return voting instructions to the depositary in a timely manner.

Fees and charges

As an ADS holder, you will be required to pay the following fees under the terms of the deposit agreement:

<u>Service</u>	<u>Fee</u>
(1) 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, or for any other reason), excluding ADS issuances as a result of distributions of ordinary shares as described in paragraph (4) below.	Up to \$0.05 per ADS issued
(2) 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, or for any other reason).	Up to \$0.05 per ADS cancelled
(3) 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
(4) Distribution of ADSs pursuant to (i) ordinary share dividends or other free ordinary share distributions, or (ii) exercise of rights to purchase additional ADSs.	Up to \$0.05 per ADS held
(5) 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
(6) ADS Services.	Up to \$0.05 per ADS held on the applicable record date(s) established by the depositary

As an ADS holder you will also be responsible to pay certain charges such as:

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

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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 any ADS offering. Note that the fees and charges you may be required to pay may vary over time and may be changed by us and by the depository. You 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 your consent. We undertake to give holders 30 days' prior notice of any modifications that would materially prejudice any of their substantial rights under the deposit agreement. We will not consider to be materially prejudicial to your substantial rights any modifications or supplements that are reasonably necessary for the ADSs to be registered under the Securities Act or to be eligible for book-entry settlement, in each case without imposing or increasing the fees and charges you are required to pay. In addition, we may not be able to provide you with prior notice of any modifications or supplements that are required to accommodate compliance with applicable provisions of law.

You will be bound by the modifications to the deposit agreement if you continue to hold your ADSs after the modifications to the deposit agreement become effective. The deposit agreement cannot be amended to prevent you from withdrawing the ordinary shares represented by your ADSs (except as permitted by law).

We have the right to direct the 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, your rights under the deposit agreement will be unaffected.

Termination

After termination, the depositary will continue to collect distributions received (but will not distribute any such property until you request the cancellation of your ADSs) and may sell the securities held on deposit. After the sale, the depositary will hold the proceeds from such sale and any other funds then held for the holders of ADSs in a non-interest bearing account. At that point, the depositary will have no further obligations to holders other than to account for the funds then held for the holders of ADSs still outstanding (after deduction of applicable fees, taxes and expenses).

In connection with any termination of the deposit agreement, the depositary bank may make available to owners of ADSs a means to withdraw the ordinary shares represented by ADSs and to direct the depositary of such ordinary shares into an unsponsored American depositary share program established by the depositary bank. The ability to receive unsponsored American depositary shares upon termination of the deposit agreement would be subject to satisfaction of certain U.S. regulatory requirements applicable to the creation of unsponsored American depositary shares and the payment of applicable depositary fees.

Books of Depositary

The depositary will maintain ADS holder records at its depositary office. You may inspect such records at such office during regular business hours but solely for the purpose of communicating with other holders in the interest of business matters relating to the ADSs and the deposit agreement.

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

Transmission of notices, reports and proxy soliciting material

The depositary will make available for your inspection at its office all communications that it receives from us as a holder of deposited securities that we make generally available to holders of deposited securities. Subject to the terms of the deposit agreement, the depositary will send you copies of those communications or otherwise make those communications available to you if we ask it to.

Limitations on obligations and liabilities

The deposit agreement limits our obligations and the depositary's obligations to you. Please note the following:

- We and the depositary are obligated only to take the actions specifically stated in the deposit agreement without negligence or bad faith.
- The depositary disclaims any liability for any failure to carry out voting instructions, for any manner in which a vote is cast or for the effect of any vote, provided it acts in good faith and in accordance with the terms of the deposit agreement.
- The depositary disclaims any liability for any failure to determine the lawfulness or practicality of any action, for the content of any document forwarded to you on our behalf or for the accuracy of any translation of such a document, for the investment risks associated with investing in ordinary shares, for the validity or worth of the ordinary shares, for any tax consequences that result from the ownership of ADSs, for the credit-worthiness of any third party, for allowing any rights to lapse under the terms of the deposit agreement, for the timeliness of any of our notices or for our failure to give notice.
- We and the depositary are not obligated to perform any act that is inconsistent with the terms of the deposit agreement.
- We and the depositary disclaim any liability if we or the depositary are prevented or forbidden from or subject to any civil or criminal penalty or restraint on account of, or delayed in, doing or performing any act or thing required by the terms of the deposit agreement, by reason of any provision, present or

future of any law or regulation, or by reason of present or future provision of any provision of our Articles of Association or any provision of or governing the securities on deposit, or by reason of any act of God or war or other circumstances beyond our control.

- We and the depositary disclaim any liability by reason of any exercise of, or failure to exercise, any discretion provided for in the deposit agreement or in our Articles of Association or in any provisions of or governing the securities on deposit.
- We and the depositary further disclaim any liability for any action or inaction in reliance on the advice or information received from legal counsel, accountants, any person presenting ordinary shares for deposit, any holder of ADSs or authorized representatives thereof, or any other person believed by either of us in good faith to be competent to give such advice or information.
- We and the depositary also disclaim liability for the inability by a holder to benefit from any distribution, offering, right or other benefit that is made available to holders of ordinary shares but is not, under the terms of the deposit agreement, made available to you.
- We and the depositary may rely without any liability upon any written notice, request or other document believed to be genuine and to have been signed or presented by the proper parties.
- We and the depositary also disclaim liability for any consequential or punitive damages for any breach of the terms of the deposit agreement.
- No disclaimer of any Securities Act liability is intended by any provision of the deposit agreement.
- Nothing in the deposit agreement gives rise to a partnership or joint venture, or establishes a fiduciary relationship, among us, the depositary bank and you as ADS holder.
- Nothing in the deposit agreement precludes Citibank (or its affiliates) from engaging in transactions in which parties adverse to us or the ADS owners have interests, and nothing in the deposit agreement obligates Citibank to disclose those transactions, or any information obtained in the course of those transactions, to us or to the ADS owners, or to account for any payment received as part of those transactions.

As the above limitations relate to our obligations and the depositary's obligations to you under the deposit agreement, we believe that, as a matter of construction of the clause, such limitations would likely to continue to apply to ADS holders who withdraw the ordinary shares from the ADS facility with respect to obligations or liabilities incurred under the deposit agreement before the cancellation of the ADSs and the withdrawal of the ordinary shares, and such limitations would most likely not apply to ADS holders who withdraw the ordinary shares from the ADS facility with respect to obligations or liabilities incurred after the cancellation of the ADSs and the withdrawal of the ordinary shares and not under the deposit agreement.

In any event, you will not be deemed, by agreeing to the terms of the deposit agreement, to have waived our or the depositary's compliance with U.S. federal securities laws and the rules and regulations promulgated thereunder. In fact, you cannot waive our or the depositary's compliance with U.S. federal securities laws and the rules and regulations promulgated thereunder.

Taxes

You will be responsible for the taxes and other governmental charges payable on the ADSs and the ordinary shares represented by the ADSs. We, the depositary and the custodian may deduct from any distribution the taxes and governmental charges payable by holders and may sell any and all property on deposit to pay the taxes and governmental charges payable by holders. You will be liable for any deficiency if the sale proceeds do not cover the taxes that are due.

The depositary may refuse to issue ADSs, to deliver, transfer, split and combine ADRs or to release securities on deposit until all taxes and charges are paid by the applicable holder. The depositary and the custodian may take reasonable administrative actions to obtain tax refunds and reduced tax withholding for any distributions on your

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behalf. However, you may be required to provide to the depository and to the custodian proof of taxpayer status and residence and such other information as the depository and the custodian may require to fulfill legal obligations. You are required to indemnify us, the depository and the custodian for any claims with respect to taxes based on any tax benefit obtained for you.

Foreign currency conversion

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

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

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

Governing Law/Waiver of Jury Trial

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

AS A PARTY TO THE DEPOSIT AGREEMENT, YOU IRREVOCABLY WAIVE, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, YOUR RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING ARISING OUT OF THE DEPOSIT AGREEMENT, THE ADRs AND ADSs AGAINST US AND/OR THE DEPOSITARY.

The deposit agreement provides that, to the extent permitted by law, ADS holders waive the right to a jury trial of any claim they may have against us or the depository arising out of or relating to our ordinary shares, the ADSs or the deposit agreement, including any claim under U.S. federal securities laws. If we or the depository opposed a jury trial demand based on the waiver, the court would determine whether the waiver was enforceable in the facts and circumstances of that case in accordance with applicable case law. However, you will not be deemed by agreeing to the terms of the deposit agreement to have waived our or the depository's compliance with U.S. federal securities laws and the rules and regulations promulgated thereunder.

DESCRIPTION OF DEBT SECURITIES

This prospectus describes the general terms and provisions of the debt securities we may offer under this prospectus. When we offer to sell a particular series of debt securities, we will describe the specific terms of the securities in a supplement to this prospectus, including any additional covenants or changes to existing covenants relating to such series. The prospectus supplement also will indicate whether any of the general terms and provisions described in this prospectus apply to a particular series of debt securities. You should read the applicable indenture if you do not fully understand a term or the way we use it in this prospectus.

We may offer senior or subordinated debt securities, which may be convertible. Each series of debt securities may have different terms. The senior debt securities will be issued under one or more senior indentures, dated as of a date prior to such issuance, between us and the trustee identified in the applicable prospectus supplement, as amended or supplemented from time to time. We will refer to any such indenture throughout this prospectus as the “senior indenture.” Any subordinated debt securities will be issued under one or more separate indentures, dated as of a date prior to such issuance, between us and the trustee identified in the applicable prospectus supplement, as amended or supplemented from time to time. We will refer to any such indenture throughout this prospectus as the “subordinated indenture” and to the trustee under the senior or subordinated indenture as the “trustee.” The senior indenture and the subordinated indenture are sometimes collectively referred to in this prospectus as the “indentures.” The indentures will be subject to and governed by the Trust Indenture Act of 1939, as amended. We included copies of the forms of the indentures as exhibits to this registration statement of which this prospectus forms a part.

If we issue debt securities at a discount from their principal amount, then, for purposes of calculating the aggregate initial offering price of the offered securities issued under this prospectus, we will include only the initial offering price of the debt securities and not the principal amount of the debt securities.

We have summarized below the material provisions of the indentures and the debt securities, or indicated which material provisions will be described in the related prospectus supplement. The prospectus supplement relating to any particular securities offered will describe the specific terms of the debt securities, which may be in addition to or different from the general terms summarized in this prospectus. Because the summary in this prospectus and in any prospectus supplement does not contain all of the information that you may find useful, you should read the documents relating to the debt securities that are described in this prospectus or in any applicable prospectus supplement. The statements below are not complete and are subject to, and qualified in their entirety by reference to, all of the provisions of the applicable indenture, as amended or supplemented from time to time. Please read “Where You Can Find More Information” to find out how you can obtain a copy of those documents. Except as otherwise indicated, the terms of the indentures are identical. As used under this caption, the term “debt securities” includes the debt securities being offered by this prospectus and all other debt securities issued by us under the indentures.

General

We expect that the indentures will:

- not limit the amount of debt securities that we may issue;
- allow us to issue debt securities in one or more series;
- not require us to issue all of the debt securities of a series at the same time;
- allow us to reopen a series to issue additional debt securities without the consent of the holders of the debt securities of such series; and
- provide that the debt securities will be unsecured, except as may be set forth in the applicable prospectus supplement.

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Unless we give you different information in the applicable prospectus supplement, the senior debt securities will be unsubordinated obligations and will rank equally with all of our other unsecured and unsubordinated indebtedness. Payments on the subordinated debt securities will be subordinated to the prior payment in full of all of our senior indebtedness, as described under “—Subordination” and in the applicable prospectus supplement.

Each indenture will provide that we may, but need not, designate more than one trustee under an indenture. Any trustee under an indenture may resign or be removed and a successor trustee may be appointed to act with respect to the series of debt securities administered by the resigning or removed trustee. If two or more persons are acting as trustee with respect to different series of debt securities, each trustee shall be a trustee of a trust under the applicable indenture separate and apart from the trust administered by any other trustee. Except as otherwise indicated in this prospectus, any action described in this prospectus to be taken by each trustee may be taken by each trustee with respect to, and only with respect to, the one or more series of debt securities for which it is trustee under the applicable indenture.

The prospectus supplement for each offering will provide the following terms, where applicable:

- the title of the debt securities and whether they are senior or subordinated;
- the aggregate principal amount of the debt securities being offered, the aggregate principal amount of the debt securities outstanding as of the most recent practicable date and any limit on their aggregate principal amount, including the aggregate principal amount of debt securities authorized;
- the price at which the debt securities will be issued, expressed as a percentage of the principal and, if other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof or, if applicable, the portion of the principal amount of such debt securities that is convertible into ordinary shares or the method by which any such portion shall be determined;
- if convertible, the terms on which such debt securities are convertible, including the initial conversion price or rate and the conversion period and any applicable limitations on the ownership or transferability of ordinary shares received on conversion;
- the date or dates, or the method for determining the date or dates, on which the principal of the debt securities will be payable;
- the fixed or variable interest rate or rates of the debt securities, or the method by which the interest rate or rates is determined;
- the date or dates, or the method for determining the date or dates, from which interest will accrue;
- the dates on which interest will be payable;
- the record dates for interest payment dates, or the method by which we will determine those dates;
- the persons to whom interest will be payable;
- the basis upon which interest will be calculated if other than that of a 360-day year of twelve 30-day months;
- any make-whole amount, which is the amount in addition to principal and interest that is required to be paid to the holder of a debt security as a result of any optional redemption or accelerated payment of such debt security, or the method for determining the make-whole amount;
- the place or places where the principal of, and any premium, or make-whole amount, and interest on, the debt securities will be payable;
- where the debt securities may be surrendered for registration of transfer or conversion or exchange;
- where notices or demands to or upon us in respect of the debt securities and the applicable indenture may be served;

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- the times, prices and other terms and conditions upon which we may redeem the debt securities;
- any obligation we have to redeem, repay or purchase the debt securities pursuant to any sinking fund or analogous provision or at the option of holders of the debt securities, and the times and prices at which we must redeem, repay or purchase the debt securities as a result of such an obligation;
- the currency or currencies in which the debt securities are denominated and payable if other than United States dollars, which may be a foreign currency or units of two or more foreign currencies or a composite currency or currencies and the terms and conditions relating thereto, and the manner of determining the equivalent of such foreign currency in United States dollars;
- whether the principal of, and any premium, or make-whole amount, or interest on, the debt securities of the series are to be payable, at our election or at the election of a holder, in a currency or currencies other than that in which the debt securities are denominated or stated to be payable, and other related terms and conditions;
- whether the amount of payments of principal of, and any premium, or make-whole amount, or interest on, the debt securities may be determined according to an index, formula or other method and how such amounts will be determined;
- whether the debt securities will be in registered form, bearer form or both and (1) if in registered form, the person to whom any interest shall be payable, if other than the person in whose name the security is registered at the close of business on the regular record date for such interest, or (2) if in bearer form, the manner in which, or the person to whom, any interest on the security shall be payable if otherwise than upon presentation and surrender upon maturity;
- any restrictions applicable to the offer, sale or delivery of debt securities in bearer form and the terms upon which securities in bearer form of the series may be exchanged for debt securities in registered form of the series and vice versa if permitted by applicable laws and regulations;
- whether any debt securities of the series are to be issuable initially in temporary global form and whether any debt securities of the series are to be issuable in permanent global form with or without coupons and, if so, whether beneficial owners of interests in any such permanent global security may or shall be required to exchange their interests for other debt securities of the series, and the manner in which interest shall be paid;
- the identity of the depositary for securities in registered form, if such series are to be issuable as a global security;
- the guarantors of each series, if any, and the extent of the guarantees (including provisions relating to seniority, subordination, security and release of the guarantees), if any;
- the date as of which any debt securities in bearer form or in temporary global form shall be dated if other than the original issuance date of the first security of the series to be issued;
- the applicability, if any, of the defeasance and covenant defeasance provisions described in this prospectus or in the applicable indenture;
- whether and under what circumstances we will pay any additional amounts on the debt securities in respect of any tax, assessment or governmental charge and, if so, whether we will have the option to redeem the debt securities in lieu of making such a payment;
- whether and under what circumstances the debt securities being offered are convertible into ordinary shares, including the conversion price or rate or the manner of calculation thereof;
- the circumstances, if any, specified in the applicable prospectus supplement, under which beneficial owners of interests in the global security may obtain definitive debt securities and the manner in which payments on a permanent global debt security will be made if any debt securities are issuable in temporary or permanent global form;

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- any provisions granting special rights to holders of securities upon the occurrence of such events as specified in the applicable prospectus supplement;
- if the debt securities of such series are to be issuable in definitive form only upon receipt of certain certificates or other documents or satisfaction of other conditions, then the form and/or terms of such certificates, documents or conditions;
- the name of the applicable trustee and the nature of any material relationship between the trustee and us or any of our affiliates, and the percentage of debt securities of the class necessary to require the trustee to take action;
- any deletions from, modifications of, or additions to our events of default or covenants and any change in the right of any trustee or any of the holders to declare the principal amount of any of such debt securities due and payable;
- provisions related to the modification of the indentures;
- applicable CUSIP numbers; and
- any other terms of such debt securities not inconsistent with the provisions of the applicable indenture or the Trust Indenture Act.

We may issue debt securities at a discount below their principal amount and provide for less than the entire principal amount thereof to be payable upon declaration of acceleration of the maturity of the debt securities. We refer to any such debt securities throughout this prospectus as “original issue discount securities.” The applicable prospectus supplement will describe the United States federal income tax consequences and other relevant considerations applicable to original issue discount securities.

We also may issue indexed debt securities. Payments of principal, premium and interest on indexed debt securities are determined with reference to the rate of exchange between the currency or currency unit in which the debt security is denominated and any other currency or currency unit specified by us, to the relationship between two or more currencies or currency units or by other similar methods or formulas specified in the prospectus supplement.

Except as described under “—Merger, Consolidation or Sale of Assets” or as may be set forth in any prospectus supplement, the debt securities will not contain any provisions that (1) would limit our ability to incur indebtedness or (2) would afford holders of debt securities protection in the event of (a) a highly leveraged or similar transaction involving us, or (b) a change of control or reorganization, restructuring, merger or similar transaction involving us that may adversely affect the holders of the debt securities. In the future, we may enter into transactions, such as the sale of all or substantially all of our assets or a merger or consolidation, that may have an adverse effect on our ability to service our indebtedness, including the debt securities, by, among other things, substantially reducing or eliminating our assets.

We will provide you with more information in the applicable prospectus supplement regarding any deletions, modifications, or additions to the events of default or covenants that are described below, including any addition of a covenant or other provision providing event risk or similar protection.

Payment

Unless we give you different information in the applicable prospectus supplement, the principal of, and any premium or make-whole amount, and interest on, any series of the debt securities will be payable at the corporate trust office of the trustee. We will provide you with the address of the trustee in the applicable prospectus supplement. We may also pay interest by mailing a check to the address of the person entitled to it as it appears in the applicable register for the debt securities or by wire transfer of funds to that person at an account maintained within the United States.

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All monies that we pay to a paying agent or a trustee for the payment of the principal of, and any premium or make-whole amount, or interest on, any debt security will be repaid to us if unclaimed at the end of two years after the obligation underlying payment becomes due and payable. After funds have been returned to us, the holder of the debt security may look only to us for payment, without payment of interest for the period which we hold the funds.

Denomination, Interest, Registration and Transfer

Unless otherwise described in the applicable prospectus supplement, the debt securities of any series will be issuable in denominations of \$1,000 and integral multiples of \$1,000.

Subject to the limitations imposed upon debt securities that are evidenced by a computerized entry in the records of a depository company rather than by physical delivery of a note, a holder of debt securities of any series may:

- exchange them for any authorized denomination of other debt securities of the same series and of a like aggregate principal amount and kind upon surrender of such debt securities at the corporate trust office of the applicable trustee or at the office of any transfer agent that we designate for such purpose; and
- surrender them for registration of transfer or exchange at the corporate trust office of the applicable trustee or at the office of any transfer agent that we designate for such purpose.

Every debt security surrendered for registration of transfer or exchange must be duly endorsed or accompanied by a written instrument of transfer satisfactory to the applicable trustee or transfer agent. Payment of a service charge will not be required for any registration of transfer or exchange of any debt securities, but we or the trustee may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection therewith. If in addition to the applicable trustee, the applicable prospectus supplement refers to any transfer agent initially designated by us for any series of debt securities, we may at any time rescind the designation of any such transfer agent or approve a change in the location through which any such transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for such series. We may at any time designate additional transfer agents for any series of debt securities.

Neither we, nor any trustee, will be required to:

- issue, register the transfer of or exchange debt securities of any series during a period beginning at the opening of business 15 calendar days before the day that the notice of redemption of any debt securities selected for redemption is mailed and ending at the close of business on the day of such mailing;
- register the transfer of or exchange any debt security, or portion thereof, so selected for redemption, in whole or in part, except the unredeemed portion of any debt security being redeemed in part; and
- issue, register the transfer of or exchange any debt security that has been surrendered for repayment at the option of the holder, except the portion, if any, of such debt security not to be so repaid.

Merger, Consolidation or Sale of Assets

The indentures provide that we may, without the consent of the holders of any outstanding debt securities, (1) consolidate with, (2) sell, lease or convey all or substantially all of our assets to, or (3) merge with or into, any other entity provided that:

- either we are the continuing entity, or the successor entity, if other than us, assumes the obligations (A) to pay the principal of, and any premium (or make-whole amount) and interest on, all of the debt securities and (B) to duly perform and observe all of the covenants and conditions contained in each indenture;
- after giving effect to the transaction, there is no event of default under the indentures and no event which, after notice or the lapse of time, or both, would become such an event of default, occurs and continues; and

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- an officers' certificate and legal opinion covering such conditions are delivered to each applicable trustee.

Covenants

Existence. Except as permitted under “—Merger, Consolidation or Sale of Assets,” the indentures require us to do or cause to be done all things necessary to preserve and keep in full force and effect our existence, rights and franchises. However, the indentures do not require us to preserve any right or franchise if we determine that any right or franchise is no longer desirable in the conduct of our business.

Payment of taxes and other claims. The indentures require us to pay, discharge or cause to be paid or discharged, before they become delinquent (1) all taxes, assessments and governmental charges levied or imposed on us, our subsidiaries or our subsidiaries' income, profits or property, and (2) all lawful claims for labor, materials and supplies which, if unpaid, might by law become a lien upon our property or the property of our subsidiaries. However, we will not be required to pay, discharge or cause to be paid or discharged any such tax, assessment, charge or claim whose amount, applicability or validity is being contested in good faith by appropriate proceedings.

Provision of financial information. The indentures require us to (1) within 15 days of each of the respective dates by which we are required to file our annual reports, quarterly reports and other documents with the SEC, file with the trustee copies of the annual report, quarterly report and other documents that we file with the SEC under Section 13 or 15(d) of the Exchange Act of 1934, as amended (the “Exchange Act”), (2) file with the trustee and the SEC any additional information, documents and reports regarding compliance by us with the conditions and covenants of the indentures, as required, (3) within 30 days after the filing with the trustee, mail to all holders of debt securities, as their names and addresses appear in the applicable register for such debt securities, without cost to such holders, summaries of any documents and reports required to be filed by us pursuant to (1) and (2) above, and (4) supply, promptly upon written request and payment of the reasonable cost of duplication and delivery, copies of such documents to any prospective holder.

Additional covenants. The applicable prospectus supplement will set forth any additional covenants relating to any series of debt securities.

Events of Default, Notice and Waiver

Unless the applicable prospectus supplement states otherwise, when we refer to “events of default” as defined in the indentures with respect to any series of debt securities, we mean:

- default in the payment of any installment of interest on any debt security of such series continuing for 30 calendar days;
- default in the payment of principal of, or any premium, or make-whole amount, on any debt security of such series for five business days at its stated maturity;
- default in making any sinking fund payment as required for any debt security of such series for five business days;
- default in the performance or breach of any covenant or warranty in the debt securities or in the indenture by us continuing for 90 calendar days after written notice as provided in the applicable indenture, but not of a covenant added to the indenture solely for the benefit of a series of debt securities issued thereunder other than such series;
- a default under any bond, debenture, note, mortgage, indenture or instrument:
 - (1) having an aggregate principal amount in excess of a minimum amount as specified in a prospectus supplement; or

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- (2) under which there may be issued, secured or evidenced any existing or later created indebtedness for money borrowed by us or our subsidiaries, if we are directly responsible or liable as obligor or guarantor, if the default results in the indebtedness becoming or being declared due and payable prior to the date it otherwise would have, without such indebtedness having been discharged, or such acceleration having been rescinded or annulled, within 30 days after notice to the issuing company specifying such default. Such notice shall be given to us by the trustee, or to us and the trustee by the holders of at least 10% in principal amount of the outstanding debt securities of that series. The written notice specifying such default and requiring us to cause such indebtedness to be discharged or cause such acceleration to be rescinded or annulled and shall state that such notice is a “Notice of Default” under such indenture;
- bankruptcy, insolvency or reorganization, or court appointment of a receiver, liquidator or trustee of Orchard Therapeutics or any significant subsidiary that, if contested, is not dismissed or stayed within 90 calendar days; and
- any other event of default provided with respect to a particular series of debt securities.

When we use the term “significant subsidiary,” we refer to the meaning ascribed to such term in Rule 1-02 of Regulation S-X promulgated under the Securities Act of 1933, as amended, or Securities Act.

If an event of default occurs and is continuing with respect to debt securities of any series outstanding, then the applicable trustee or the holders of 33% or more in principal amount of the debt securities of that series will have the right to declare the principal amount of all the debt securities of that series to be due and payable. If the debt securities of that series are original issue discount securities or indexed securities, then the applicable trustee or the holders of 33% or more in principal amount of the debt securities of that series will have the right to declare the portion of the principal amount as may be specified in the terms thereof to be due and payable. However, at any time after such a declaration of acceleration has been made, but before a judgment or decree for payment of the money due has been obtained by the applicable trustee, the holders of at least a majority in principal amount of outstanding debt securities of such series or of all debt securities then outstanding under the applicable indenture may rescind and annul such declaration and its consequences if:

- we have deposited with the applicable trustee all required payments of the principal, any premium, or make-whole amount, interest and, to the extent permitted by law, interest on overdue installment of interest, plus applicable fees, expenses, disbursements and advances of the applicable trustee; and
- all events of default, other than the non-payment of accelerated principal, or a specified portion thereof, and any premium, or make-whole amount, have been cured or waived.

We expect that the indentures will also provide that the holders of at least a majority in principal amount of the outstanding debt securities of any series or of all debt securities then outstanding under the applicable indenture may, on behalf of all holders, waive any past default with respect to such series and its consequences, except a default:

- in the payment of the principal, any premium, or make-whole amount, or interest;
- in respect of a covenant or provision contained in the applicable indenture that cannot be modified or amended without the consent of the holders of the outstanding debt security that is affected by the default; or
- in respect of a covenant or provision for the benefit or protection of the trustee, without its express written consent.

We expect that the indentures will require each trustee to give notice to the holders of debt securities within 90 days of a default unless such default has been cured or waived. However, the trustee may withhold notice if specified persons of such trustee consider such withholding to be in the interest of the holders of debt securities.

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The trustee may not withhold notice of a default in the payment of principal, any premium or interest on any debt security of such series or in the payment of any sinking fund installment in respect of any debt security of such series.

We expect that the indentures will provide that holders of debt securities of any series may not institute any proceedings, judicial or otherwise, with respect to such indenture or for any remedy under the indenture, unless the trustee fails to act for a period of 60 days after the trustee has received a written request to institute proceedings in respect of an event of default from the holders of 25% or more in principal amount of the outstanding debt securities of such series, as well as an offer of indemnity reasonably satisfactory to the trustee. However, this provision will not prevent any holder of debt securities from instituting suit for the enforcement of payment of the principal of, and any premium, or make-whole amount, and interest on, such debt securities at the respective due dates thereof.

We expect that the indentures will provide that, subject to provisions in each indenture relating to its duties in the case of a default, a trustee has no obligation to exercise any of its rights or powers at the request or direction of any holders of any series of debt securities then outstanding under the indenture, unless the holders have offered to the trustee reasonable security or indemnity. The holders of at least a majority in principal amount of the outstanding debt securities of any series or of all debt securities then outstanding under an indenture shall have the right to direct the time, method and place of conducting any proceeding for any remedy available to the applicable trustee, or of exercising any trust or power conferred upon such trustee. However, a trustee may refuse to follow any direction which:

- is in conflict with any law or the applicable indenture;
- may involve the trustee in personal liability; or
- may be unduly prejudicial to the holders of debt securities of the series not joining the proceeding.

Within 120 days after the close of each fiscal year, we will be required to deliver to each trustee a certificate, signed by one of our several specified officers, stating whether or not that officer has knowledge of any default under the applicable indenture. If the officer has knowledge of any default, the notice must specify the nature and status of the default.

Modification of the Indentures

We expect that the indentures will provide that modifications and amendments may be made only with the consent of the affected holders of at least a majority in principal amount of all outstanding debt securities issued under that indenture. However, no such modification or amendment may, without the consent of each of the affected holders of the debt securities affected by the modification or amendment:

- change the stated maturity of the principal of, or any premium, or make-whole amount, on, or any installment of principal of or interest on, any such debt security;
- reduce the principal amount of, the rate or amount of interest on or any premium, or make-whole amount, payable on redemption of any such debt security;
- reduce the amount of principal of an original issue discount security that would be due and payable upon declaration of acceleration of the maturity thereof or would be provable in bankruptcy, or adversely affect any right of repayment of the holder of any such debt security;
- change the place of payment or the coin or currency for payment of principal of, or any premium, or make-whole amount, or interest on, any such debt security;
- impair the right to institute suit for the enforcement of any payment on or with respect to any such debt security;

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- reduce the percentage in principal amount of any outstanding debt securities necessary to modify or amend the applicable indenture with respect to such debt securities, to waive compliance with particular provisions thereof or defaults and consequences thereunder or to reduce the quorum or voting requirements set forth in the applicable indenture; or
- modify any of the foregoing provisions or any of the provisions relating to the waiver of particular past defaults or covenants, except to increase the required percentage to effect such action or to provide that some of the other provisions may not be modified or waived without the consent of the holder of such debt security.

The holders of a majority in aggregate principal amount of the outstanding debt securities of each series may, on behalf of all holders of debt securities of that series, waive, insofar as that series is concerned, our compliance with material restrictive covenants of the applicable indenture.

We and our respective trustee may make modifications and amendments of an indenture without the consent of any holder of debt securities for any of the following purposes:

- to evidence the succession of another person to us as obligor under such indenture;
- to add to our covenants for the benefit of the holders of all or any series of debt securities or to surrender any right or power conferred upon us in such indenture;
- to add events of default for the benefit of the holders of all or any series of debt securities;
- to add or change any provisions of an indenture (1) to change or eliminate restrictions on the payment of principal of, or premium, or make-whole amount, or interest on, debt securities in bearer form, or (2) to permit or facilitate the issuance of debt securities in uncertificated form, provided that such action shall not adversely affect the interests of the holders of the debt securities of any series in any material respect;
- to change or eliminate any provisions of an indenture, provided that any such change or elimination shall become effective only when there are no debt securities outstanding of any series created prior thereto which are entitled to the benefit of such provision;
- to secure the debt securities;
- to establish the form or terms of debt securities of any series;
- to provide for the acceptance of appointment by a successor trustee or facilitate the administration of the trusts under an indenture by more than one trustee;
- to cure any ambiguity, defect or inconsistency in an indenture, provided that such action shall not adversely affect the interests of holders of debt securities of any series issued under such indenture; and
- to supplement any of the provisions of an indenture to the extent necessary to permit or facilitate defeasance and discharge of any series of such debt securities, provided that such action shall not adversely affect the interests of the holders of the outstanding debt securities of any series.

Voting

We expect the indentures will provide that in determining whether the holders of the requisite principal amount of outstanding debt securities of a series have given any request, demand, authorization, direction, notice, consent or waiver under the indentures or whether a quorum is present at a meeting of holders of debt securities:

- the principal amount of an original issue discount security that shall be deemed to be outstanding shall be the amount of the principal thereof that would be due and payable as of the date of such determination upon declaration of acceleration of the maturity thereof;

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- the principal amount of any debt security denominated in a foreign currency that shall be deemed outstanding shall be the United States dollar equivalent, determined on the issue date for such debt security, of the principal amount or, in the case of an original issue discount security, the United States dollar equivalent on the issue date of such debt security of the amount determined as provided in the preceding bullet point;
- the principal amount of an indexed security that shall be deemed outstanding shall be the principal face amount of such indexed security at original issuance, unless otherwise provided for such indexed security under such indenture; and
- debt securities owned by us or any other obligor upon the debt securities or by any affiliate of ours or of such other obligor shall be disregarded.

The indentures contain provisions for convening meetings of the holders of debt securities of a series. A meeting will be permitted to be called at any time by the applicable trustee, and also, upon request, by us or the holders of at least 25% in principal amount of the outstanding debt securities of such series, in any such case upon notice given as provided in such indenture. Except for any consent that must be given by the holder of each debt security affected by the modifications and amendments of an indenture described above, any resolution presented at a meeting or adjourned meeting duly reconvened at which a quorum is present may be adopted by the affirmative vote of the holders of a majority of the aggregate principal amount of the outstanding debt securities of that series represented at such meeting.

Notwithstanding the preceding paragraph, except as referred to above, any resolution relating to a request, demand, authorization, direction, notice, consent, waiver or other action that may be made, given or taken by the holders of a specified percentage, which is less than a majority of the aggregate principal amount of the outstanding debt securities of a series, may be adopted at a meeting or adjourned meeting duly reconvened at which a quorum is present by the affirmative vote of such specified percentage.

Any resolution passed or decision taken at any properly held meeting of holders of debt securities of any series will be binding on all holders of such series. The quorum at any meeting called to adopt a resolution, and at any reconvened meeting, will be persons holding or representing a majority in principal amount of the outstanding debt securities of a series. However, if any action is to be taken relating to a consent or waiver which may be given by the holders of at least a specified percentage in principal amount of the outstanding debt securities of a series, the persons holding such percentage will constitute a quorum.

Notwithstanding the foregoing provisions, we expect that the indentures will provide that if any action is to be taken at a meeting with respect to any request, demand, authorization, direction, notice, consent, waiver or other action that such indenture expressly provides may be made, given or taken by the holders of a specified percentage in principal amount of all outstanding debt securities affected by such action, or of the holders of such series and one or more additional series:

- there shall be no minimum quorum requirement for such meeting; and
- the principal amount of the outstanding debt securities of such series that vote in favor of such request, demand, authorization, direction, notice, consent, waiver or other action shall be taken account in determining whether such request, demand, authorization, direction, notice, consent, waiver or other action has been made, given or taken under such indenture.

Subordination

Unless otherwise provided in the applicable prospectus supplement and indenture, subordinated securities will be subject to the following subordination provisions.

Upon any distribution to our creditors in a liquidation, dissolution or reorganization, the payment of the principal of and interest on any subordinated securities will be subordinated to the extent provided in the applicable

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indenture in right of payment to the prior payment in full of all senior debt. However, our obligation to make payments of the principal of and interest on such subordinated securities otherwise will not be affected. No payment of principal or interest will be permitted to be made on subordinated securities at any time if a default on senior debt exists that permits the holders of such senior debt to accelerate its maturity and the default is the subject of judicial proceedings or we receive notice of the default. After all senior debt is paid in full and until the subordinated securities are paid in full, holders of subordinated securities will be subrogated to the rights of holders of senior debt to the extent that distributions otherwise payable to holders of subordinated securities have been applied to the payment of senior debt. The subordinated indenture will not restrict the amount of senior debt or other indebtedness of Orchard Therapeutics and its subsidiaries. As a result of these subordination provisions, in the event of a distribution of assets upon insolvency, holders of subordinated securities may recover less, ratably, than our general creditors.

The term “senior debt” will be defined in the applicable indenture as the principal of and interest on, or substantially similar payments to be made by us in respect of, other outstanding indebtedness, whether outstanding at the date of execution of the applicable indenture or subsequently incurred, created or assumed. The prospectus supplement may include a description of additional terms implementing the subordination feature.

No restrictions will be included in any indenture relating to subordinated securities upon the creation of additional senior debt.

If this prospectus is being delivered in connection with the offering of a series of subordinated securities, the accompanying prospectus supplement or the information incorporated in this prospectus by reference will set forth the approximate amount of senior debt outstanding as of the end of our most recent fiscal quarter.

Defeasance and Discharge

The terms of each indenture are expected to provide us with the option to be discharged from any and all obligations in respect of the debt securities issued thereunder upon the deposit with the trustee, in trust, of money or government obligations, or both, which through the payment of interest and principal in accordance with their terms will provide money in an amount sufficient to pay any installment of principal, premium and interest on, and any mandatory sinking fund payments in respect of, the debt securities on the stated maturity of the payments in accordance with the terms of the debt securities and the indenture governing the debt securities. We expect that this right may only be exercised if, among other things, we have received from, or there has been published by, the Internal Revenue Service a ruling to the effect that such a discharge will not be deemed, or result in, a taxable event with respect to holders. This discharge would not apply to our obligations to register the transfer or exchange of debt securities, to replace stolen, lost or mutilated debt securities, to maintain paying agencies and hold moneys for payment in trust.

Defeasance of Certain Covenants

We expect that the terms of the debt securities will provide us with the right not to comply with specified covenants and that specified events of default described in a prospectus supplement will not apply provided we deposit with the trustee money or government obligations, or both, which through the payment of interest and principal will provide money in an amount sufficient to pay any installment of principal, premium, and interest on, and any mandatory sinking fund payments in respect of, the debt securities on the stated maturity of such payments in accordance with the terms of the debt securities and the indenture governing such debt securities. We expect that to exercise this right, we will also be required to deliver to the trustee an opinion of counsel to the effect that the deposit and related covenant defeasance should not cause the holders of such series to recognize income, gain or loss for federal income tax purposes.

Conversion Rights

The terms and conditions, if any, upon which the debt securities are convertible into ordinary shares will be set forth in the applicable prospectus supplement. The terms will include whether the debt securities are convertible into ordinary shares, the conversion price, or manner of calculation thereof, the conversion period, provisions as to whether conversion will be at the issuing company's option or the option of the holders, the events requiring an adjustment of the conversion price and provisions affecting conversion in the event of the redemption of the debt securities and any restrictions on conversion.

Global Securities

The debt securities of a series may be issued in whole or in part in the form of one or more global securities that will be deposited with, or on behalf of, a depository identified in the applicable prospectus supplement relating to such series. Global securities, if any, issued in the United States are expected to be deposited with The Depository Trust Company, or DTC, as depository. We may issue global securities in either registered or bearer form and in either temporary or permanent form. We will describe the specific terms of the depository arrangement with respect to a series of debt securities in the applicable prospectus supplement relating to such series. We expect that unless the applicable prospectus supplement provides otherwise, the following provisions will apply to depository arrangements.

Once a global security is issued, the depository for such global security or its nominee will credit on its book-entry registration and transfer system the respective principal amounts of the individual debt securities represented by such global security to the accounts of participants that have accounts with such depository. Such accounts shall be designated by the underwriters, dealers or agents with respect to such debt securities or by us if we offer such debt securities directly. Ownership of beneficial interests in such global security will be limited to participants with the depository or persons that may hold interests through those participants.

We expect that, under procedures established by DTC, ownership of beneficial interests in any global security for which DTC is the depository will be shown on, and the transfer of that ownership will be effected only through, records maintained by DTC or its nominee, with respect to beneficial interests of participants with the depository, and records of participants, with respect to beneficial interests of persons who hold through participants with the depository. Neither we nor the trustee will have any responsibility or liability for any aspect of the records of DTC or for maintaining, supervising or reviewing any records of DTC or any of its participants relating to beneficial ownership interests in the debt securities. The laws of some states require that certain purchasers of securities take physical delivery of such securities in definitive form. Such limits and laws may impair the ability to own, pledge or transfer beneficial interest in a global security.

So long as the depository for a global security or its nominee is the registered owner of such global security, such depository or such nominee, as the case may be, will be considered the sole owner or holder of the debt securities represented by the global security for all purposes under the applicable indenture. Except as described below or in the applicable prospectus supplement, owners of beneficial interest in a global security will not be entitled to have any of the individual debt securities represented by such global security registered in their names, will not receive or be entitled to receive physical delivery of any such debt securities in definitive form and will not be considered the owners or holders thereof under the applicable indenture. Beneficial owners of debt securities evidenced by a global security will not be considered the owners or holders thereof under the applicable indenture for any purpose, including with respect to the giving of any direction, instructions or approvals to the trustee under the indenture. Accordingly, each person owning a beneficial interest in a global security with respect to which DTC is the depository must rely on the procedures of DTC and, if such person is not a participant with the depository, on the procedures of the participant through which such person owns its interests, to exercise any rights of a holder under the applicable indenture. We understand that, under existing industry practice, if DTC requests any action of holders or if an owner of a beneficial interest in a global security desires to give or take any action which a holder is entitled to give or take under the applicable indenture, DTC would

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authorize the participants holding the relevant beneficial interest to give or take such action, and such participants would authorize beneficial owners through such participants to give or take such actions or would otherwise act upon the instructions of beneficial owners holding through them.

Payments of principal of, and any premium, or make-whole amount, and interest on, individual debt securities represented by a global security registered in the name of a depository or its nominee will be made to or at the direction of the depository or its nominee, as the case may be, as the registered owner of the global security under the applicable indenture. Under the terms of the applicable indenture, we and the trustee may treat the persons in whose name debt securities, including a global security, are registered as the owners thereof for the purpose of receiving such payments. Consequently, neither we nor the trustee have or will have any responsibility or liability for the payment of such amounts to beneficial owners of debt securities including principal, any premium, or make-whole amount, or interest. We believe, however, that it is currently the policy of DTC to immediately credit the accounts of relevant participants with such payments, in amounts proportionate to their respective holdings of beneficial interests in the relevant global security as shown on the records of DTC or its nominee. We also expect that payments by participants to owners of beneficial interests in such global security held through such participants will be governed by standing instructions and customary practices, as is the case with securities held for the account of customers in bearer form or registered in street name, and will be the responsibility of such participants. Redemption notices with respect to any debt securities represented by a global security will be sent to the depository or its nominee. If less than all of the debt securities of any series are to be redeemed, we expect the depository to determine the amount of the interest of each participant in such debt securities to be redeemed to be determined by lot. Neither we, the trustee, any paying agent nor the security registrar for such debt securities will have any responsibility or liability for any aspect of the records relating to or payments made on account of beneficial ownership interests in the global security for such debt securities or for maintaining any records with respect thereto.

Neither we nor the trustee will be liable for any delay by the holders of a global security or the depository in identifying the beneficial owners of debt securities, and we and the trustee may conclusively rely on, and will be protected in relying on, instructions from the holder of a global security or the depository for all purposes. The rules applicable to DTC and its participants are on file with the SEC.

If a depository for any debt securities is at any time unwilling, unable or ineligible to continue as depository and we do not appoint a successor depository within 90 days, we will issue individual debt securities in exchange for the global security representing such debt securities. In addition, we may at any time and in our sole discretion, subject to any limitations described in the applicable prospectus supplement relating to such debt securities, determine not to have any of such debt securities represented by one or more global securities and in such event will issue individual debt securities in exchange for the global security or securities representing such debt securities. Individual debt securities so issued will be issued in denominations of \$1,000 and integral multiples of \$1,000.

The debt securities of a series may also be issued in whole or in part in the form of one or more bearer global securities that will be deposited with a depository, or with a nominee for such depository, identified in the applicable prospectus supplement. Any such bearer global securities may be issued in temporary or permanent form. The specific terms and procedures, including the specific terms of the depository arrangement, with respect to any portion of a series of debt securities to be represented by one or more bearer global securities will be described in the applicable prospectus supplement.

No Recourse

There is no recourse under any obligation, covenant or agreement in the applicable indenture or with respect to any security against any of our or our successor's past, present or future shareholders, employees, officers or directors.

We refer you to any applicable prospectus supplement with respect to any deletions or additions or modifications to the descriptions above.

DESCRIPTION OF WARRANTS

We may offer warrants for the purchase of ordinary shares, each of which may be represented by one American Depositary Share, and/or senior or subordinated debt securities in one or more series, from time to time. We may issue warrants independently or together with ordinary shares, each of which may be represented by one American Depositary Share, and/or senior or subordinated debt securities, and the warrants may be attached to or separate from those securities.

If we offer warrants, they will be evidenced by warrant certificates issued under one or more warrant agreements, which are contracts between us and an agent for the holders of the warrants. We will indicate the name and address of the warrant agent in the applicable prospectus supplement relating to a particular series of warrants.

The prospectus supplement for each offering will provide the following terms, where applicable:

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- in the case of warrants to purchase securities, the number of shares purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreement and the warrants;
- the terms of any rights to redeem or call the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the periods during which, and places at which, the warrants are exercisable;
- the manner of exercise;
- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrant agreement and warrants may be modified;
- federal income tax consequences of holding or exercising the warrants;
- the terms of the securities issuable upon exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

We urge you to read the prospectus supplement related to any series of warrants we may offer, as well as the complete warrant agreement and warrant certificate that contain the terms of the warrants. If we offer warrants, forms of warrant agreements and warrant certificates relating to warrants for the purchase of such ordinary shares and debt securities will be incorporated by reference into the registration statement of which this prospectus is a part from reports we would subsequently file with the SEC.

DESCRIPTION OF UNITS

We may offer units consisting of ordinary shares, ordinary shares in the form of ADSs, debt securities and/or warrants for the purchase of ordinary shares and/or debt securities in any combination in one or more series, from time to time.

If we offer units, they will be evidenced by unit certificates issued under one or more unit agreements, which are contracts between us and an agent for the holders of the units.

If we offer any units, certain terms of that series of units will be described in the applicable prospectus supplement, including, without limitation, the following, as applicable:

- the title of the series of units;
- identification and description of the separate constituent securities comprising the units;
- the price or prices at which the units will be issued;
- the date, if any, on and after which the constituent securities comprising the units will be separately transferable;
- a discussion of certain United States federal income tax considerations applicable to the units; and
- any other terms of the units and their constituent securities.

We urge you to read the prospectus supplement related to any series of units we may offer, as well as the complete unit agreement and unit certificate that contain the terms of the unit. If we offer units, forms of unit agreements and unit certificates relating to units will be incorporated by reference into the registration statement of which this prospectus is a part from reports we would subsequently file with the SEC.

TAXATION

U.S. Federal Income Tax Considerations For U.S. Holders

Our most recent Annual Report on Form 10-K for the year ended December 31, 2020, as updated by other reports and documents we file with the SEC after the date of this prospectus and that are incorporated by reference herein, provides a discussion of the material U.S. federal income tax considerations that may be relevant to prospective investors in our ordinary shares. The applicable prospectus supplement may also contain information about any material U.S. federal income tax considerations relating to the securities covered by such prospectus supplement.

U.K. Taxation

Our most recent Annual Report on Form 10-K for the year ended December 31, 2020, as updated by other reports and documents we file with the SEC after the date of this prospectus and that are incorporated by reference herein, provides a discussion of the material U.K. tax consequences that may be relevant to prospective investors in our ordinary shares. The applicable prospectus supplement may also contain information about any U.K. tax considerations relating to the securities covered by such prospectus supplement.

USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds from the sale of our securities offered by us under this prospectus. Except as described in any prospectus supplement, we currently anticipate using the net proceeds from the sale of our securities offered hereby primarily for general corporate purposes which include, but are not limited to: funding our ongoing commercialization of Libmeldy™ (formerly OTL-200) in the European Union and other regions of the world; research and development and clinical development costs to support the advancement of our potential product candidates; discovering additional product candidates; and the potential expansion of our manufacturing capabilities. We may also use a portion of the net proceeds to pay interest or principal on outstanding indebtedness, if any, and/or acquire or invest in complementary businesses, products and technologies. Although we have no specific agreements, commitments or understandings with respect to any acquisition, we evaluate acquisition opportunities and engage in related discussions with other companies from time to time.

Pending the use of the net proceeds, we intend to invest the net proceeds in a variety of capital preservation instruments, including short-term, interest-bearing, investment-grade securities.

PLAN OF DISTRIBUTION

We may sell our securities from time to time in one or more transactions. We may sell our securities to or through agents, underwriters, dealers, remarketing firms or other third parties or directly to one or more purchasers or through a combination of any of these methods. In some cases, we or dealers acting with us or on our behalf may also purchase our securities and reoffer them to the public. We may also offer and sell, or agree to deliver, securities pursuant to, or in connection with, any option agreement or other contractual arrangement.

Agents whom we designate may solicit offers to purchase our securities.

- We will name any agent involved in offering or selling our securities, and disclose any commissions that we will pay to the agent, in the applicable prospectus supplement.
- Unless indicate otherwise in the applicable prospectus supplement, agents will act on a best efforts basis for the period of their appointment.
- Agents may be deemed to be underwriters under the Securities Act of any of our securities that they offer or sell.

We may use an underwriter or underwriters in the offer or sale of our securities.

- If we use an underwriter or underwriters, we will execute an underwriting agreement with the underwriter or underwriters at the time that we reach an agreement for the sale of our securities.
- We will include the names of the specific managing underwriter or underwriters, as well as the names of any other underwriters, and the terms of the transactions, including the compensation the underwriters and dealers will receive, in the applicable prospectus supplement.
- The underwriters will use the applicable prospectus supplement, together with the prospectus, to sell our securities.

We may use a dealer to sell our securities.

- If we use a dealer, we will sell our securities to the dealer, as principal.
- The dealer will then sell our securities to the public at varying prices that the dealer will determine at the time it sells our securities.
- We will include the name of the dealer and the terms of the transactions with the dealer in the applicable prospectus supplement.

One or more firms, referred to as “remarketing firms,” may also offer or sell the securities, if a prospectus supplement so indicates, in connection with a remarketing arrangement upon their purchase. Remarketing firms will act as principals for their own accounts or as our agents. These remarketing firms will offer or sell the securities in accordance with the terms of the securities. Each prospectus supplement will identify and describe any remarketing firm and the terms of its agreement, if any, with us and will describe the remarketing firm’s compensation. Remarketing firms may be deemed to be underwriters in connection with the securities they remarket. Remarketing firms may be entitled under agreements that may be entered into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

We may solicit directly offers to purchase our securities, and we may directly sell our securities to institutional or other investors. We will describe the terms of direct sales in the applicable prospectus supplement.

We may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) of the Securities Act.

We may enter into derivative or hedging transactions with third parties or sell securities not covered by this prospectus to third parties in privately negotiated transactions. In connection with such a transaction, the third

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parties may sell securities covered by and pursuant to this prospectus and any accompanying prospectus supplement. If so, the third party may use securities borrowed from us or others to settle such sales and may use securities received from us to close out any related short positions. We may also loan or pledge securities covered by this prospectus and any accompanying prospectus supplement to third parties, who may sell the loaned securities or, in an event of default in the case of a pledge, sell the pledged securities pursuant to this prospectus and any accompanying prospectus supplement.

Agents, underwriters and dealers participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. In addition, the underwriters' commissions, discounts or concessions may qualify as underwriters' compensation under the Securities Act and the rules of the Financial Industry Regulatory Authority, Inc. We may indemnify agents, underwriters and dealers against certain liabilities, including liabilities under the Securities Act. Agents, underwriters and dealers, or their affiliates, may be customers of, engage in transactions with or perform services for us or our respective affiliates, in the ordinary course of business.

We may authorize agents and underwriters to solicit offers by certain institutions to purchase our securities at the public offering price under delayed delivery contracts.

- If we use delayed delivery contracts, we will disclose that we are using them in the prospectus supplement and will tell you when we will demand payment and when delivery of our securities will be made under the delayed delivery contracts.
- These delayed delivery contracts will be subject only to the conditions that we describe in the prospectus supplement.
- We will describe in the applicable prospectus supplement the commission that underwriters and agents soliciting purchases of our securities under delayed delivery contracts will be entitled to receive.

Unless otherwise specified in connection with a particular underwritten offering of our securities, the underwriters will not be obligated to purchase offered securities unless specified conditions are satisfied, and if the underwriters do purchase any offered securities, they will purchase all offered securities.

Certain underwriters may use this prospectus and any accompanying prospectus supplement for offers and sales related to market-making transactions in the securities. These underwriters may act as principal or agent in these transactions, and the sales will be made at prices related to prevailing market prices at the time of sale.

In order to facilitate the offering of the securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than we sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing the applicable security in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if the securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

The underwriters, dealers and agents may engage in other transactions with us, or perform other services for us, in the ordinary course of their business.

We may effect sales of securities in connection with forward sale, option, swap or other types of agreements with third parties.

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Any distribution of securities pursuant to any sale may be effected from time to time in one or more transactions that may take place through a stock exchange, including block trades or ordinary broker's transactions, or through broker-dealers acting either as principal or agent, or through privately-negotiated transactions, or through an underwritten public offering, or through a combination of any such methods of sale, at market prices prevailing at the time of sale, prices relating to such prevailing market prices or at negotiated or fixed prices.

The specific terms of the lock-up provisions, if any, with respect to any given offering will be described in the applicable prospectus supplement.

The expenses of any offering of our securities will be detailed in the applicable prospectus supplement.

We will identify the specific plan of distribution, including any agents, underwriters, dealers, remarketing firms or other third parties and their compensation in a prospectus supplement.

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. Any underwriters will be advised about other issues relating to any offering by their own legal counsel.

EXPERTS

The financial statements incorporated in this Prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2020 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.

SERVICE OF PROCESS AND ENFORCEMENT OF LIABILITIES

We are incorporated and currently existing under the laws of England and Wales. In addition, certain of our directors and officers reside outside of the United States and most of the assets of our non-U.S. subsidiaries are located outside of the United States. As a result, it may be difficult for investors to effect service of process on us or those persons in the United States or to enforce in the United States judgments obtained in United States courts against us or those persons based on the civil liability or other provisions of the United States securities laws or other laws. In addition, uncertainty exists as to whether the courts of England and Wales would:

- recognize or enforce judgments of United States courts obtained against us or our directors or officers predicated upon the civil liabilities provisions of the securities laws of the United States or any state in the United States; or
- entertain original actions brought in England and Wales against us or our directors or officers predicated upon the securities laws of the United States or any state in the United States.

There is currently no treaty between (i) the United States and (ii) England and Wales providing for reciprocal recognition and enforcement of judgments of United States courts in civil and commercial matters (although the United States and the United Kingdom are both parties to the New York Convention on the Recognition and Enforcement of Foreign Arbitral Awards) and that a final judgment for the payment of money rendered by any general or state court in the United States based on civil liability, whether predicated solely upon the United States securities laws, would not be automatically enforceable in England and Wales. Any final and conclusive monetary judgment for a definite sum obtained against us in United States courts would be treated by the courts of England and Wales as a cause of action in itself and sued upon as a debt at common law so that no retrial of the issues would be necessary, provided that:

- the relevant U.S. court had jurisdiction over the original proceedings according to English conflicts of laws principles at the time when proceedings were initiated;
- England and Wales courts had jurisdiction over the matter on enforcement and we either submitted to such jurisdiction or were resident or carrying on business within such jurisdiction and were duly served with process;
- the U.S. judgment was final and conclusive on the merits in the sense of being final and unalterable in the court that pronounced it and being for a definite sum of money;
- the judgment given by the courts was not in respect of penalties, taxes, fines or similar fiscal or revenue obligations (or otherwise based on a U.S. law that an English court considers to relate to a penal, revenue or other public law);
- the judgment was not procured by fraud;

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- recognition or enforcement of the judgment in England and Wales would not be contrary to public policy or the Human Rights Act 1998;
- the proceedings pursuant to which judgment was obtained were not contrary to natural justice;
- the U.S. judgment was not arrived at by doubling, trebling or otherwise multiplying a sum assessed as compensation for the loss or damages sustained and not being otherwise in breach of Section 5 of the UK Protection of Trading Interests Act 1980, or is a judgment based on measures designated by the Secretary of State under Section 1 of that Act;
- there is not a prior decision of an English court or the court of another jurisdiction on the issues in question between the same parties; and
- the English enforcement proceedings were commenced within the limitation period.

Whether these requirements are met in respect of a judgment based upon the civil liability provisions of the United States securities laws, including whether the award of monetary damages under such laws would constitute a penalty, is an issue for the court making such decision.

Subject to the foregoing, investors may be able to enforce in England and Wales judgments in civil and commercial matters that have been obtained from U.S. federal or state courts. Nevertheless, we cannot assure you that those judgments will be recognized or enforceable in England and Wales.

If an English court gives judgment for the sum payable under a U.S. judgment, the English judgment will be enforceable by methods generally available for this purpose. These methods generally permit the English court discretion to prescribe the manner of enforcement. In addition, it may not be possible to obtain an English judgment or to enforce that judgment if the judgment debtor is or becomes subject to any insolvency or similar proceedings, or if the judgment debtor has any set-off or counterclaim against the judgment creditor. Also note that, in any enforcement proceedings, the judgment debtor may raise any counterclaim that could have been brought if the action had been originally brought in England unless the subject of the counterclaim was in issue and denied in the U.S. proceedings.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public at the SEC's website at www.sec.gov. Copies of certain information filed by us with the SEC are also available on our website at www.orchard-tx.com. Our website is not a part of this prospectus and is not incorporated by reference in this prospectus.

This prospectus is part of the registration statement we filed with the SEC. This prospectus omits some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the registration statement for further information about us and our consolidated subsidiaries and the securities we are offering. Statements in this prospectus concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements. 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 into this prospectus the information contained in other documents we file with the SEC, which means that we can disclose important information to you by referring you to those documents. Any statement contained in any document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded, for purposes of this prospectus, to the extent that a statement contained in or omitted from this prospectus, or in any other subsequently filed document that also is or is deemed to be incorporated by reference herein, modifies or supersedes such statement. Any such statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus. We incorporate by reference the documents listed below which have been filed by us:

- Our Annual Report on [Form 10-K](#) for the year ended December 31, 2020, filed with the SEC on March 2, 2021;
- The information specifically incorporated by reference into our Annual Report on [Form 10-K](#) for the year ended December 31, 2020 from our definitive proxy statement on [Schedule 14A](#) (other than information furnished rather than filed), which was filed with the SEC on April 28, 2021;
- Quarterly Reports on Form 10-Q filed with the SEC for the quarters ended March 31, 2021, June 30, 2021 and September 30, 2021, filed with the SEC on [May 13, 2021](#), [August 4, 2021](#) and [November 4, 2021](#), respectively;
- Current Reports on Form 8-K filed with the SEC on [January 11, 2021](#), [January 14, 2021](#), [January 19, 2021](#), [January 29, 2021](#), [February 9, 2021](#), [April 14, 2021](#), [May 11, 2021](#), [May 28, 2021](#), [June 4, 2021](#), [June 22, 2021](#), [June 29, 2021](#), [July 1, 2021](#), [September 14, 2021](#), [September 14, 2021](#), [November 18, 2021](#), [January 10, 2022](#), [January 21, 2022](#) and [February 4, 2022](#) (except that, with respect to the foregoing Current Reports, any portions thereof which are furnished and not filed shall not be deemed incorporated by reference); and
- The description of our ordinary shares and ADSs contained in our Registration Statement on [Form 8-A](#), as filed with the SEC under Section 12(b) of the Exchange Act on October 29, 2018, including any amendment or report filed for the purpose of updating such description (File No. 001-38722).

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act on or after the date of this prospectus, including our annual Proxy Statement on Schedule 14A relating to our annual general meeting of shareholders, until the earlier of the date on which all of the securities registered hereunder have been sold or the registration statement of which this prospectus is a part has been withdrawn, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

We will provide to each person at their request, including any beneficial owner, to whom a prospectus is delivered, a copy of any or all of the reports or documents that have been incorporated by reference into this prospectus but not delivered with this prospectus free of charge. We will provide these reports upon written or oral request at no cost to the requester. Please direct your request, either in writing or by telephone, to the following address and telephone number:

Orchard Therapeutics plc
108 Cannon Street
London EC4N 6EU
United Kingdom
+44 (0) 203 808 8286

You may also access these documents on our website, www.orchard-tx.com. The information contained on, or that can be accessed through, our website is not a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

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You should rely only on the information incorporated by reference or provided in this prospectus. We have not authorized anyone else to provide you with different or additional information. An offer of these securities is not being made in any jurisdiction where the offer or sale is not permitted. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front of those documents.



\$200,000,000

Ordinary Shares
American Depositary Shares representing Ordinary Shares
Debt Securities
Warrants
Units

PROSPECTUS

March 30, 2022

PART II

INFORMATION NOT REQUIRED IN THE PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution

The following is an estimate of the expenses (all of which are to be paid by us) that we may incur in connection with the securities being registered hereby, other than the FINRA filing fee.

SEC registration fee	\$ 18,540(1)
FINRA filing fee	225,500
Legal fees and expenses	*
Accounting fees and expenses	*
Miscellaneous expenses	*
Total	<u>\$ *</u>

* Estimated expenses not presently known.

(1) The registrant previously paid a fee of \$12,980.

Item 15. Indemnification of Directors and Officers

Subject to the Companies Act 2006, members of the registrant's board of directors and its officers (excluding auditors) have the benefit of the following indemnification provisions in the registrant's Articles of Association:

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

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

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

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

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Item 16. Exhibits

The following exhibits are filed with this registration statement or are incorporated herein by reference.

Exhibit Number	<u>Description of Exhibit</u>
1.1*	Form of Underwriting Agreement
3.1	<u>Articles of Association of Orchard Therapeutics plc (Incorporated herein by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-38722), filed with the Securities and Exchange Commission on June 19, 2020).</u>
4.1	<u>Deposit Agreement (Incorporated herein by reference to 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).</u>
4.2	<u>Form of American Depositary Receipt (Incorporated herein by reference to Exhibit 2.2 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).</u>
4.3	<u>Form of Indenture for Senior Debt Securities (Exhibit 4.3 to the Registrant's Registration Statement on Form F-3 (File No. 333-234439), filed with the Securities and Exchange Commission on November 1, 2019).</u>
4.4	<u>Form of Senior Debt Security (included in Exhibit 4.3 hereto).</u>
4.5	<u>Form of Indenture for Subordinated Debt Securities (Exhibit 4.5 to the Registrant's Registration Statement on Form F-3 (File No. 333-234439), filed with the Securities and Exchange Commission on November 1, 2019).</u>
4.6	<u>Form of Subordinated Debt Security (included in Exhibit 4.5 hereto).</u>
4.7*	Form of Warrant Agreement
4.8*	Form of Warrant Certificate
4.9*	Form of Unit Agreement
4.10*	Form of Unit Certificate
5.1	<u>Opinion of Goodwin Procter (UK) LLP</u>
5.2	<u>Opinion of Goodwin Procter LLP</u>
10.1	<u>Investment and shareholders' agreement by and between the registrant and the shareholders named therein, dated August 2, 2018, as amended (Incorporated herein by reference to Exhibit 10.1 to the Company's Registration Statement on Form F-1, File No. 333-231916, filed with the Securities and Exchange Commission on June 3, 2019).</u>
23.1	<u>Consent of Goodwin Procter (UK) LLP (included in Exhibit 5.1 hereto).</u>
23.2	<u>Consent of Goodwin Procter LLP (included in Exhibit 5.2 hereto).</u>
23.3	<u>Consent of PricewaterhouseCoopers LLP</u>
24.1	<u>Power of Attorney (included on signature page)</u>
25.1**	Form T-1 Statement of Eligibility of Trustee for Senior Indenture under the Trust Indenture Act of 1939.
25.2**	Form T-1 Statement of Eligibility of Trustee for Subordinated Indenture under the Trust Indenture Act of 1939.
107	<u>Filing Fee Table</u>

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- * To be filed, if necessary, as an exhibit to a post-effective amendment to this registration statement or as an exhibit to a report filed under the Securities Exchange Act of 1934, as amended, and incorporated herein by reference.
- ** To be filed pursuant to Section 305(b)(2) of the Trust Indenture Act of 1939, as amended.

Item 17. Undertakings

The undersigned registrant hereby undertakes:

- (a) 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;
 - (ii) To reflect in the prospectus any facts or events arising after the effective date of the 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 the 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 SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement.
 - (iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement.

Provided, however, that paragraphs (a)(1)(i), (a)(1)(ii) and (a)(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 SEC by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the 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 that 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) (i) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:
 - (A) Each prospectus filed by a 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
 - (B) 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,

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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 the 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 the 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, the 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 the 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 the undersigned registrant or used or referred to by the undersigned registrant;
 - (iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and
 - (iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.
- (b) The undersigned registrant hereby undertakes 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 Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the 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.
- (h) 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 foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act 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.
- (j) The undersigned registrant hereby undertakes to file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of section 310 of the Trust Indenture Act in accordance with the rules and regulations prescribed by the SEC under section 305(b)2 of the Trust Indenture Act.

SIGNATURES

Pursuant to the requirements of the Securities Act, the registrant has duly caused this Post-Effective Amendment No. 2 to Registration Statement on Form S-3 to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of London, United Kingdom, on this 30th day of March, 2022.

ORCHARD THERAPEUTICS PLC

By: /s/ Bobby Gaspar
Bobby Gaspar, M.D., Ph.D.
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 and in his name, place and stead, and in any and all capacities, to sign for us and in our names in the capacities indicated below any and all amendments (including post-effective amendments) to this Post-Effective Amendment No. 2 to Registration Statement on Form S-3 (or any other registration statement for the same offering that is to be effective upon filing pursuant to Rule 462(b) under the Securities Act of 1933, as amended), and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises, as full to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this Post-Effective Amendment No. 2 to Registration Statement on Form S-3 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, M.D., Ph.D.	Chief Executive Officer and Director <i>(Principal Executive Officer)</i>	March 30, 2022
<u>/s/ Frank E. Thomas</u> Frank E. Thomas	President and Chief Operating Officer <i>(Principal Financial Officer and Principal Accounting Officer)</i>	March 30, 2022
<u>/s/ James A. Geraghty</u> James A. Geraghty	Chairman of the Board of Directors	March 30, 2022
<u>/s/ Joanne T. Beck</u> Joanne T. Beck, Ph.D.	Director	March 30, 2022
<u>/s/ John Curnutte</u> John Curnutte	Director	March 30, 2022

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Signature	Title	Date
<u>/s/ Marc Dunoyer</u> Marc Dunoyer	Director	March 30, 2022
<u>/s/ Steven M. Altschuler</u> Steven M. Altschuler, M.D.	Director	March 30, 2022
<u>/s/ Charles A. Rowland, Jr.</u> Charles A. Rowland, Jr.	Director	March 30, 2022
<u>/s/ Alicia Secor</u> Alicia Secor	Director	March 30, 2022

SIGNATURE OF AUTHORIZED REPRESENTATIVE OF THE REGISTRANT

Pursuant to the Securities Act, the undersigned, the duly authorized representative in the United States of the registrant has signed this Post-Effective Amendment No. 2 to Form S-3 on the 30th day of March, 2022.

Cogency Global Inc.
Authorized U.S. Representative

By: /s/ Coleen A. De Vries
Name: Coleen A. De Vries
Title: Sr. Vice President on behalf of
Cogency Global Inc.



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

goodwinlaw.com
+44 (0) 20 7447 4200

30 March 2022

Orchard Therapeutics plc
108 Cannon Street
London, EC4N 6EU

Ladies and Gentlemen:

Orchard Therapeutics plc – Post-Effective Amendment (No. 2) to 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 post-effective amendment (No. 2) to the registration statement on Form S-3 (the “**Registration Statement**”) including a base prospectus (the “**Base Prospectus**”), which provides that it may be supplemented by one or more prospectus supplements (each such prospectus supplement, together with the Base Prospectus, a “**Prospectus**”) pursuant to the U.S. Securities Act of 1933, as amended (the “**Securities Act**”).

The Registration Statement relates to the registration for the issue and sale by the Company of (a) ordinary shares at a nominal value of £0.10 per share (“**Ordinary Shares**”), including Ordinary Shares in the form of American Depositary Shares (the “**ADSs**” and together with the Ordinary Shares, the “**Shares**”), (b) debt securities (“**Debt Securities**”), (c) warrants (“**Warrants**”) for the purchase of Shares and/or Debt Securities in one or more series, and/or (d) units (“**Units**”) comprised of Shares, Debt Securities and Warrants in any combination (the Shares, Debt Securities, Warrants and Units, together, the “**Securities**”).

1. INTRODUCTION

1.1 Purpose

In connection with the preparation and filing of the Registration Statement, to which this letter is attached as an exhibit, with the SEC pursuant to the Securities Act we have been asked to provide opinions on certain matters, as set out below. We have taken instruction in this regard solely from the Company.

1.2 Defined terms and headings

In this letter:

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

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

1.3 Legal review

For the purpose of issuing this letter, we have examined such questions of law as we have considered appropriate. We have reviewed only 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 30 March 2022 at 10:00 am (London time);
- (b) an enquiry of the Central Index of Winding Up Petitions, London on 30 March 2022 at 10:00 am (London time) ((a) and (b) together, the "**Searches**");
- (c) a certificate dated 30 March 2022 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:
 - a. a PDF copy of resolutions of the board of directors of the Company (the "**Board**") dated 23 March 2022 authorising the Company, inter alia, to execute and file the Registration Statement with the SEC;
 - b. a PDF executed copy of the resolutions passed by the shareholders of the Company at the general meeting of the Company held on 16 June 2021 at 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 Ordinary Shares or grant rights to subscribe for Ordinary Shares;
 - c. a PDF copy of the current articles of association of the Company adopted on 17 June 2020 (the "**Articles**");
 - d. 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
- (d) a draft copy of the Registration Statement (which for the avoidance of doubt includes the Prospectus) to be filed with the SEC on 30 March 2022.

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; and
- (b) the Shares, when issued and sold as contemplated in the Registration Statement, the Base Prospectus and any related Prospectus supplement(s), and in accordance with a duly authorised, executed and delivered purchase, underwriting or similar agreement, or upon conversion of any Debt Securities in accordance with their terms, or upon exercise of any Warrants or Units in each case in accordance with their terms, 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.

Orchard Therapeutics plc
30 March 2022
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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.

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;
- (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, 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) 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;
- (j) an appropriate prospectus supplement with respect to the Securities has been prepared, delivered and filed in compliance with the Securities Act and the rules and regulations thereunder;

- (k) that the resolutions described in the resolutions of the Board provided to us in connection with the giving of this opinion or otherwise contemplated in connection with the matters referred to herein were and/or will be duly passed as resolutions of the Board, all constitutional, statutory and other formalities were and/or will be observed and such resolutions have not been, and will not be, revoked or varied and remain in full force and effect at the date of this letter;
- (l) that the resolutions of the shareholders of the Company provided to us in connection with the giving of this opinion and as referred to in paragraph 1.3(c)(b) of this letter or otherwise contemplated in connection with the matters referred to herein were and/or will be duly passed, all constitutional, statutory and other formalities were and/or will be observed in relation to such resolutions and such resolutions have not been revoked or varied as at the date of this letter and remain in full force and effect;
- (m) that in relation to the allotment and issue of the Shares, the directors of the Company have acted and will act in the manner required by section 172 of the 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;
- (n) the Securities will be sold or issued in accordance with a duly authorised, executed and delivered purchase, underwriting or similar agreement;
- (o) that the Securities 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 the relevant Securities 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);
- (p) that the Securities, and the obligations created by them, constitute the legal, valid, binding and enforceable obligations of each of the parties to them under the laws by which they are expressed to be governed; and that the Securities will remain in full force and effect at all relevant times in the form examined by us;
- (q) the directors of the Company, including the pricing 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 Shares and related matters;
- (r) 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;
- (s) 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;

- (t) that no 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);
- (u) that no Securities or rights to subscribe for Shares have been or shall be offered to the public in the United Kingdom in breach of the Financial Services and Markets Act 2000 (“**FSMA**”) or of any other United Kingdom laws or regulations concerning offers of securities to the public, and no communication has been or shall be made in relation to the Shares in breach of section 21 of 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;
- (v) 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
- (w) 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.



Goodwin Procter LLP
100 Northern Avenue
Boston, MA 02210
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+1 617 570 1000

March 30, 2022

Orchard Therapeutics plc
108 Cannon Street
London, EC4N 6EU
United Kingdom

Re: Securities Being Registered under Registration Statement on Form S-3

We have acted as U.S. counsel to you in connection with your filing of a Post-Effective Amendment No. 2 (the "Amendment") to the Registration Statement on Form S-3 (as amended or supplemented, the "Registration Statement") pursuant to the Securities Act of 1933, as amended (the "Securities Act"), which pursuant to the Amendment relates to the registration by Orchard Therapeutics plc, a public limited company organized under the laws of England and Wales (the "Company"), of up to \$200,000,000 of any combination of (i) ordinary shares, nominal value £0.10 per share (the "Ordinary Shares") of the Company, which may be represented by American Depositary Shares ("American Depositary Shares"), (ii) debt securities of the Company, which may be either senior debt securities or subordinated debt securities ("Debt Securities"), (iii) warrants to purchase Ordinary Shares, ordinary shares represented by American Depositary Shares or Debt Securities ("Warrants") and (iv) units comprised of Ordinary Shares, ordinary shares represented by American Depositary Shares, Debt Securities and Warrants in any combination ("Units"). The American Depositary Shares, Debt Securities, Warrants to purchase ordinary shares represented by American Depositary Shares or Debt Securities and Units comprised of American Depositary Shares, Debt Securities or Warrants, are sometimes referred to collectively herein as the "Securities." Pursuant to the Amendment, up to \$200,000,000 of the Securities may be issued in an unspecified number (with respect to American Depositary Shares, Warrants and Units) or in an unspecified principal amount (with respect to Debt Securities). The Registration Statement provides that the Securities may be offered separately or together, in separate series, in amounts, at prices and on terms to be set forth in one or more prospectus supplements (each a "Prospectus Supplement") to the prospectus contained in the Registration Statement.

We have reviewed such documents and made such examination of law as we have deemed appropriate to give the opinions set forth below. We have relied, without independent verification, on certificates of public officials and, as to matters of fact material to the opinions set forth below, on certificates of officers of the Company.

The opinions set forth below are limited to the law of New York.

For purposes of the opinions set forth below, without limiting any other exceptions or qualifications set forth herein, we have assumed that (i) each of the Debt Securities, Warrants and Units, and the indentures, warrant agreements, unit agreements and other agreements governing Securities offered pursuant to the Registration Statement will be governed by the internal law of New York and (ii) after the issuance of any Securities offered pursuant to the Registration Statement, the total number of Ordinary Shares, together with the total number of Ordinary Shares issuable in exchange for American Depositary Shares, upon the exercise, exchange, conversion or settlement, as the case may be, of any exercisable, exchangeable or convertible security (including without limitation any Warrants, Debt Securities or Units), as the case may be, then outstanding, will not exceed the total number of authorized Ordinary Shares available for issuance under the Company's articles of association as then in effect.

For purposes of the opinions set forth below, we refer to the following as the “Future Authorization and Issuance” of Securities:

- with respect to any of the Securities, (a) the authorization by the Company of the amount, terms and issuance of such Securities (the “Authorization”) and (b) the issuance of such Securities in accordance with the Authorization therefor upon the receipt by the Company of the consideration to be paid therefor in accordance with the Authorization;
- with respect to Debt Securities, (a) the authorization, execution and delivery of the indenture or a supplemental indenture relating to such Securities by the Company and the trustee thereunder and/or (b) the establishment of the terms of such Securities by the Company in conformity with the applicable indenture or supplemental indenture and applicable law, and (c) the execution, authentication and issuance of such Securities in accordance with the applicable indenture or supplemental indenture and applicable law; and
- with respect to Warrants or Units, (a) the authorization, execution and delivery by the Company and the other parties thereto of any agreement under which such Securities are to be issued, and (b) the establishment of the terms of such Securities and the issuance of such Securities in conformity with those terms, the terms of any applicable agreement and applicable law.

Based upon the foregoing, and subject to the additional qualifications set forth below, we are of the opinion that:

1. Upon the Future Authorization and Issuance of Debt Securities, such Debt Securities will be valid and binding obligations of the Company.
2. Upon the Future Authorization and Issuance of Warrants, such Warrants will be valid and binding obligations of the Company.
3. Upon the Future Authorization and Issuance of Units, such Units will be valid and binding obligations of the Company.

The opinions expressed above are subject to bankruptcy, insolvency, fraudulent transfer, reorganization, moratorium and other similar laws of general application affecting the rights and remedies of creditors and to general principles of equity.

This opinion letter and the opinions it contains shall be interpreted in accordance with the Core Opinion Principles as published in *74 Business Lawyer* 815 (Summer 2019).

We hereby consent to the inclusion of this opinion as Exhibit 5.2 to the Registration Statement and to the references to our firm under the caption “Legal Matters” in the Registration Statement. In giving our consent, we do not 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.

Very truly yours,

/S/ Goodwin Procter LLP

GOODWIN PROCTER LLP

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 2, 2021 relating to the financial statements, which appears in Orchard Therapeutics plc's Annual Report on Form 10-K for the year ended December 31, 2020. We also consent to the reference to us under the heading "Experts" in such Registration Statement.

/s/PricewaterhouseCoopers LLP

Boston, Massachusetts
March 30, 2022

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 and Carry Forward Securities

	Security Type	Security Class Title	Fee Calculation or Carry Forward Rule	Amount Registered(2)	Proposed Maximum Offering Price Per Unit(3)	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee	Carry Forward Form Type	Carry Forward File Number	Carry Forward Initial effective date	Filing Fee Previously Paid In Connection with Unsold Securities to be Carried Forward
Newly Registered Securities												
Fees to Be Paid	Equity(1)	Ordinary Shares, nominal value £0.10 per share	457(r)	\$ —	\$ —	\$ —	—	\$ —				
Fees to Be Paid	Debt(1)	Debt Securities	457(r)	—	—	—	—	—				
Fees to Be Paid	Other(1)	Warrants	457(r)	—	—	—	—	—				
Fees to Be Paid	Other(1)	Units	457(r)	—	—	—	—	—				
Fees to Be Paid	Unallocated (Universal) Shelf(1)		457(o)	—	—	\$200,000,000	0.0000927	\$18,540				
Fees to Be Paid	Total Registration Fee:							\$18,540				
Carry Forward Securities												
Carry Forward Securities	Equity	Ordinary Shares, nominal value £0.10 per share	457(b)	\$100,000,000(4)	N/A	\$100,000,000			POSASR	333-234439	February 27, 2020	\$12,980
Total Offering Amounts								\$18,540				
Total Fees Previously Paid								—				
Total Fee Offsets								\$12,980				
Net Fee Due								\$5,560				

- (1) The amount to be registered consists of up to \$200,000,000 of an indeterminate amount of ordinary shares, debt securities, warrants and/or units that may be offered and sold from time to time in one or more offerings. The ordinary shares may be represented by American Depositary Shares, each of which currently represents one ordinary share. A separate registration statement on Form F-6 has been or will be filed for the registration of American Depositary Shares issuable upon deposit of the ordinary shares.
- (2) Such indeterminate number or amount of ordinary shares, debt securities, warrants and/or units to purchase any combination of the foregoing securities, as may from time to time be issued at indeterminate prices, and units composed of one or more of the foregoing securities, with an aggregate initial offering price not to exceed \$200,000,000. Securities registered hereunder may be sold separately or together in any combination with other securities registered hereunder. Warrants may be exercised to purchase any of the other securities registered hereby. The securities registered hereunder also include such indeterminate number of ordinary shares and amount of debt securities as may be issued upon conversion of or exchange for securities that provide for conversion or exchange, upon exercise of securities or pursuant to the antidilution provisions of any other securities.
- (3) The proposed maximum offering price per security will be determined from time to time by the registrant in connection with the issuance by the registrant of the securities registered hereunder and is not specified as to each class of security pursuant to General Instruction II.D. of Form S-3 under the Securities Act of 1933, as amended (the "Securities Act").
- (4) The registrant previously paid a fee of \$12,980 related to \$100,000,000 of the registrant's ordinary shares, which could have been represented by American Depositary Shares, that could have been issued and sold under a certain sales agreement with Cowen and Company, LLC pursuant to a prospectus supplement filed by the registrant on February 27, 2020. Of such shares, \$100,000,000 were unsold, and the registration fee in the amount of \$12,980 related thereto is applied to the registrant's total registration fee. Accordingly, the registrant is paying the registration fee due less the \$12,980 that was previously paid.

Table 2: Fee Offset Claims and Sources

	Registrant or Filer Name	Form or Filing Type	File Number	Initial Filing Date	Filing Date	Fee Offset Claimed	Security Type Associated with Fee Offset Claimed	Security Title Associated with Fee Offset Claimed	Unsold Securities Associated with Fee Offset Claimed	Unsold Aggregate Offering Amount Associated with Fee Offset Claimed	Fee Paid with Fee Offset Source
Rule 457(b) and 0-11(a)(2)											
Fee Offset Claims		—	—	—		—					
Fee Offset Sources	Orchard Therapeutics plc	POSASR	333-234439	February 27, 2020	February 27, 2020	\$12,980	Equity	American Depositary Shares representing Ordinary Shares, nominal value £0.10 per share	N/A	\$100,000,000	\$12,980
Rule 457(p)											
Fee Offset Claims		—	—	—		—					