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

**Post-Effective Amendment No. 1
to
Form F-3 on
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.)

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

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

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+1 212 947 7200**

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

Copies of all communications, including communications sent to agent for service, should be sent to:

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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
Non-accelerated filer

Accelerated filer
Smaller reporting company
Emerging growth company

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

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered	Proposed Maximum Offering Price Per Share	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee
Primary Offering of Securities				
Ordinary Shares, nominal value £0.10 per share(4)(5)	(1)(2)	(1)(2)	(1)(2)	(3)
Debt Securities	(1)(2)	(1)(2)	(1)(2)	(3)
Warrants(6)	(1)(2)	(1)(2)	(1)(2)	(3)
Units(7)	(1)(2)	(1)(2)	(1)(2)	(3)
Primary Offering of Securities				
Ordinary Shares, nominal value £0.10 per share(4)(5)	\$100,000,000	N/A*	\$100,000,000	\$12,980(9)
Total(8)	(1)(2)	(1)(2)	(1)(2)	(3)

* The proposed maximum offering price per share is not applicable in that these securities are not issued in predetermined amounts.

- (1) An indeterminate number of securities or aggregate principal amount, as applicable, of each identified class is being registered as may at various times be issued at indeterminate prices.
- (2) Not applicable pursuant to General Instruction II.E of Form S-3 under the Securities Act of 1933, as amended, or the Securities Act.
- (3) In reliance on, and in accordance with, Rules 456(b) and 457(r) under the Securities Act, the registrant is deferring payment of all applicable registration fees. Any registration fees will be paid subsequently on a pay-as-you-go basis in accordance with Rule 457(r).
- (4) In addition to any securities that may be registered hereunder, the registrant is also registering an indeterminate number of ordinary shares as may be issued upon conversion or exercise of the securities issued directly hereunder. No separate consideration will be received for any ordinary shares so issued upon conversion or exercise.
- (5) The Ordinary Shares may be represented by American Depositary Shares, or ADSs, 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 ADSs issuable upon deposit of the Ordinary Shares.
- (6) Warrants may be exercised to purchase any of the other securities registered hereby.
- (7) These offered securities may be sold separately or together as units.
- (8) The securities registered hereunder may be sold separately or in a combination with other securities registered hereby.
- (9) Calculated in accordance with Rules 457(o) and 457(r) under the Securities Act.

EXPLANATORY NOTE

As of November 1, 2019, the date on which Orchard Therapeutics plc (the “Registrant”) filed a registration statement on Form F-3, Registration No. 333-234439 (the “Registration Statement”), to which this post-effective amendment No. 1 on Form S-3 relates, the Registrant was a foreign private issuer within the meaning of the Securities Exchange Act of 1934, as amended, which required the Registrant to file Annual Reports on Form 20-F, furnish Reports on Form 6-K and file registration statements on Forms F-1, F-3 and F-4. The Registrant has determined that, effective as of January 1, 2020, it is no longer a foreign private issuer, and, as a result is subject to the registration and reporting requirements applicable to a United States domestic registrant, including the requirement to file Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K and registration statements on Forms S-1, S-3 or S-4. This Registration Statement on Form S-3 serves as a post-effective amendment on Form S-3 to the Registration Statement. The Registration Statement became automatically effective upon filing with the Securities and Exchange Commission on November 1, 2019.

This post-effective amendment contains:

- a base prospectus, which covers the offering, issuance and sale by the Registrant or our security holders of the securities identified above from time to time in one or more offerings; and
- a sales agreement prospectus supplement relating to the offering and sale by the Registrant of up to a maximum aggregate offering price of \$100,000,000 of the Registrant’s ADSs representing Ordinary Shares that may be issued and sold from time to time under a sales agreement with Cowen and Company, LLC.

The base prospectus immediately follows this explanatory note. The specific terms of any securities to be offered pursuant to the base prospectus will be specified in a prospectus supplement to the base prospectus. The specific terms of the securities to be issued and sold under the sales agreement are specified in the sales agreement prospectus supplement that immediately follows the base prospectus.

PROSPECTUS



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

We and/or our selling security holders may offer and sell from time to time up to an indeterminate number 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 will not receive any proceeds from the sale of securities by our selling security holders.

We and/or our selling security holders may offer these securities in amounts, at prices and on terms determined at the time of offering. We and/or our selling security holders may sell the securities directly to you, through agents, or through underwriters and dealers. If we and/or our selling security holders 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 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 February 26, 2020, the closing price of our American Depositary Shares on The Nasdaq Global Select Market was \$11.49 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 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 February 27, 2020

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ABOUT THIS PROSPECTUS

This prospectus is part of an automatic shelf registration statement, as amended, that we filed with the U.S. Securities and Exchange Commission, or SEC, as a “well-known seasoned issuer” as defined in Rule 405 under the Securities Act of 1933, as amended.

Under this shelf registration process, we and/or our selling security holders may offer the securities described in this prospectus from time to time 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 and/or our selling security holders may offer. Each time we and/or our selling security holders 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, including, to the extent applicable:

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 and/or our selling security holders may sell the securities directly to or through underwriters, dealers or agents. We and/or our selling security holders, and our underwriters or agents, reserve the right to accept or reject all or part of any proposed purchase of securities. If we and/or our selling security holders 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 or our selling security holders.

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 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

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

To date, over 170 patients have been treated with our commercial product and clinical-stage product candidates across seven different diseases, with follow-up periods of more than 18 years following a single administration. We believe the data observed across these programs, in combination with our deep expertise in the development, manufacturing and commercialization of gene and cell therapies, position us to provide potentially transformative therapies to people suffering from a broad range of diseases.

We are currently focusing our *ex vivo* autologous HSC gene therapy approach on three therapeutic rare disease franchise areas: primary immune deficiencies, neurometabolic disorders and blood disorders. Our portfolio includes Strimvelis, our commercial-stage gammaretroviral-based product approved in Europe for the treatment of adenosine deaminase-severe combined immunodeficiency, or ADA-SCID, seven lentiviral-based product candidates in clinical-stage development and several other product candidates in preclinical development.

For each of our lead product candidates, we are in ongoing discussions with the applicable regulatory authorities with respect to the clinical and other data required for regulatory submissions. We filed a marketing authorization application, or MAA, with the European Medicines Agency, or EMA, for OTL-200 for the treatment of metachromatic leukodystrophy, or MLD, in 2019, and we anticipate filing a biologics license application, or BLA, with the U.S. Food & Drug Administration, or FDA, for OTL-200 for the same indication by 2021. We plan to make additional regulatory submissions over the next two years with the FDA for OTL-101 for the treatment of ADA-SCID and with the FDA and EMA for OTL-103 for the treatment of Wiskott-Aldrich syndrome, or WAS.

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, in light of your particular investment objectives and financial circumstances. 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, the period during which the results of the trials will become available and our research and development programs;
- the timing, scope or likelihood of regulatory submissions, filings, and approvals;
- our ability to develop and advance product candidates into, and successfully complete, clinical trials;
- our expectations regarding the size of the patient populations for our product candidates, if approved for commercial use;
- the implementation of our business model and our strategic plans for our business, commercial product, product candidates and technology;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the pricing and reimbursement of our commercial product and product candidates, if approved;
- the scalability and commercial viability of our manufacturing methods and processes, including our plans to develop our in-house manufacturing operations;
- the rate and degree of market acceptance and clinical utility of our commercial product and product candidates, in particular, and gene therapy, in general;
- our ability to establish or maintain collaborations or strategic relationships or obtain additional funding;
- our competitive position;
- the scope of protection we and/or our licensors are able to establish and maintain for intellectual property rights covering our commercial product and product candidates;
- developments and projections relating to our competitors and our industry;
- our expectations related to the use of proceeds from this offering;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- the impact of laws and regulations;
- our ability to attract and retain qualified employees and key personnel;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately; and

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- 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 and/or our selling security holders 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 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 and/or our selling security holders 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 2019 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 issue shares in the company and grant rights to subscribe for or convert any securities into shares in the company up to a maximum aggregate nominal amount of £13,023,851.50 for a period of five years from the date of the meeting; and
- empowering of our directors pursuant to Section 570 of Companies Act 2006 to issue equity securities for cash pursuant to the Section 551 authority referred to above as if the statutory preemption rights under Section 561(1) of the Companies Act 2006 did not apply to such allotments.

Issued share capital

As of December 31, 2019, our issued share capital was 96,923,729 ordinary shares with a nominal value of £0.10 per share.

Ordinary shares

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

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

Registered shares

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

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their nominees is the holder of the shares underlying our ADSs. Holders of our ADSs have a right to receive the ordinary shares underlying their ADSs. For 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 also are required by the Companies Act 2006 to register a transfer of shares (or give the transferee notice of and reasons for refusal as the transferee may reasonably request) as soon as practicable and in any event within two months of receiving notice of the transfer.

We, any of our shareholders or any other affected person may apply to the court for rectification of the share register if:

- the name of any person, without sufficient cause, is wrongly entered in or omitted from our register of members; or
- there is a default or unnecessary delay in entering on the register the fact of any person having ceased to be a member or on which we have a lien, provided that such delay does not prevent dealings in the shares taking place on an open and proper basis.

Preemptive rights

English law generally provides shareholders with preemptive rights when new shares are issued for cash; however, it is possible for the articles of association, or shareholders in general meeting, to exclude preemptive rights. Such an exclusion of preemptive rights may be for a maximum period of up to five years from the date of adoption of the articles of association, if the exclusion is contained in the articles of association, or from the date of the shareholder resolution, if the exclusion is by shareholder resolution. In either case, this exclusion would need to be renewed by our shareholders upon its expiration (i.e., at least every five years). At our annual general meeting in June 2019 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 24,699,842 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 24,699,842 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, if we are eligible to file a registration statement on Form F-3 or Form S-3, upon the written request of holders of a majority of these securities at an aggregate offer price

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

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

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

Share capital

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

Voting

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

Variation of rights

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

Dividends

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

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

Liquidation Preference

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

Transfer of ordinary shares

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

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

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

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

Allotment of shares and preemption rights

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

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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 2019 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 2019.

Alteration of share capital

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

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

Board of directors

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

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.

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

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

Directors shall be entitled to receive such remuneration as the board shall determine for their services to 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. Save as otherwise provided by the Articles, two shareholders present in person or by proxy and entitled to vote shall be a quorum for all purposes.

Borrowing Powers

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

- (a) borrow money;

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- (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.

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	Under Delaware law, any director or the entire board of directors may be

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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.

removed, with or without cause, by the holders of a majority of the shares then entitled to vote at an election of directors, except (i) unless the certificate of incorporation provides otherwise, in the case of a corporation whose board of directors is classified, stockholders may effect such removal only for cause, or (ii) in the case of a corporation having cumulative voting, if less than the entire board of directors is to be removed, no director may be removed without cause if the votes cast against his removal would be sufficient to elect him if then cumulatively voted at an election of the entire board of directors, or, if there are classes of directors, at an election of the class of directors of which he is a part.

Vacancies on the Board of Directors

Under English law, the procedure by which directors, other than a company's initial directors, are appointed is generally set out in a company's articles of association, provided that where two or more persons are appointed as directors of a public limited company by resolution of the shareholders, resolutions appointing each director must be voted on individually.

Under Delaware law, vacancies and newly created directorships may be filled by a majority of the directors then in office (even though less than a quorum) or by a sole remaining director unless (i) otherwise provided in the certificate of incorporation or bylaws of the corporation or (ii) the certificate of incorporation directs that a particular class of stock is to elect such director, in which case a majority of the other directors elected by such class, or a sole remaining director elected by such class, will fill such vacancy.

Annual General Meeting

Under the Companies Act 2006, a public limited company must hold an annual general meeting in each six-month period following the company's annual accounting reference date.

Under Delaware law, the annual meeting of stockholders shall be held at such place, on such date and at such time as may be designated from time to time by the board of directors or as provided in the certificate of incorporation or by the bylaws.

General Meeting

Under the Companies Act 2006, a general meeting of the shareholders of a public limited company may be called by the directors.

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.

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

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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.

Notice of
General
Meetings

Under the Companies Act 2006, at least 21 days' notice must be given for an annual general meeting and any resolutions to be proposed at the meeting. Subject to a company's articles of association providing for a longer period, at least 14 days' notice is required for any other general meeting of a public limited company. In addition, certain matters, such as the removal of directors or auditors, require special notice, which is 28 days' notice. The shareholders of a company may in all cases consent to a shorter notice period, the proportion of shareholders' consent required being 100% of those entitled to attend and vote in the case of an annual general meeting and, in the case of any other general meeting, a majority in number of the members having a right to attend and vote at the meeting, being a majority who together hold not less than 95% in nominal value of the shares giving a right to attend and vote at the meeting.

Under Delaware law, unless otherwise provided in the certificate of incorporation or bylaws, written notice of any meeting of the stockholders must be given to each stockholder entitled to vote at the meeting not less than ten nor more than 60 days before the date of the meeting and shall specify the place, date, hour and purpose or purposes of the meeting.

Proxy

Under the Companies Act 2006, at any meeting of shareholders, a shareholder may designate another person to attend, speak and vote at the meeting on their behalf by proxy.

Under Delaware law, at any meeting of stockholders, a stockholder may designate another person to act for such stockholder by proxy, but no such proxy shall be voted or acted upon after three years from its date, unless the proxy provides for a longer period. A director of a Delaware corporation may not issue a proxy representing the director's voting rights as a director.

Preemptive Rights

Under the Companies Act 2006, "equity securities," being (i) shares in the company other than shares that, with respect to dividends and capital, carry a right to participate only up to a specified amount in a distribution, referred to as "ordinary shares," or (ii) rights to subscribe for, or to convert securities

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.

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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.

Authority to Allot

Under the Companies Act 2006, the directors of a company must not allot shares or grant rights to subscribe for or convert any security into shares unless an exception applies or an ordinary resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise, in each case in accordance with the provisions of the Companies Act.

Under Delaware law, if the corporation’s charter or certificate of incorporation so provides, the board of directors has the power to authorize the issuance of stock. The board may authorize capital stock to be issued for consideration consisting of cash, any tangible or intangible property or any benefit to the corporation or any combination thereof. It may determine the amount of such consideration by approving a formula. In the absence of actual fraud in the transaction, the judgment of the directors as to the value of such consideration is conclusive.

Liability of Directors and Officers

Under the Companies Act 2006, any provision, whether contained in a company’s articles of association or any contract or otherwise, that purports to exempt a director of a company, to any extent, from any liability that would otherwise attach to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company, is void. Any provision by which a company directly or indirectly provides an indemnity, to any extent, for a director of the company or of an associated company against any liability attaching to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company of which he is a director is also void except as permitted by the Companies Act, which provides exceptions for the

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

- any breach of the director’s duty of loyalty to the corporation or its stockholders;
- acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;

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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.

- 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

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

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.

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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.

Shareholder
Vote on
Certain
Transactions

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

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

Standard of
Conduct for
Directors

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

- to act in the way he considers, in good faith, would be most likely to promote the success of the company for the benefit of its members as a whole;
- to avoid a situation in which he has, or can have, a direct or indirect interest that conflicts, or possibly conflicts, with the interests of the company;

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

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

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

Directors of a Delaware corporation owe fiduciary duties of care and loyalty to the corporation and to its shareholders. The duty of care generally requires that a

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- 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.

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

In addition, under Delaware law, when the board of directors of a Delaware corporation approves the sale or break-up of a corporation, the board of directors may, in certain circumstances, have a duty to obtain the highest value reasonably available to the shareholders.

Shareholder Suits

Under English law, generally, the company, rather than its shareholders, is the proper claimant in an action in respect of a wrong done to the company or where there is an irregularity in the company's internal management. Notwithstanding this general position, the Companies Act 2006 provides that (i) a court may allow a shareholder to bring a derivative claim (that is, an action in respect of and on behalf of the company) in respect of a cause of action arising from a director's negligence, default, breach of duty or breach of trust and (ii) a shareholder may bring a claim for a court order where the company's affairs have been or are being conducted in a manner that is unfairly prejudicial to some of its shareholders.

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

- state that the plaintiff was a stockholder at the time of the transaction of which the plaintiff complains or that the plaintiff's shares thereafter devolved on the plaintiff by operation of law; and
- allege with particularity the efforts made by the plaintiff to obtain the action the plaintiff desires from the directors and the reasons for the plaintiff's failure to obtain the action; or

- state the reasons for not making the effort.

Additionally, the plaintiff must remain a stockholder through the duration of the derivative suit. The action will not be dismissed or compromised without the approval of the Delaware Court of Chancery.

Stock exchange listing

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

Transfer agent and registrar of shares

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

DESCRIPTION OF AMERICAN DEPOSITARY SHARES

American depositary shares

Citibank, N.A., or Citibank, 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.

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 other distributions

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

Distributions of cash

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

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

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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 purchase 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 purchase additional ADSs to holders.

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

The 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 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.

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

Issuance of ADSs upon deposit of ordinary shares

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

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To have 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.

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

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

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- *In the event of voting by poll*, the depositary will vote (or cause the custodian to vote) the ordinary shares represented by ADSs in accordance with the voting instructions received from the holders of ADSs.

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>
Issuance of ADSs (e.g., an issuance of ADS upon a deposit of ordinary shares or upon a change in the ADS(s)-to-ordinary shares ratio), excluding ADS issuances as a result of distributions of ordinary shares	Up to \$0.05 per ADS issued
Cancellation of ADSs (e.g., a cancellation of ADSs for delivery of deposited property or upon a change in the ADS(s)-to-ordinary shares ratio)	Up to \$0.05 per ADS cancelled
Distribution of cash dividends or other cash distributions (e.g., upon a sale of rights and other entitlements)	Up to \$0.05 per ADS held
Distribution of ADSs pursuant to (i) share dividends or other free share distributions, or (ii) exercise of rights to purchase additional ADSs	Up to \$0.05 per ADS held
Distribution of securities other than ADSs or rights to purchase additional ADSs (e.g., upon a spin-off)	Up to \$0.05 per ADS held
ADS Services	Up to \$0.05 per ADS held on the applicable record date(s) established by the depositary

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

- taxes (including applicable interest and penalties) and other governmental charges;
- the registration fees as may from time to time be in effect for the registration of ordinary shares on the share register and applicable to transfers of ordinary shares to or from the name of the custodian, the depositary, or any nominees upon the making of deposits and withdrawals, respectively;
- certain cable, telex and facsimile transmission and delivery expenses;
- the expenses and charges incurred by the depositary in the conversion of foreign currency;
- the fees and expenses incurred by the depositary in connection with compliance with exchange control regulations and other regulatory requirements applicable to ordinary shares, ADSs and ADRs; and
- the fees and expenses incurred by the depositary, the custodian or any nominee in connection with the servicing or delivery of deposited property.

ADS fees and charges payable upon (i) the issuance of ADSs, and (ii) the cancellation of ADSs are charged to the person for whom the ADSs are issued (in the case of ADS issuances) and to the person for whom ADSs are

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cancelled (in the case of ADS cancellations). In the case of ADSs issued by the depositary into DTC, the ADS issuance and cancellation fees and charges may be deducted from distributions made through DTC, and may be charged to the DTC participant(s) receiving the ADSs being issued or the DTC participant(s) holding the ADSs being cancelled, as the case may be, on behalf of the beneficial owner(s) and will be charged by the DTC participant(s) to the account of the applicable beneficial owner(s) in accordance with the procedures and practices of the DTC participants as in effect at the time. ADS fees and charges in respect of distributions and the ADS service fee are charged to the holders as of the applicable ADS record date. In the case of distributions of cash, the amount of the applicable ADS fees and charges is deducted from the funds being distributed. In the case of (i) distributions other than cash and (ii) the ADS service fee, holders as of the ADS record date will be invoiced for the amount of the ADS fees and charges and such ADS fees and charges may be deducted from distributions made to holders of ADSs. For ADSs held through DTC, the ADS fees and charges for distributions other than cash and the ADS service fee may be deducted from distributions made through DTC, and may be charged to the DTC participants in accordance with the procedures and practices prescribed by DTC and the DTC participants in turn charge the amount of such ADS fees and charges to the beneficial owners for whom they hold ADSs.

In the event of refusal to pay the depositary fees, the depositary may, under the terms of the deposit agreement, refuse the requested service until payment is received or may set off the amount of the depositary fees from any distribution to be made to the ADS holder. Certain depositary fees and charges (such as the ADS services fee) may become payable shortly after the closing of 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 depositary. You will receive prior notice of such changes. The depositary may reimburse us for certain expenses incurred by us in respect of the ADR program, by making available a portion of the ADS fees charged in respect of the ADR program or otherwise, upon such terms and conditions as we and the depositary agree from time to time.

Amendments and termination

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

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

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

Termination

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

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In connection with the termination of the deposit agreement, the depositary may, independently and without the need for any action by us, make available to holders a means to withdraw the ordinary shares and other deposited securities represented by their ADSs and to direct the deposit of such ordinary shares and other deposited securities into an unsponsored ADS program established by the depositary, upon such terms and conditions as the depositary may deem reasonably appropriate, subject however, in each case, to satisfaction of the applicable registration requirements by the unsponsored ADS program under the Securities Act, and to receipt by the depositary of payment of the applicable fees and charges of, and reimbursement of the applicable expenses incurred by, the depositary.

Books of depositary

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

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

Transmission of notices, reports and proxy soliciting material

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

Limitations on obligations and liabilities

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

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

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- We and the depositary disclaim any liability by reason of any exercise of, or failure to exercise, any discretion provided for in the deposit agreement or in our Articles of Association or in any provisions of or governing the securities on deposit.
- We and the depositary further disclaim any liability for any action or inaction in reliance on the advice or information received from legal counsel, accountants, any person presenting ordinary shares for deposit, any holder of ADSs or authorized representatives thereof, or any other person believed by either of us in good faith to be competent to give such advice or information.
- We and the depositary also disclaim liability for the inability by a holder to benefit from any distribution, offering, right or other benefit that is made available to holders of ordinary shares but is not, under the terms of the deposit agreement, made available to you.
- We and the depositary may rely without any liability upon any written notice, request or other document believed to be genuine and to have been signed or presented by the proper parties.
- We and the depositary also disclaim liability for any consequential or punitive damages for any breach of the terms of the deposit agreement.
- No disclaimer of any Securities Act liability is intended by any provision of the deposit agreement.

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

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

Taxes

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

The depositary may refuse to issue ADSs, to deliver, transfer, split and combine ADRs or to release securities on deposit until all taxes and charges are paid by the applicable holder. The depositary and the custodian may take reasonable administrative actions to obtain tax refunds and reduced tax withholding for any distributions on your behalf. However, you may be required to provide to the depositary and to the custodian proof of taxpayer status and residence and such other information as the depositary and the custodian may require to fulfill legal obligations. You are required to indemnify us, the depositary and the custodian for any claims with respect to taxes based on any tax benefit obtained for you.

Foreign currency conversion

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

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

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

Governing Law/Waiver of Jury Trial

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

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

DESCRIPTION OF DEBT SECURITIES

This prospectus describes the general terms and provisions of the debt securities we and/or our selling security holders may offer under this prospectus. When we and/or our selling security holders 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 and/or our selling security holders 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 depository 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
- 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
 - (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

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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. 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

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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;
- 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.

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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;
- 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.

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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 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.

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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

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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 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

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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 and/or our selling security holders 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 and/or our selling security holders 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 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 and/or our selling security holders 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 and/or our selling security holders 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 and/or our selling security holders 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. 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 and/or our selling security holders 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, 2019, 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, 2019, 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 ongoing commercialization of Strimvelis, the development and, if approved, the commercialization of our product candidates, to discover 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.

We will not receive any proceeds from the sale by selling security holders of the securities covered by this prospectus.

SELLING SECURITY HOLDERS

Information about selling security holders, where applicable, will be set forth in a prospectus supplement, in a post-effective amendment, or in filings we make with the SEC which are incorporated into this prospectus by reference.

PLAN OF DISTRIBUTION

We and/or our selling securityholders may sell our securities from time to time in one or more transactions. We and/or our selling securityholders 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 or with our selling securityholders or on their behalf may also purchase our securities and reoffer them to the public. We and/or our selling securityholders 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 and/or our selling securityholders designate may solicit offers to purchase our securities.

- We and/or our selling securityholders will name any agent involved in offering or selling our securities, and disclose any commissions that we and/or our selling securityholders will pay to the agent, in the applicable prospectus supplement.
- Unless we and/or our selling securityholders 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 and/or our selling securityholders may use an underwriter or underwriters in the offer or sale of our securities.

- If we and/or our selling securityholders use an underwriter or underwriters, we and/or our selling securityholders will execute an underwriting agreement with the underwriter or underwriters at the time that we and/or our selling securityholders reach an agreement for the sale of our securities.
- We and/or our selling securityholders 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 and/or our selling securityholders may use a dealer to sell our securities.

- If we and/or our selling securityholders use a dealer, we and/or our selling securityholders 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 and/or our selling securityholders 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.

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

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

We and/or our selling securityholders 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 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 and/or our selling securityholders 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 and/or our selling securityholders 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 and/or our selling securityholders 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 and/or our selling securityholders use delayed delivery contracts, we and/or our selling securityholders will disclose that we and/or our selling securityholders are using them in the prospectus supplement and will tell you when we and/or our selling securityholders 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 and/or our selling securityholders 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 and/or our selling securityholders sold to them. In these circumstances, these persons would

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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 and/or our selling securityholders may effect sales of securities in connection with forward sale, option, swap or other types of agreements with third parties.

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 and/or our selling securityholders 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 as of and for the year ended December 31, 2019 and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Annual Report on Internal Control Over Financial Reporting) incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2019 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP (a Delaware limited liability partnership), an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

The financial statements as of December 31, 2018 and for each of the two years in the period ended December 31, 2018 incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2019 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP (a United Kingdom entity), an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

Change in Accountants

On June 26, 2019, our Audit Committee of the Board of Directors, or the Audit Committee, dismissed PwC UK as our independent registered public accounting firm and separately approved the engagement of PricewaterhouseCoopers LLP, a Delaware limited liability partnership, or PwC USA, as our new independent registered public accounting firm effective immediately. This decision was made by the Audit Committee in connection with our centralization of our accounting and finance functions to our Boston, Massachusetts office.

The reports of PwC UK on our consolidated financial statements for each of the fiscal years ended December 31, 2018 and 2017 did not contain an adverse opinion or a disclaimer of opinion and were not qualified or modified as to uncertainty, audit scope or accounting principles. During our two most recent fiscal years ended December 31, 2018 and 2017, and the subsequent interim period through June 26, 2019, there were:

- no "disagreements" (as that term is defined in Item 16F(a)(1)(iv) of Form 20-F and the instructions to Item 16F) between us and PwC UK on any matters of accounting principles or practices, financial statement disclosure, or auditing scope or procedures, which disagreements, if not resolved to PwC UK's satisfaction would have caused PwC UK to make reference to the subject matter of the disagreement(s) in connection with its report, and
- no "reportable events" (as that term is defined in Item 16F(a)(1)(v) of Form 20-F), except for: (i) the material weakness in our internal control over financial reporting related to the recognition and accrual of research and development related expenses and reimbursements, and (ii) the restatement of our interim condensed consolidated financial statements as of June 30, 2018 and the six month period then ended for an error in accounting for contingent assets and the related material weakness in internal control over financial reporting which has since been remediated, each as disclosed in our prior filings with the SEC.

We provided PwC UK with a copy of the statements made in this registration statement and requested that PwC UK furnish a letter addressed to the SEC stating whether it agrees with the above statements and, if not, stating the respects in which it does not agree. A copy of PwC UK's letter dated November 1, 2019, is included herein as Exhibit 16.1 to the Registration Statement of which this prospectus forms a part.

During our two most recent fiscal years ended December 31, 2018 and 2017 and the subsequent interim period through June 26, 2019, neither we nor anyone on our behalf consulted with PwC USA regarding any of the matters or events set forth in Item 16F(a)(2)(i) and (ii) of Form 20-F.

SERVICE OF PROCESS AND ENFORCEMENT OF LIABILITIES

We are a public limited company incorporated under the laws of England and Wales. Certain of our directors and executive officers and experts reside outside of the United States. As a result, it may be difficult for an investor to serve process on us or our directors and executive officers or to compel any of them to appear in Court in the United States or to enforce judgments obtained in U.S. courts against them or us, including judgments based on civil liability provisions of the securities laws of the United States. In addition, awards of punitive damages in actions brought in the United States or elsewhere may be unenforceable in the United Kingdom. An award for monetary damages under the U.S. securities laws would be considered punitive in the United Kingdom if it does not seek to compensate the claimant for loss or damage suffered and is intended to punish the defendant. The enforceability of any judgment in the United Kingdom will depend on the particular facts of the case as well as the laws and treaties in effect at the time. The United States and the United Kingdom do not currently have a treaty providing for the mutual recognition and enforcement of judgments (other than arbitration awards) in civil and commercial matters.

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, 2019, filed with the SEC on February 27, 2020; 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.

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

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.



\$100,000,000

American Depositary Shares representing Ordinary Shares

We have entered into a sales agreement with Cowen and Company, LLC, or Cowen, relating to the sale of American Depositary Shares, or ADSs, offered by this prospectus supplement. Each ADS represents one ordinary share, nominal value £0.10 per share. In accordance with the terms of the sales agreement, we may offer and sell our ADSs having an aggregate offering price of up to \$100,000,000 from time to time through Cowen acting as our sales agent.

Our ADSs are listed on The Nasdaq Global Select Market under the symbol "ORTX". On February 26, 2020, the last reported sale price of our ADSs was \$11.49 per ADS.

Sales of our ADSs, if any, under this prospectus supplement will be made in sales deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, or the Securities Act. Cowen is not required to sell any specific number or dollar amount of securities, but will act as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices, on mutually agreed terms between Cowen and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

The compensation to Cowen for sales of ADSs sold pursuant to the sales agreement will be an amount up to 3.0% of the gross proceeds of any ADSs sold under the sales agreement. In connection with the sale of the ADSs on our behalf, Cowen may be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Cowen may be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Cowen with respect to certain liabilities, including liabilities under the Securities Act.

Investing in our ADSs involves risks. These risks are described under the caption "[Risk Factors](#)" beginning on page S-9 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement.

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

Cowen

The date of this prospectus supplement is February 27, 2020.

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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 supplement 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 supplement. 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 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.

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus are part of an automatic shelf registration statement, as amended, that we filed with the SEC as a “well-known seasoned issuer” as defined in Rule 405 under the Securities Act of 1933, as amended. We may from time to time sell our ADSs representing our ordinary shares having an aggregate offering price of up to \$100,000,000 under this prospectus supplement at prices and on terms to be determined at the time of each such offering.

Before buying any of the ADSs that we are offering, we urge you to carefully read this prospectus supplement, together with the accompanying prospectus and the information incorporated by reference as described under the headings “Where You Can Find More Information” and “Incorporation by Reference” in this prospectus supplement, and any free writing prospectus that we have authorized for use in connection with this offering. These documents contain important information that you should consider when making your investment decision.

This prospectus supplement describes the terms of this offering of ADSs and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in any document incorporated by reference into this prospectus supplement that was filed with the SEC before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference into this prospectus supplement—the statement in the document having the later date modifies or supersedes the earlier statement.

We have not, and Cowen has not, authorized anyone to provide you with information in addition to or different from that contained in or incorporated by reference into this prospectus supplement and any related free writing prospectus filed by us with the SEC. We and Cowen take no responsibility for, and can provide no assurances as to the reliability of, any information that others may provide to you. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus supplement does not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in this prospectus supplement or an offer to sell or the solicitation of an offer to buy any securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information in this prospectus supplement or any related free writing prospectus is accurate only as of the date on the front of such document and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus supplement or any related free writing prospectus, or any sale of a security. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

This prospectus supplement contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus supplement forms a part. You may obtain copies of those documents as described below under the heading “Where You Can Find More Information”.

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

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We own various U.S. federal trademark registrations and applications and unregistered trademarks, including our corporate logo. This prospectus supplement and the information incorporated herein by reference contains references to trademarks, service marks and trade names referred to in this prospectus supplement and the information incorporated herein, including logos, artwork, and other visual displays, may appear without the ® or TM symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks, service marks or trade names. We do not intend our use or display of other companies' trade names, service marks or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus supplement or any related free writing prospectus are the property of their respective owners.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement 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 supplement and our periodic filings with the SEC incorporated by reference in this 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 supplement include, but are not limited to, statements about:

- the timing, progress and results of clinical trials and preclinical studies for our programs and product candidates, including statements regarding the timing of initiation and completion of trials or studies and related preparatory work, the period during which the results of the trials will become available and our research and development programs;
- the timing, scope or likelihood of regulatory submissions, filings, and approvals;
- our ability to develop and advance product candidates into, and successfully complete, clinical trials;
- our expectations regarding the size of the patient populations for our product candidates, if approved for commercial use;
- the implementation of our business model and our strategic plans for our business, commercial product, product candidates and technology;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the pricing and reimbursement of our commercial product and product candidates, if approved;
- the scalability and commercial viability of our manufacturing methods and processes, including our plans to develop our in-house manufacturing operations;
- the rate and degree of market acceptance and clinical utility of our commercial product and product candidates, in particular, and gene therapy, in general;
- our ability to establish or maintain collaborations or strategic relationships or obtain additional funding;
- our competitive position;
- the scope of protection we and/or our licensors are able to establish and maintain for intellectual property rights covering our commercial product and product candidates;
- developments and projections relating to our competitors and our industry;
- our expectations related to the use of proceeds from any securities offering;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- the impact of laws and regulations;
- our ability to attract and retain qualified employees and key personnel;

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- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately; and
- other risks and uncertainties, including those listed under the caption “Risk Factors” in this prospectus supplement as well as those risk factors that are incorporated by reference in this prospectus supplement.

The forward-looking statements made or incorporated by reference in this prospectus supplement 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 supplement 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.

PROSPECTUS SUPPLEMENT SUMMARY

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

Business Overview

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

To date, over 170 patients have been treated with our commercial product and clinical-stage product candidates across seven different diseases, with follow-up periods of more than 18 years following a single administration. We believe the data observed across these programs, in combination with our deep expertise in the development, manufacturing and commercialization of gene and cell therapies, position us to provide potentially transformative therapies to people suffering from a broad range of diseases.

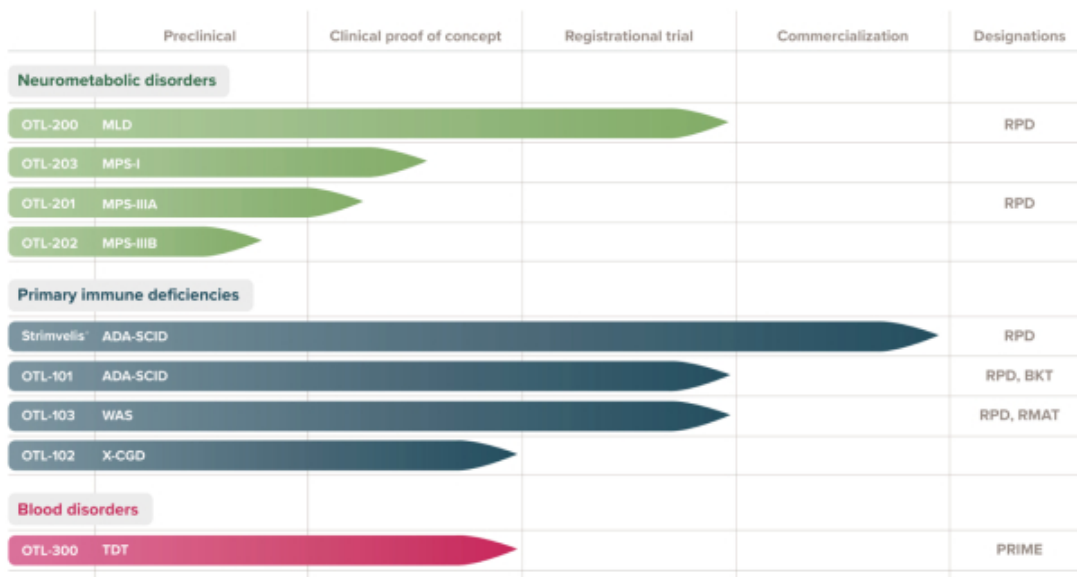
We are currently focusing our *ex vivo* autologous HSC gene therapy approach on three therapeutic rare disease franchise areas: primary immune deficiencies, neurometabolic disorders and blood disorders. Our portfolio includes Strimvelis, our commercial-stage gammaretroviral-based product approved in Europe for the treatment of adenosine deaminase-severe combined immunodeficiency, or ADA-SCID, seven lentiviral-based product candidates in clinical-stage development and several other product candidates in preclinical development.

For each of our lead product candidates, we are in ongoing discussions with the applicable regulatory authorities with respect to the clinical and other data required for regulatory submissions. We filed a marketing authorization application, or MAA, with the European Medicines Agency, or EMA, for OTL-200 for the treatment of metachromatic leukodystrophy, or MLD, in 2019, and we anticipate filing a biologics license application, or BLA, with the U.S. Food & Drug Administration, or FDA, for OTL-200 for the same indication by 2021. We plan to make additional regulatory submissions over the next two years with the FDA for OTL-101 for the treatment of ADA-SCID and with the FDA and EMA for OTL-103 for the treatment of Wiskott-Aldrich syndrome, or WAS.

Our pipeline

Our advanced portfolio of *ex vivo* autologous HSC gene therapies targets serious and life-threatening rare diseases. Our primary immune deficiencies franchise consists of Strimvelis for ADA-SCID, two advanced registrational clinical programs, OTL-101 for ADA-SCID and OTL-103 for WAS, and one clinical proof of concept-stage program, OTL-102 for X-linked chronic granulomatous disease, or X-CGD. Our neurometabolic disorders franchise consists of one advanced registrational clinical program, OTL-200 for MLD, two clinical proof of concept-stage programs, OTL-203 for mucopolysaccharidosis type I, or MPS-I, and OTL-201 for mucopolysaccharidosis type IIIA, or MPS-III A, and a preclinical program, OTL-202 for mucopolysaccharidosis type IIIB, or MPS-IIIB. Our blood disorders franchise consists of one clinical proof of concept-stage program, OTL-300 for transfusion-dependent beta-thalassemia, or TDT.

The status of these programs is outlined below:



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 supplement, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus supplement.

THE OFFERING

ADSs offered by us	Ordinary shares represented by ADSs, having an aggregate offering price of up to \$100,000,000.
Manner of offering	“At the market offering” that may be made from time to time through our sales agent, Cowen. See “Plan of Distribution” on page S-15 of this prospectus supplement.
The ADSs	Each ADS represents one ordinary share, nominal value £0.10 per share. The offered ADSs may be evidenced by American Depositary Receipts, or ADRs.
Depositary	Citibank, N.A.
Use of proceeds	<p>We currently anticipate using such proceeds primarily for general corporate purposes and to fund ongoing commercialization of Strimvelis, the development and, if approved, the commercialization of our product candidates, to discover or license additional product candidates, pay interest on outstanding indebtedness, if any, and the potential expansion of our manufacturing facilities and capabilities.</p> <p>See “Use of Proceeds” on page S-12 of this prospectus supplement.</p>
Risk Factors	You should read the “Risk Factors” section of this prospectus supplement beginning on page S-9, as well as those risk factors that are incorporated by reference herein, for a discussion of factors to consider carefully before deciding to invest in our securities.
The Nasdaq Global Select Market symbol	“ORTX”

RISK FACTORS

Investing in our ADSs and ordinary shares involves a high degree of risk. You should carefully consider the risks and uncertainties described in the following risk factors as well as the other information contained in this prospectus supplement and in the documents incorporated by reference into this prospectus supplement before making an investment decision. Our business, financial condition or results of operations could be materially adversely affected by the materialization of any of these risks. The trading price of our ADSs could decline due to the materialization of any of these risks, and you may lose all or part of your investment. This prospectus supplement and the documents incorporated herein by reference also contain forward-looking statements that involve risks and uncertainties. Actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks described in the documents incorporated herein by reference, including our Annual Report on Form 10-K for the year ended December 31, 2019, which is on file with the SEC and is incorporated by reference into this prospectus supplement, and other documents we file with the SEC that are deemed incorporated by reference into this prospectus supplement. The risks and uncertainties we have described are not the only ones facing our company. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our business, financial condition, and results of operations.

Risks Related to this Offering

The market price of our ADSs may be highly volatile, and may fluctuate due to factors beyond our control.

The trading price of our ADSs has fluctuated, and is likely to continue to fluctuate significantly. The market price of our ADSs depends on a number of factors, some of which are beyond our control. In addition to the factors discussed in our Annual Report on Form 10-K for the fiscal year ended December 31, 2019, these factors include:

- adverse results or delays in preclinical studies or clinical trials;
- reports of adverse events in other gene therapy products or clinical trials of such products;
- an inability to obtain additional funding;
- failure by us to successfully develop and commercialize our product candidates;
- failure by us to succeed in our ongoing commercialization of Strimvelis;
- failure by us to gain broad insurance coverage and reimbursement for our product candidates, if approved;
- failure by us to maintain our existing strategic collaborations or enter into new collaborations;
- failure by us or our licensors and strategic partners to prosecute, maintain or enforce our intellectual property rights;
- changes in laws or regulations applicable to future products;
- an inability to obtain adequate product supply for our product candidates or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- the introduction of new products, services or technologies by our competitors;
- failure by us to meet or exceed financial or other projections we may provide to the public;
- failure by us to meet or exceed the financial or other projections of the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;

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- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us, our strategic partner or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent or shareholder litigation;
- changes in the market valuations of similar companies;
- sales of our ADSs by us or our shareholders in the future; and
- the trading volume of our ADSs.

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

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

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

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

The ADSs sold in this offering, if any, will be sold from time to time at various prices. However, we expect that the offering price of our ADSs in this offering will be substantially higher than the net tangible book value per ADS. Therefore, if you purchase ADSs in this offering, you will pay a price per ADS that substantially exceeds our net tangible book value per ADS after this offering. To the extent outstanding options are exercised, you will incur further dilution. After giving effect to the assumed sales of our ADSs in the aggregate amount of \$100,000,000 in this offering at an assumed public offering price of \$11.49 per ADS, the last reported sale price of our ADSs on The Nasdaq Global Select Market on February 26, 2020, and after deducting estimated discounts and commissions and estimated offering expenses payable by us, you would experience immediate dilution of \$7.74 per ADS as of December 31, 2019, representing the difference between our as adjusted net tangible book value per ADS after giving effect to this offering and the assumed public offering price. See the section titled “Dilution” below for a more detailed illustration of the dilution you will incur if you participate in this offering.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional of our ADSs or other securities convertible into or exchangeable for our ADSs. We cannot assure you that we will be able to sell ADSs or other securities in any other offering at a price per ADS or per share that is equal to or greater than the price per ADS paid by investors in this offering, and investors purchasing ADSs or other securities in the future could have rights superior to existing shareholders. The price per ADS at which we sell additional ADSs or other securities convertible into or exchangeable for our ADSs in future transactions may be higher or lower than the price per ADS in this offering.

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

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

USE OF PROCEEDS

We may issue and sell ADSs having aggregate sales proceeds of up to \$100,000,000 from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and net proceeds to us, if any, are not determinable at this time.

We currently anticipate using the net proceeds primarily for general corporate purposes and to fund our ongoing commercialization of Strimvelis, the development and, if approved, the commercialization of our product candidates, to discover and license additional product candidates, pay interest on outstanding indebtedness, if any, and the potential expansion of our manufacturing facilities and capabilities.

We have not determined the exact amounts we plan to spend on any of the items indicated above or the timing of these expenditures. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the actual net proceeds from this offering, the factors described under “Risk Factors” in this prospectus supplement and in the documents incorporated by reference herein, the progress of our development efforts, the status of and results from clinical trials, as well as any collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering. We have no current understandings, agreements or commitments for any material acquisitions or licenses of any products, businesses or technologies.

Pending application of the net proceeds as described above, if any, we may temporarily invest the net proceeds in a variety of capital preservation instruments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

DIVIDEND POLICY

Since our inception, we have not declared or paid any dividends on our ADSs. We intend to retain any earnings for use in our business and do not currently intend to pay dividends on our ADSs.

The payment of dividends by us is governed by English law. Further, our existing debt agreement restricts us from paying dividends. The declaration and payment of any future dividends will be at the discretion of our board of directors and will depend upon our results of operations, cash requirements, financial condition, contractual restrictions, restrictions imposed by our indebtedness, any current or future debt agreements or applicable laws and other factors that our board of directors may deem relevant.

DILUTION

If you invest in our ADSs in this offering, your ownership interest will be diluted immediately to the extent of the difference between the price per ADS you pay in this offering and the net tangible book value per ADS immediately after this offering.

Our net tangible book value as of December 31, 2019, was \$299.2 million, or \$3.09 per ordinary share (equivalent to \$3.09 per ADS). Net tangible book value per ADS is determined by dividing our total tangible assets, less total liabilities, by 96,923,729, the total number of our ordinary shares outstanding as of December 31, 2019.

After giving effect to the assumed sale by us of our ADSs in the aggregate amount of \$100,000,000 in this offering at an assumed public offering price of \$11.49 per ADS, the last reported sale price of our ADSs on The Nasdaq Global Select Market on February 26, 2020 and after deducting estimated discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of December 31, 2019, would have been \$396.2 million, or \$3.75 per ordinary share (equivalent to \$3.75 per ADS). This represents an immediate increase in net tangible book value of \$0.66 per ordinary share and ADS to our existing shareholders. Dilution per share to new investors is determined by subtracting as adjusted net tangible book value per ADS after this offering from the public offering price per ADS paid by new investors participating in this offering. Investors purchasing our ADSs in this offering will have paid \$7.74 more than the as adjusted net tangible book value per ADS after this offering. The following table illustrates this dilution on a per ADS basis.

Assumed public offering price per ADS		\$11.49
Net tangible book value per ADS as of December 31, 2019	\$3.09	
Increase in net tangible book value per ADS attributable to the offering	<u>0.66</u>	
As adjusted net tangible book value per ADS after giving effect to the offering		<u>3.75</u>
Dilution per ADS to new investors participating in the offering		<u>\$ 7.74</u>

The as adjusted information above is illustrative only and will change based on the actual price to the public, the actual number of ADSs sold and other terms of the offering determined at the time our ADSs are sold pursuant to this prospectus supplement. The ADSs sold in this offering, if any, will be sold from time to time at various prices.

The above discussion and table are based on 96,923,729 of our ordinary shares outstanding as of December 31, 2019, and exclude:

- 12,216,140 ordinary shares issuable upon the exercise of options for ordinary shares outstanding as of December 31, 2019, at a weighted-average exercise price of \$6.61 per share;
- 556,422 ordinary shares issuable upon the vesting of performance-based restricted stock units, or RSUs, outstanding as of December 31, 2019;
- 183,069 ordinary shares associated with a consulting agreement issuable to a non-employee advisor, of which 91,034 are issuable over a four-year period and 92,035 are issuable upon achievement of certain performance conditions;
- 4,687,029 ordinary shares available for future issuance under our 2018 Share Option and Incentive Plan as of December 31, 2019; and
- 1,580,887 ordinary shares available for future issuance under our 2018 Employee Share Purchase Plan as of December 31, 2019.

PLAN OF DISTRIBUTION

We have entered into a sales agreement with Cowen, under which we may issue and sell from time to time up to an aggregate of \$100,000,000 of our ADSs, each representing one ordinary share, through Cowen as our sales agent. Sales of our ADSs, if any, will be made at market prices by any method that is deemed to be an “at the market offering” as defined in Rule 415(a)(4) under the Securities Act, including sales made directly on The Nasdaq Global Select Market or any other trading market for our ADSs. If authorized by us in writing, Cowen may purchase our ADSs as principal.

Cowen will offer our ADSs subject to the terms and conditions of the sales agreement on a daily basis or as otherwise agreed upon by us and Cowen. We will designate the maximum amount of ADSs to be sold through Cowen on a daily basis or otherwise determine such maximum amount together with Cowen. Subject to the terms and conditions of the sales agreement, Cowen will use its commercially reasonable efforts to sell on our behalf all of the ADSs requested to be sold by us. We may instruct Cowen not to sell ADSs if the sales cannot be effected at or above the price designated by us in any such instruction. Cowen or we may suspend the offering of our ADSs being made through Cowen under the sales agreement upon proper notice to the other party. Cowen and we each have the right, by giving written notice as specified in the sales agreement, to terminate the sales agreement in each party’s sole discretion at any time.

The compensation to Cowen for sales of ADSs sold pursuant to the sales agreement will be an amount up to 3.0% of the gross proceeds of any ADSs sold under the sales agreement. We have also agreed to reimburse Cowen up to \$50,000 of Cowen’s actual outside legal expenses incurred by Cowen in connection with this offering, as well as Cowen’s FINRA counsel fees in an amount up to \$15,000. We estimate that the total expenses of the offering payable by us, excluding commissions payable to Cowen under the sales agreement, will be approximately \$0.5 million.

The remaining sales proceeds, after deducting any expenses payable by us and any transaction fees imposed by any governmental, regulatory, or self-regulatory organization in connection with the sales, will equal our net proceeds for the sale of such ADSs.

Cowen will provide written confirmation to us following the close of trading on The Nasdaq Global Select Market on each day in which ADSs are sold through it as sales agent under the sales agreement. Each confirmation will include the number of ADSs sold through it as sales agent on that day, the volume weighted average price of the ADSs sold, the percentage of the daily trading volume and the net proceeds to us.

We will report at least quarterly the number of ADSs sold through Cowen under the sales agreement, the net proceeds to us and the compensation paid by us to Cowen in connection with the sales of ADSs.

Settlement for sales of ADSs will occur, unless the parties agree otherwise, on the second business day that is also a trading day following the date on which any sales were made in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

In connection with the sales of our ADSs on our behalf, Cowen may be deemed to be an “underwriter” within the meaning of the Securities Act, and the compensation paid to Cowen may be deemed to be underwriting commissions or discounts. We have agreed in the sales agreement to provide indemnification and contribution to Cowen against certain liabilities, including liabilities under the Securities Act. As sales agent, Cowen will not engage in any transactions that stabilizes our ADSs.

Our ADSs are listed on The Nasdaq Global Select Market and trade under the symbol “ORTX.” The transfer agent of our ordinary shares is Equiniti Limited and the depositary is Citibank, N.A.

Cowen and/or its affiliates have provided, and may in the future provide, various investment banking and other financial services for us for which services they have received and, may in the future receive, customary fees.

The address of Cowen is 599 Lexington Avenue, New York, New York 10022.

LEGAL MATTERS

The validity of the ordinary shares underlying the ADSs offered hereby and certain matters governed by English law will be passed upon for us by Goodwin Procter (UK) LLP. Certain matters of U.S. federal law will be passed upon for us by Goodwin Procter LLP, New York, New York. Cowen and Company, LLC is being represented in connection with this offering by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts.

EXPERTS

The financial statements as of and for the year ended December 31, 2019 and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Annual Report on Internal Control Over Financial Reporting) incorporated in this prospectus supplement by reference to the Annual Report on Form 10-K for the year ended December 31, 2019 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP (a Delaware limited liability partnership), an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

The financial statements as of December 31, 2018 and for each of the two years in the period ended December 31, 2018 incorporated in this prospectus supplement by reference to the Annual Report on Form 10-K for the year ended December 31, 2019 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP (a United Kingdom entity), 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 a public limited company incorporated under the laws of England and Wales. Certain of our directors and executive officers and experts reside outside of the United States. As a result, it may be difficult for an investor to serve process on us or our directors and executive officers or to compel any of them to appear in Court in the United States or to enforce judgments obtained in U.S. courts against them or us, including judgments based on civil liability provisions of the securities laws of the United States. In addition, awards of punitive damages in actions brought in the United States or elsewhere may be unenforceable in the United Kingdom. An award for monetary damages under the U.S. securities laws would be considered punitive in the United Kingdom if it does not seek to compensate the claimant for loss or damage suffered and is intended to punish the defendant. The enforceability of any judgment in the United Kingdom will depend on the particular facts of the case as well as the laws and treaties in effect at the time. The United States and the United Kingdom do not currently have a treaty providing for the mutual recognition and enforcement of judgments (other than arbitration awards) in civil and commercial matters.

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 supplement and is not incorporated by reference in this prospectus supplement.

This prospectus supplement is part of the Registration Statement we filed with the SEC. This prospectus supplement 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 supplement 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 much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus supplement is considered to be part of this prospectus supplement. Because we are incorporating by reference future filings with the SEC, this prospectus supplement is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus supplement. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus supplement or in any document previously incorporated by reference have been modified or superseded. This prospectus supplement incorporates by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) until the offering of the securities under the Registration Statement is terminated or completed:

- Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2019, filed on February 27, 2020 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).

We are also incorporating by reference all subsequent Annual Reports on Form 10-K that we file with the SEC, Quarterly Reports on Form 10-Q that we file with the SEC, our annual Proxy Statement on Schedule 14A relating to our annual general meeting of shareholders that we file with the SEC, certain Current Reports on Form 8-K that we file with the SEC and certain Current Reports on Form 8-K that we furnish to the SEC after the date of this prospectus supplement (if they state that they are incorporated by reference into our Registration Statement on Form S-3 (Registration No. 333-234439)) prior to the termination of this offering. In all cases, you should rely on the later information over different information included in this prospectus supplement or any accompanying prospectus.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address or 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 supplement. We have included our website address in this prospectus supplement solely as an inactive textual reference.

You should rely only on the information incorporated by reference or provided in this prospectus supplement. 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 supplement is accurate as of any date other than the date on the front of those documents.



\$100,000,000

American Depositary Shares representing Ordinary Shares

PROSPECTUS SUPPLEMENT

Cowen

February 27, 2020

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	\$ 12,980
FINRA filing fee	225,500
Legal fees and expenses	*
Accounting fees and expenses	*
Miscellaneous expenses	*
Total	\$ *

* Estimated expenses not presently known.

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 purported execution of the duties of his or her office or the exercise of his or her powers.

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

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

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Item 16. Exhibits

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

Exhibit Number	Description of Exhibit
1.1*	Form of Underwriting Agreement
1.2	<u>Sales Agreement, dated February 27, 2020, by and between the Registrant and Cowen and Company, LLC</u>
3.1	<u>Articles of Association of Orchard Therapeutics plc (Incorporated herein by reference to Exhibit 1.1 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>
4.1	<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 (Exhibit 5.1 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>
5.2	<u>Opinion of Goodwin Procter LLP (Exhibit 5.2 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>
5.3	<u>Opinion of Goodwin Procter (UK) 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>
16.1	<u>Letter of PricewaterhouseCoopers LLP, a United Kingdom entity, dated November 1, 2019 regarding changes in Registrant's certifying accountants (Exhibit 16.1 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>

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<u>Exhibit Number</u>	<u>Description of Exhibit</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 Goodwin Procter (UK) LLP (included in Exhibit 5.3 hereto)</u>
23.4	<u>Consent of PricewaterhouseCoopers LLP, a Delaware limited liability partnership</u>
23.5	<u>Consent of PricewaterhouseCoopers LLP, a United Kingdom entity</u>
24.1	<u>Power of Attorney (included on signature page) (Exhibit 24.1 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>
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.

* 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, 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

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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.
- (e) The undersigned registrant hereby undertakes to deliver or cause to be delivered with the prospectus, to each person to whom the prospectus is sent or given, the latest annual report, to security holders that is incorporated by reference in the prospectus and furnished pursuant to and meeting the requirements of Rule 14a-3 or Rule 14c-3 under the Securities Exchange Act of 1934; and, where interim financial information required to be presented by Article 3 of Regulation S-X is not set forth in the prospectus, to deliver, or cause to be delivered to each person to whom the prospectus is sent or given, the latest quarterly report that is specifically incorporated by reference in the prospectus to provide such interim financial information.
- (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.

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SIGNATURES

Pursuant to the requirements of the Securities Act, the registrant has duly caused this Post-Effective Amendment to Registration Statement on Form F-3 to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of London, United Kingdom, on this 27th day of February, 2020.

ORCHARD THERAPEUTICS PLC

By: /s/ Mark Rothera
Mark Rothera
President and Chief Executive Officer

No other person is required to sign this Post-Effective Amendment in reliance upon Rule 478 under the Securities Act.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
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Cogency Global Inc.

By: <u>/s/ Colleen A. De Vries</u> Name: Colleen A. De Vries Title: Senior Vice President on behalf of Cogency Global Inc.	Authorized Representative in the United States	February 27, 2020
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ORCHARD THERAPEUTICS PLC

\$100,000,000

AMERICAN DEPOSITARY SHARES

EACH REPRESENTING ONE ORDINARY SHARE

(NOMINAL VALUE £0.10 PER SHARE)

SALES AGREEMENT

February 27, 2020

Cowen and Company, LLC
599 Lexington Avenue
New York, NY 10022

Ladies and Gentlemen:

Orchard Therapeutics plc, a public limited company incorporated under the laws of England and Wales (the "**Company**"), confirms its agreement (this "**Agreement**") with Cowen and Company, LLC ("**Cowen**"), as follows:

1. **Issuance and Sale of Placement Shares.** The Company agrees that, from time to time during the term of this Agreement, on the terms and subject to the conditions set forth herein, it may issue and sell through Cowen, acting as agent and/or principal, American Depositary Shares (the "**ADSs**"), each representing one (1) of the Company's ordinary shares, nominal value £0.10 per share (the "**Ordinary Shares**"), having an aggregate offering price of up to \$100,000,000 (the "**Placement Shares**"). Notwithstanding anything to the contrary contained herein, the parties hereto agree that compliance with the limitation set forth in this **Section 1** on the number or dollar amount of ADSs issued and sold under this Agreement shall be the sole responsibility of the Company, and Cowen shall have no obligation in connection with such compliance. The issuance and sale of ADSs through Cowen will be effected pursuant to the Registration Statement (as defined below) filed by the Company and which became effective under Rule 462(e) of the Securities Act (as defined below) upon filing with the Securities and Exchange Commission (the "**Commission**"), although nothing in this Agreement shall be construed as requiring the Company to use the Registration Statement (as defined below) to issue the ADSs. The ADSs are to be issued pursuant to that certain deposit agreement (the "**Deposit Agreement**"), dated as of November 2, 2018, among the Company, Citibank, N.A. as depository (the "**Depository**"), and the holders and beneficial owners from time to time of the ADSs. Each ADS will represent the right to receive one Ordinary Share deposited pursuant to the Deposit Agreement.

The Company has filed, in accordance with the provisions of the Securities Act of 1933, as amended, and the rules and regulations thereunder (collectively, the "**Securities Act**"), with the Commission an automatic shelf registration statement on Form F-3ASR (File No. 333-234439), which was subsequently converted to an automatic shelf registration statement on Form S-3ASR pursuant to an immediately effective Post-Effective Amendment on the date hereof (the

“Post-Effective Amendment”), including a base prospectus, relating to certain securities, including the ADSs, to be issued from time to time by the Company, and which incorporates by reference documents that the Company has filed or will file in accordance with the provisions of the Securities Exchange Act of 1934, as amended, and the rules and regulations thereunder (collectively, the **“Exchange Act”**). The Company has prepared a prospectus supplement specifically relating to the Placement Shares (the **“Prospectus Supplement”**) to the base prospectus, both of which are included as part of such registration statement. The Company has furnished to Cowen, for use by Cowen, copies of the prospectus included as part of such registration statement, as supplemented by the Prospectus Supplement, relating to the Placement Shares. Except where the context otherwise requires, such registration statement, as amended when it and the Post-Effective Amendment became effective, including all documents filed as part thereof or incorporated by reference therein, and including any information contained in a Prospectus (as defined below) subsequently filed with the Commission pursuant to Rule 424(b) under the Securities Act or deemed to be a part of such registration statement pursuant to Rule 430B of the Securities Act, is herein called the **“Registration Statement.”** The base prospectus, including all documents incorporated therein by reference, included in the Registration Statement, as it may be supplemented by the Prospectus Supplement, in the form in which such prospectus and/or Prospectus Supplement have most recently been filed by the Company with the Commission as part of the Registration Statement or pursuant to Rule 424(b) under the Securities Act, together with any “issuer free writing prospectus,” as defined in Rule 433 of the Securities Act regulations (**“Rule 433”**), relating to the Placement Shares that (i) is required to be filed with the Commission by the Company or (ii) is exempt from filing pursuant to Rule 433(d)(5)(i), in each case in the form filed or required to be filed with the Commission or, if not required to be filed, in the form retained in the Company’s records pursuant to Rule 433(g), is herein called the **“Prospectus.”** The Company has filed with the Commission a registration statement on Form F-6, as amended (File No. 333-227905) relating to the ADSs. Such registration statement, as amended, including the financial statements, exhibits and schedules thereto, in the form in which it became effective under the Securities Act is called the **“F-6 Registration Statement.”** Any reference herein to the Registration Statement, the F-6 Registration Statement, the Prospectus or any amendment or supplement thereto shall be deemed to refer to and include the documents incorporated by reference therein, and any reference herein to the terms “amend,” “amendment” or “supplement” with respect to the Registration Statement or the Prospectus shall be deemed to refer to and include the filing after the execution hereof of any document with the Commission deemed to be incorporated by reference therein. For purposes of this Agreement, all references to the Registration Statement, the Prospectus or to any amendment or supplement thereto shall be deemed to include any copy filed with the Commission pursuant to the Electronic Data Gathering Analysis and Retrieval system (**“EDGAR”**).

2. **Placements.** Each time that the Company wishes to issue and sell the Placement Shares hereunder (each, a **“Placement”**), it will notify Cowen by email notice (or other method mutually agreed to in writing by the parties) (a **“Placement Notice”**) containing the parameters in accordance with which it desires the Placement Shares to be sold, which shall at a minimum include the number or dollar amount of Placement Shares to be issued, the time period during which sales are requested to be made, any limitation on the number of Placement Shares that may be sold in any one Trading Day (as defined in Section 3) and any minimum price below which sales may not be made, a form of which containing such minimum sales parameters necessary is attached hereto as **Schedule 1**. The Placement Notice shall originate from any of the individuals from the Company set forth on **Schedule 2** (with a copy to each of the other individuals from the

Company listed on such schedule), and shall be addressed to each of the individuals from Cowen set forth on **Schedule 2**, as such **Schedule 2** may be amended from time to time. The Placement Notice shall be effective upon receipt by Cowen unless and until (i) in accordance with the notice requirements set forth in Section 4, Cowen declines to accept the terms contained therein for any reason, in its sole discretion, (ii) the entire amount of the Placement Shares have been sold, (iii) in accordance with the notice requirements set forth in Section 4, the Company suspends or terminates the Placement Notice, (iv) the Company issues a subsequent Placement Notice with parameters superseding those on the earlier dated Placement Notice, or (v) this Agreement has been terminated under the provisions of **Section 11**. The amount of any discount, commission or other compensation to be paid by the Company to Cowen in connection with the sale of the Placement Shares shall be calculated in accordance with the terms set forth in **Schedule 3**. It is expressly acknowledged and agreed that neither the Company nor Cowen will have any obligation whatsoever with respect to a Placement or any Placement Shares unless and until the Company delivers a Placement Notice to Cowen and Cowen does not decline such Placement Notice pursuant to the terms set forth above, and then only upon the terms specified therein and herein. In the event of a conflict between the terms of this Agreement and the terms of a Placement Notice, the terms of the Placement Notice will control.

3. **Sale of Placement Shares by Cowen.** Subject to the terms and conditions herein set forth, upon the Company's delivery of a Placement Notice, and unless the sale of the Placement Shares described therein has been declined, suspended, or otherwise terminated in accordance with the terms of this Agreement, Cowen, for the period specified in the Placement Notice, will use its commercially reasonable efforts consistent with its normal trading and sales practices and applicable state and federal laws, rules and regulations and the rules of the Nasdaq Global Select Market ("**Nasdaq**") to sell such Placement Shares up to the amount specified, and otherwise in accordance with the terms of such Placement Notice. Cowen will provide written confirmation to the Company (including by email correspondence to each of the individuals of the Company set forth on **Schedule 2**, if receipt of such correspondence is actually acknowledged by any of the individuals to whom the notice is sent, other than via auto-reply) on the Trading Day (as defined below) on which it has made sales of Placement Shares hereunder setting forth the number of Placement Shares sold on such day, the volume-weighted average price of the Placement Shares sold, and the Net Proceeds (as defined below) payable to the Company. Cowen may sell Placement Shares by any method permitted by law deemed to be an "at the market" offering as defined in Rule 415(a)(4) of the Securities Act, including without limitation sales made through Nasdaq or on any other existing trading market for the ADSs. Cowen shall not purchase Placement Shares for its own account as principal unless expressly authorized to do so by the Company in a Placement Notice. The Company acknowledges and agrees that (i) there can be no assurance that Cowen will be successful in selling Placement Shares, and (ii) Cowen will incur no liability or obligation to the Company or any other person or entity if it does not sell Placement Shares for any reason other than a failure by Cowen to use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such Placement Shares as required under this **Section 3**. For the purposes hereof, "**Trading Day**" means any day on which the Company's ADSs are purchased and sold on the principal market on which the ADSs are listed or quoted.

4. Suspension of Sales.

(a) The Company or Cowen may, upon notice to the other party in writing (including by email correspondence to each of the individuals of the other party set forth on **Schedule 2**, if receipt of such correspondence is actually acknowledged by any of the individuals to whom the notice is sent, other than via auto-reply) or by telephone (confirmed immediately by verifiable facsimile transmission or email correspondence to each of the individuals of the other party set forth on **Schedule 2**), suspend any sale of Placement Shares; *provided, however,* that such suspension shall not affect or impair either party's obligations with respect to any Placement Shares sold hereunder prior to the receipt of such notice. Each of the parties agrees that no such notice under this **Section 4** shall be effective against the other unless it is made to one of the individuals named on **Schedule 2** hereto, as such schedule may be amended from time to time.

(b) Notwithstanding any other provision of this Agreement, during any period in which the Company is in possession of material non-public information, the Company and Cowen agree that (i) no sale of Placement Shares will take place, (ii) the Company shall not request the sale of any Placement Shares, and (iii) Cowen shall not be obligated to sell or offer to sell any Placement Shares.

(c) If either Cowen or the Company has reason to believe that the exemptive provisions set forth in Rule 101(c)(1) of Regulation M under the Exchange Act are not satisfied with respect to the Ordinary Shares or ADSs, it shall promptly notify the other party, and Cowen may, at its sole discretion and upon delivery of notice to the Company, suspend sales of the Placement Shares under this Agreement.

(d) The Registration Statement became automatically effective upon filing with the Commission on November 1, 2019. Notwithstanding any other provision of this Agreement, during any period in which the Registration Statement or the F-6 Registration Statement is no longer effective under the Securities Act, the Company shall promptly notify Cowen, the Company shall not request the sale of any Placement Shares, and Cowen shall not be obligated to sell or offer to sell any Placement Shares.

5. Settlement.

(a) Settlement of Placement Shares. Unless otherwise specified in the applicable Placement Notice or otherwise agreed by the parties hereto, settlement for sales of Placement Shares will occur on the second (2nd) Trading Day following the date on which such sales are made (each, a "**Settlement Date**" and the first such settlement date, the "**First Delivery Date**"). The amount of proceeds to be delivered to the Company on a Settlement Date against receipt of the Placement Shares sold (the "**Net Proceeds**") will be equal to the aggregate sales price received by Cowen at which such Placement Shares were sold, after deduction for (i) Cowen's commission, discount or other compensation for such sales payable by the Company pursuant to **Section 2** hereof, (ii) any other amounts due and payable by the Company

to Cowen hereunder pursuant to Section 7(g) (Expenses) hereof, and (iii) any transaction fees imposed by any governmental or self-regulatory organization in respect of such sales.

(b) Delivery of Placement Shares. On or before each Settlement Date and against payment of the purchase price for the relevant Placement Shares, the Company will, or will cause the Depositary or its transfer agent (if applicable) to, electronically transfer the Placement Shares being sold by crediting Cowen's or its designee's account (provided Cowen shall have given the Company written notice of such designee prior to the Settlement Date) at The Depositary Trust Company through its Deposit and Withdrawal at Custodian System or by such other means of delivery as may be mutually agreed upon by the parties hereto which in all cases shall be freely tradeable, transferable, registered shares in good deliverable form. On each Settlement Date, Cowen will deliver the related Net Proceeds in same day funds to an account designated by the Company on, or prior to, the Settlement Date. The Company agrees that if the Company, or its transfer agent (if applicable), or the Depositary, defaults in its obligation to deliver duly authorized Placement Shares on a Settlement Date, the Company agrees that in addition to and in no way limiting the rights and obligations set forth in Section 9(a) (Indemnification and Contribution) hereto, it will (i) hold Cowen harmless against any loss, claim, damage, or reasonable documented expense (including reasonable documented legal fees and expenses), as incurred, arising out of or in connection with such default by the Company and (ii) pay to Cowen any commission, discount, or other compensation to which it would otherwise have been entitled absent such default.

6. Representations and Warranties of the Company. The Company represents and warrants to, and agrees with, Cowen that as of the date of this Agreement, each Representation Date (as defined in Section 7(m)), each date on which a Placement Notice is given, and any date on which Placement Shares are sold hereunder:

(a) Registration Statement and Prospectus. The Registration Statement has become effective under the Securities Act. No order suspending the effectiveness of the Registration Statement has been issued by the Commission, and no proceeding for that purpose or pursuant to Section 8A of the Securities Act against the Company or related to the offering of the Placement Shares has been initiated or, to the knowledge of the Company, threatened by the Commission. The Company meets the requirements for use of Form S-3 under the Securities Act. The sale of the Placement Shares hereunder meets the requirements or General Instruction I.B.1 of Form S-3. As of the applicable effective date of the Registration Statement and any post-effective amendment thereto, the Registration Statement and any such post-effective amendment complied and as of each Applicable Time, complied and will comply in all material respects with the applicable requirements of the Securities Act, and did not and as of each Applicable Time, did not and will not contain any untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary in order to make the statements therein not misleading; and as of the date of the Prospectus and any amendment or supplement thereto and as of each Applicable Time, the Prospectus will comply in all material

respects with the applicable requirements of the Securities Act and will not contain any untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading; provided that the Company makes no representation or warranty with respect to any statements or omissions made in reliance upon and in conformity with information relating to Cowen furnished to the Company in writing by Cowen expressly for use in the Registration Statement and the Prospectus and any amendment or supplement thereto, it being understood and agreed that the only such information furnished by Cowen consists of the information described as such in Section 9(b) hereof.

(b) Form F-6. The F-6 Registration Statement and any amendments thereto, in respect of the Placement Shares has been filed with the Commission; such registration statement in the form heretofore delivered to Cowen and has been declared effective by the Commission; no stop order suspending the effectiveness of such registration statement has been issued and, to the knowledge of the Company, no proceeding for that purpose has been initiated or threatened by the Commission (the various parts of such registration statement, including all exhibits thereto, each as amended at the time such part of the registration statement became effective, being hereinafter called the “**ADS Registration Statement**”); as of the applicable effective date of the ADS Registration Statement and any post-effective amendment thereto, the ADS Registration Statement and any such post-effective amendment complied and as of each Applicable Time, complied and will comply in all material respects with the applicable requirements of the Securities Act, and did not and as of each Applicable Time, did not and will not contain any untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary in order to make the statements therein not misleading.

(c) Incorporated Documents. The documents incorporated by reference in the Registration Statement and the Prospectus, when they were filed with the Commission, conformed in all material respects to the requirements of the Exchange Act, and as of each Applicable Time none of such documents contained any untrue statement of a material fact or omitted to state a material fact necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading; and any further documents so filed and incorporated by reference in the Registration Statement and the Prospectus, when such documents are filed with the Commission, will conform in all material respects to the requirements of the Exchange Act and as of each Applicable Time will not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading.

(d) Financial Statements. The financial statements (including the related notes thereto) of the Company and its consolidated subsidiaries included or incorporated by reference in the Registration Statement and the Prospectus comply in all material respects with the applicable requirements of the Securities Act and the Exchange Act, as applicable, and present fairly the financial position of the

Company and its consolidated subsidiaries as of the dates indicated and the results of their operations and the changes in their cash flows for the periods specified; such financial statements have been prepared in conformity with generally accepted accounting principles (“GAAP”) in the United States applied on a consistent basis throughout the periods covered thereby, except in the case of unaudited financial statements, which are subject to normal year-end adjustments and do not contain footnotes as permitted by the applicable rules of the Commission, and any supporting schedules included or incorporated by reference in the Registration Statement present fairly in all material respects the information required to be stated therein; and the other financial information included or incorporated by reference in the Registration Statement and the Prospectus has been derived from the accounting records of the Company and its consolidated subsidiaries and presents fairly in all material respects the information shown thereby..

(e) No Material Adverse Change. Since the date of the most recent financial statements of the Company included or incorporated by reference in the Registration Statement and the Prospectus, (i) there has not been any change in the capital stock (other than the issuance of Ordinary Shares upon exercise of stock options and warrants described as outstanding in, and the grant of options and awards under existing equity incentive plans and certain other agreements described in, or as incorporated by reference in, the Registration Statement and the Prospectus or otherwise publicly disclosed), short-term debt or long-term debt of the Company or any of its subsidiaries, or any dividend or distribution of any kind declared, set aside for payment, paid or made by the Company on any class of capital stock, or any material adverse change, or any development involving a prospective material adverse change, in or affecting the business, properties, management, financial position, stockholders’ equity, results of operations or prospects of the Company and its subsidiaries taken as a whole; (ii) neither the Company nor any of its subsidiaries has entered into any transaction or agreement (whether or not in the ordinary course of business) that is material to the Company and its subsidiaries taken as a whole or incurred any liability or obligation, direct or contingent, that is material to the Company and its subsidiaries taken as a whole; and (iii) neither the Company nor any of its subsidiaries has sustained any loss or interference with its business that is material to the Company and its subsidiaries taken as a whole and that is either from fire, explosion, flood or other calamity, whether or not covered by insurance, or from any labor disturbance or dispute or any action, order or decree of any court or arbitrator or governmental or regulatory authority, except in each case as otherwise disclosed in the Registration Statement and the Prospectus.

(f) Organization and Good Standing. The Company and each of its subsidiaries have been duly incorporated and are validly existing and in good standing under the laws of their respective jurisdictions of incorporation, are duly qualified to do business and are in good standing in each jurisdiction in which their respective ownership or lease of property or the conduct of their respective businesses requires such qualification, and have all power and authority necessary to own or hold their respective properties and to conduct the businesses in which they are engaged, except where the failure to be so qualified or in good standing or

have such power or authority would not, individually or in the aggregate, reasonably be expected to have a material adverse effect on the business, properties, management, financial position, stockholders' equity, results of operations or prospects of the Company and its subsidiaries taken as a whole or on the performance by the Company of its obligations under this Agreement (a "**Material Adverse Effect**"). The Company does not own or control, directly or indirectly, any corporation, association or other entity other than the subsidiaries listed in Exhibit 21.1 to the Registration Statement.

(g) **Capitalization.** The Company has an authorized share capital as set forth in the Registration Statement and the Prospectus under the heading "Capitalization"; all the outstanding shares of capital stock of the Company have been duly and validly authorized and issued and are fully paid and non-assessable and are not subject to any pre-emptive or similar rights (save for those granted under applicable law); except as described in or expressly contemplated by the Registration Statement and the Prospectus, there are no outstanding rights (including, without limitation, pre-emptive rights (save for those granted under applicable law)), warrants or options to acquire, or instruments convertible into or exchangeable for, any shares of capital stock or other equity interest in the Company or any of its subsidiaries, or any contract, commitment, agreement, understanding or arrangement of any kind relating to the issuance of any capital stock of the Company or any such subsidiary, any such convertible or exchangeable securities or any such rights, warrants or options; the capital stock of the Company conforms in all material respects to the description thereof contained in the Registration Statement and the Prospectus; and all the outstanding shares of capital stock or other equity interests of each subsidiary owned, directly or indirectly, by the Company have been duly and validly authorized and issued, are fully paid and non-assessable and are owned directly or indirectly by the Company, free and clear of any lien, charge, encumbrance, security interest, restriction on voting or transfer or any other claim of any third party.

(h) **Stock Options.** With respect to the stock options (the "**Stock Options**") granted pursuant to the stock-based compensation plans of the Company and its subsidiaries (the "**Company Stock Plans**"), (i) each Stock Option intended to qualify as an "incentive stock option" under Section 422 of the Code so qualifies, (ii) each grant of a Stock Option was duly authorized no later than the date on which the grant of such Stock Option was by its terms to be effective by all necessary corporate action, including, as applicable, approval by the board of directors of the Company (or a duly constituted and authorized committee thereof) and any required stockholder approval by the necessary number of votes or written consents, and the award agreement governing such grant (if any) was duly executed and delivered by each party thereto, (iii) each such grant was made in all material respects in accordance with the terms of the Company Stock Plans, the Exchange Act and all other applicable laws, and regulatory rules or requirements, including the rules of the Nasdaq Global Select Market and (iv) each such grant or issuance was properly accounted for in accordance with GAAP in the financial statements (including the related notes) of the Company and disclosed in the Company's filings with the

Commission in accordance with the Exchange Act and all other applicable laws. The Company has not knowingly granted, and there is not currently and has been no policy or practice of the Company of coordinating the grant of Stock Options with, the release or other public announcement of material information regarding the Company or its subsidiaries or their results of operations or prospects.

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

(j) Sales Agreement. This Agreement has been duly authorized, executed and delivered by the Company.

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

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

(m) Description of the Transaction Documents. Each Transaction Document conforms in all material respects to the description thereof contained in the Registration Statement and the Prospectus.

(n) No Violation or Default. Neither the Company nor any of its subsidiaries is (i) in violation of its charter or by-laws or similar organizational documents; (ii) in default, and no event has occurred that, with notice or lapse of time or both, would constitute such a default, in the due performance or observance of any term, covenant or condition contained in any indenture, mortgage, deed of trust, loan agreement or other agreement or instrument to which the Company or any of its subsidiaries is a party or by which the Company or any of its subsidiaries is bound or to which any property or asset of the Company or any of its subsidiaries is subject; or (iii) in violation of any law or statute or any judgment, order, rule or regulation of any court or arbitrator or governmental or regulatory authority, except, in the case of clauses (ii) and (iii) above, for any such default or violation that would not, individually or in the aggregate, have a Material Adverse Effect.

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

(p) No Consents Required. No consent, approval, authorization, order, registration or qualification of or with any court or arbitrator or governmental or regulatory authority is required for the execution, delivery and performance by the Company of each of the Transaction Documents, the issuance and sale of the Placement Shares and the consummation of the transactions contemplated by the Transaction Documents, except for the registration of the ADSs under the Securities Act and such consents, approvals, authorizations, orders and registrations or qualifications as may be required by the Financial Industry Regulatory Authority, Inc. ("**FINRA**"), the Nasdaq Global Select Market or under applicable state securities laws in connection with the purchase and distribution of the Placement Shares by Cowen.

(q) Legal Proceedings. Except as described in the Registration Statement and the Prospectus, there are no legal, governmental or regulatory investigations, actions, demands, claims, suits, arbitrations, inquiries or proceedings

(“**Actions**”) current or pending or, to the knowledge of the Company, threatened Actions to which the Company or any of its subsidiaries is or may be a party or to which any property of the Company or any of its subsidiaries is or may be the subject that, individually or in the aggregate, if determined adversely to the Company or any of its subsidiaries, could reasonably be expected to have a Material Adverse Effect; no such Actions are threatened or, to the knowledge of the Company, contemplated by any governmental or regulatory authority or threatened by others; and (i) there are no current or pending Actions that are required under the Securities Act to be described in the Registration Statement or the Prospectus that are not so described in the Registration Statement and the Prospectus and (ii) there are no statutes, regulations or contracts or other documents that are required under the Securities Act to be filed as exhibits to the Registration Statement or described in the Registration Statement or the Prospectus that are not so filed as exhibits to the Registration Statement or described in the Registration Statement and the Prospectus.

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

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

(t) Intellectual Property. Except as described in the Registration Statement and the Prospectus or as could not reasonably be expected, individually or in the aggregate, to have a Material Adverse Effect, (i) the Company and its subsidiaries own or possess adequate rights to use all patents, trademarks, service marks, trade names, domain names and other source indicators, copyrights and copyrightable works, licenses and know-how, trade secrets and other unpatented and/or unpatentable proprietary or confidential information, systems or procedures, and all other worldwide intellectual property, industrial property and proprietary rights (including all registrations and applications for registration of, and all goodwill associated with, any of the foregoing) (collectively, “**Intellectual Property**”) used or held for use in, or otherwise necessary for, the conduct of their respective businesses as currently conducted and as proposed to be conducted in the Registration Statement and the Prospectus; provided that this clause (i) shall not be construed as a representation or warranty of non-infringement of Intellectual

Property; (ii) the Company and its subsidiaries' conduct of their respective businesses has not conflicted with, infringed, misappropriated or otherwise violated any Intellectual Property rights other than patent rights of any third party and, to knowledge of the Company, the Company and its subsidiaries' conduct of their respective business has not infringed or otherwise violated any patent of any third party (it being understood that the foregoing representation and warranty is made without giving effect to any exemption under applicable law to which the Company may be entitled (e.g., 35 U.S.C. Section 271(e)(1)); (iii) the Company and its subsidiaries have not received any written notice of any claim of infringement, misappropriation or other violation of, or conflict with, any Intellectual Property of any third party, or any written notice challenging the ownership, validity, enforceability or scope of any Intellectual Property of the Company or any of its subsidiaries; (iv) to the knowledge of the Company, the Intellectual Property of the Company and its subsidiaries has not been in conflict with, infringed, misappropriated or otherwise violated by any third party; (v) to the knowledge of the Company, all Intellectual Property of the Company and its subsidiaries is valid and enforceable; and (vi) the Company and its subsidiaries have taken reasonable steps in accordance with normal industry practice to maintain the confidentiality of all Intellectual Property of the Company and its subsidiaries the value of which to the Company or any of its subsidiaries is contingent upon maintaining the confidentiality thereof and no such Intellectual Property has been disclosed other than to employees, representatives and agents of the Company or any of its subsidiaries, all of whom are bound by written confidentiality agreements.

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

(v) Investment Company Act. The Company is not and, after giving effect to the offering and sale of the Placement Shares and the application of the proceeds thereof as described in the Registration Statement and the Prospectus, will not be required to register as an "investment company" or an entity "controlled" by an "investment company" within the meaning of the Investment Company Act of 1940, as amended, and the rules and regulations of the Commission thereunder (collectively, the "**Investment Company Act**").

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

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

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

(z) Certain Environmental Matters. (i) The Company and its subsidiaries (x) are in compliance with all, and have not violated any, applicable federal, state, local and foreign laws (including common law), rules, regulations, requirements, decisions, judgments, decrees, orders and other legally enforceable requirements relating to pollution or the protection of human health or safety, the environment, natural resources, hazardous or toxic substances or wastes, pollutants or contaminants (collectively, "Environmental Laws"); (y) have received and are in compliance with all, and have not violated any, permits, licenses, certificates or other authorizations or approvals required of them under any Environmental Laws to conduct their respective businesses; and (z) have not received notice of any actual or potential liability or obligation under or relating to, or any actual or potential violation of, any Environmental Laws, including for the investigation or remediation of any disposal or release of hazardous or toxic substances or wastes, pollutants or contaminants, and have no knowledge of any event or condition that would reasonably be expected to result in any such notice, and (ii) there are no costs or liabilities associated with Environmental Laws of or relating to the Company or its subsidiaries, except in the case of each of (i) and (ii) above, for any such matter as would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect; and (iii) except as described in the Prospectus, (x) there is no proceeding that is pending, or that is known to be contemplated, against the Company or any of its subsidiaries under any Environmental Laws in which a governmental entity is also a party, other than such proceeding regarding which it is

reasonably believed no monetary sanctions of \$100,000 or more will be imposed, (y) the Company and its subsidiaries are not aware of any facts or issues regarding compliance with Environmental Laws, or liabilities or other obligations under Environmental Laws or concerning hazardous or toxic substances or wastes, pollutants or contaminants, that could reasonably be expected to have a material effect on the capital expenditures, earnings or competitive position of the Company and its subsidiaries, and (z) none of the Company or its subsidiaries anticipates material capital expenditures relating to any Environmental Laws.

(aa) Compliance with ERISA. (i) Each employee benefit plan, within the meaning of Section 3(3) of the Employee Retirement Income Security Act of 1974, as amended ("ERISA"), for which the Company or any member of its "Controlled Group" (defined as any entity, whether or not incorporated, that is under common control with the Company within the meaning of Section 4001(a)(14) of ERISA or any entity that would be regarded as a single employer with the Company under Section 414(b),(c),(m) or (o) of the Internal Revenue Code of 1986, as amended (the "Code")) would have any liability (each, a "Plan") has been maintained in compliance with its terms and the requirements of any applicable statutes, orders, rules and regulations, including but not limited to ERISA and the Code; (ii) no prohibited transaction, within the meaning of Section 406 of ERISA or Section 4975 of the Code, has occurred with respect to any Plan, excluding transactions effected pursuant to a statutory or administrative exemption; (iii) for each Plan that is subject to the funding rules of Section 412 of the Code or Section 302 of ERISA, no Plan has failed (whether or not waived), or is reasonably expected to fail, to satisfy the minimum funding standards (within the meaning of Section 302 of ERISA or Section 412 of the Code) applicable to such Plan; (iv) no Plan is, or is reasonably expected to be, in "at risk status" (within the meaning of Section 303(i) of ERISA) and no Plan that is a "multiemployer plan" within the meaning of Section 4001(a)(3) of ERISA is in "endangered status" or "critical status" (within the meaning of Sections 304 and 305 of ERISA) (v) the fair market value of the assets of each Plan exceeds the present value of all benefits accrued under such Plan (determined based on those assumptions used to fund such Plan); (vi) no "reportable event" (within the meaning of Section 4043(c) of ERISA and the regulations promulgated thereunder) has occurred or is reasonably expected to occur; (vii) each Plan that is intended to be qualified under Section 401(a) of the Code is so qualified, and nothing has occurred, whether by action or by failure to act, which would cause the loss of such qualification; (viii) neither the Company nor any member of the Controlled Group has incurred, nor reasonably expects to incur, any liability under Title IV of ERISA (other than contributions to the Plan or premiums to the Pension Benefit Guarantee Corporation, in the ordinary course and without default) in respect of a Plan (including a "multiemployer plan" within the meaning of Section 4001(a)(3) of ERISA); and (ix) none of the following events has occurred or is reasonably likely to occur: (A) a material increase in the aggregate amount of contributions required to be made to all Plans by the Company or its Controlled Group affiliates in the current fiscal year of the Company and its Controlled Group affiliates compared to the amount of such contributions made in the Company's and its Controlled Group affiliates' most recently completed fiscal

year; or (B) a material increase in the Company and its subsidiaries' "accumulated post-retirement benefit obligations" (within the meaning of Accounting Standards Codification Topic 715-60) compared to the amount of such obligations in the Company and its subsidiaries' most recently completed fiscal year, except in each case with respect to the events or conditions set forth in (i) through (ix) hereof, as would not, individually or in the aggregate, have a Material Adverse Effect.

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

(cc) Accounting Controls. The Company and its subsidiaries maintain systems of "internal control over financial reporting" (as defined in Rule 13a-15(f) of the Exchange Act) that comply with the requirements of the Exchange Act and have been designed by, or under the supervision of, their respective principal executive and principal financial officers, or persons performing similar functions, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with GAAP. The Company and its subsidiaries maintain internal accounting controls sufficient to provide reasonable assurance that (i) transactions are executed in accordance with management's general or specific authorizations; (ii) transactions are recorded as necessary to permit preparation of financial statements in conformity with GAAP and to maintain asset accountability; (iii) access to assets is permitted only in accordance with management's general or specific authorization; (iv) the recorded accountability for assets is compared with the existing assets at reasonable intervals and appropriate action is taken with respect to any differences; and (v) the interactive data in eXtensible Business Reporting Language included or incorporated by reference in the Registration Statement and the Prospectus fairly presents the information called for in all material respects and is prepared in accordance with the Commission's rules and guidelines applicable thereto. Based on the Company's most recent evaluation of its internal controls over financial reporting pursuant to Rule 13a-15(c) of the Exchange Act, except as disclosed in the Registration Statement and the Prospectus, there are no material weaknesses in the Company's internal controls. The Company's auditors and the Audit Committee of the Board of Directors of the Company have been advised of: (i) all significant deficiencies and material weaknesses in the design or operation of internal controls over financial reporting which have adversely affected or are reasonably likely to adversely affect the Company's ability to record, process, summarize and report

financial information; and (ii) any fraud, whether or not material, that involves management or other employees who have a significant role in the Company's internal controls over financial reporting.

(dd) Insurance. The Company and its subsidiaries have insurance covering their respective properties, operations, personnel and businesses, including business interruption insurance, which insurance is in amounts and insures against such losses and risks which the Company believes are adequate to protect the Company and its subsidiaries and their respective businesses; and neither the Company nor any of its subsidiaries has (i) received notice from any insurer or agent of such insurer that capital improvements or other expenditures are required or necessary to be made in order to continue such insurance or (ii) any reason to believe that it will not be able to renew its existing insurance coverage as and when such coverage expires or to obtain similar coverage at reasonable cost from similar insurers as may be necessary to continue its business.

(ee) Cybersecurity. (i)(x) Except as disclosed in the Registration Statement and the Prospectus, to the Company's knowledge, there has been no security breach or other compromise of or relating to any of the Company's or any of its subsidiaries' information technology and computer systems, networks, hardware, software, data (including the data of their respective customers, employees, suppliers, vendors and any third party data maintained by or on behalf of them), equipment or technology (collectively, "**IT Systems and Data**") which could have a Material Adverse Effect and (y) the Company and its subsidiaries have not been notified of, and have no knowledge of any material event or condition that would reasonably be expected to result in, any security breach or other compromise to their IT Systems and Data; (ii) the Company and its subsidiaries are presently in compliance with all applicable laws or statutes and all judgments, orders, rules and regulations of any court or arbitrator or governmental or regulatory authority, internal policies and contractual obligations relating to the privacy and security of IT Systems and Data and to the protection of such IT Systems and Data from unauthorized use, access, misappropriation or modification, except as would not, in the case of this clause (ii), individually or in the aggregate, have a Material Adverse Effect; and (iii) the Company and its subsidiaries have implemented backup and disaster recovery technology consistent with industry standards and practices. Except as would not reasonably be expected to have a Material Adverse Effect, the Company and its subsidiaries are presently in compliance with all applicable laws or statutes and all judgments, orders, rules and regulations of any court or arbitrator or governmental or regulatory authority, including Regulation (EU) 2016/679 (the General Data Protection Regulation), and all internal policies and contractual obligations of the Company relating to the privacy and security of IT Systems and Personal Data and to the protection of such IT Systems and Personal Data from unauthorized use, access, misappropriation or modification.

(ff) No Unlawful Payments. Neither the Company nor any of its subsidiaries nor any director, officer or employee of the Company or any of its subsidiaries nor, to the knowledge of the Company, any agent, affiliate or other

person associated with or acting on behalf of the Company or any of its subsidiaries has (i) used any corporate funds for any unlawful contribution, gift, entertainment or other unlawful expense relating to political activity; (ii) made or taken an act in furtherance of an offer, promise or authorization of any direct or indirect unlawful payment or benefit to any foreign or domestic government official or employee, including of any government-owned or controlled entity or of a public international organization, or any person acting in an official capacity for or on behalf of any of the foregoing, or any political party or party official or candidate for political office; (iii) violated or is in violation of any provision of the Foreign Corrupt Practices Act of 1977, as amended, or any applicable law or regulation implementing the OECD Convention on Combating Bribery of Foreign Public Officials in International Business Transactions, or committed an offence under the Bribery Act 2010 of the United Kingdom or any other applicable anti-bribery or anti-corruption law; or (iv) made, offered, agreed, requested or taken an act in furtherance of any unlawful bribe or other unlawful benefit, including, without limitation, any rebate, payoff, influence payment, kickback or other unlawful or improper payment or benefit. The Company and its subsidiaries have instituted, maintain and enforce, and will continue to maintain and enforce policies and procedures designed to promote and ensure compliance with all applicable anti-bribery and anti-corruption laws.

(gg) Compliance with Anti-Money Laundering Laws. The operations of the Company and its subsidiaries are and have been conducted at all times in compliance with applicable financial recordkeeping and reporting requirements, including, where applicable, those of the Currency and Foreign Transactions Reporting Act of 1970, as amended, the applicable money laundering statutes of all jurisdictions where the Company or any of its subsidiaries conducts business, the rules and regulations thereunder and any related or similar rules, regulations or guidelines issued, administered or enforced by any governmental agency (collectively, the “**Anti-Money Laundering Laws**”) and no action, suit or proceeding by or before any court or governmental agency, authority or body or any arbitrator involving the Company or any of its subsidiaries with respect to the Anti-Money Laundering Laws is pending or, to the knowledge of the Company, threatened.

(hh) No Conflicts with Sanctions Laws. Neither the Company nor any of its subsidiaries, directors, officers, or employees, nor, to the knowledge of the Company, any agent, affiliate or other person associated with or acting on behalf of the Company or any of its subsidiaries is currently the subject or the target of any sanctions administered or enforced by the U.S. government, (including, without limitation, the Office of Foreign Assets Control of the U.S. Department of the Treasury (“**OFAC**”) or the U.S. Department of State and including, without limitation, the designation as a “specially designated national” or “blocked person”), the United Nations Security Council (“**UNSC**”), the European Union, Her Majesty’s Treasury (“**HMT**”) or other relevant sanctions authority (collectively, “**Sanctions**”), nor is the Company or any of its subsidiaries located, organized or resident in a country or territory that is the subject or target of Sanctions, including, without limitation, Crimea, Cuba, Iran, North Korea, Sudan and Syria (each, a “**Sanctioned**”).

Country”); and the Company will not directly or indirectly use the proceeds of the offering of the Placement Shares hereunder, or lend, contribute or otherwise make available such proceeds to any subsidiary, joint venture partner or other person or entity (i) to fund or facilitate any activities of or business with any person that, at the time of such funding or facilitation, is the subject or target of Sanctions, (ii) to fund or facilitate any activities of or business in any Sanctioned Country or (iii) in any other manner that will result in a violation by any person (including any person participating in the transaction, whether as underwriter, advisor, investor or otherwise) of Sanctions. Since the Company’s inception, the Company and its subsidiaries have not knowingly engaged in and are not now knowingly engaged in any dealings or transactions with any person that at the time of the dealing or transaction is or was the subject or the target of Sanctions or with any Sanctioned Country.

(ii) **No Restrictions on Subsidiaries.** No subsidiary of the Company is currently prohibited, directly or indirectly, under any agreement or other instrument to which it is a party or is subject, from paying any dividends to the Company, from making any other distribution on such subsidiary’s capital stock or similar ownership interest, from repaying to the Company any loans or advances to such subsidiary from the Company or from transferring any of such subsidiary’s properties or assets to the Company or any other subsidiary of the Company.

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

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

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

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

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

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

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

(qq) Status under the Securities Act. At the time of filing the Registration Statement and any post-effective amendment thereto, at the earliest time thereafter that the Company or any offering participant made a *bona fide* offer (within the meaning of Rule 164(h)(2) under the Securities Act) of the Placement Shares and at the date hereof, the Company was not and is not an "ineligible issuer," as defined in Rule 405 under the Securities Act. The Company agrees to notify Cowen promptly upon the Company becoming an "ineligible issuer."

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

(ss) Preclinical Studies and Clinical Trials. (i) Except as described in the Registration Statement and the Prospectus, the preclinical studies and clinical trials conducted by or, to the knowledge of the Company, on behalf of or sponsored by the Company or its subsidiaries, or in which the Company or its subsidiaries have participated, that are described in the Registration Statement and the Prospectus, or the results of which are referred to in the Registration Statement and the Prospectus, as applicable, were, and if still pending are, being conducted in all material respects in accordance with all applicable statutes and all applicable rules and regulations of the applicable regulatory agencies to which they are subject, including the U.S. Food and Drug Administration and the European Medicines Agency (collectively, the "Regulatory Authorities") and Good Clinical Practice and Good Laboratory Practice requirements; (ii) the descriptions in the Registration Statement and the Prospectus of the results of such studies and trials are accurate and complete descriptions in all material respects and fairly present the data derived therefrom as of the dates given for such data in the Registration Statement; (iii) the Company has no knowledge of any other studies or trials conducted by or on behalf of the Company not described in the Registration Statement and the Prospectus, the results of which are inconsistent with or call into question the results described or referred to in the Registration Statement and the Prospectus; (iv) the Company and its

subsidiaries have operated at all times and are currently in compliance in all respects with all applicable statutes, rules and regulations of the Regulatory Authorities, except that where such non-compliance would not, individually or in the aggregate, have a Material Adverse Effect; (v) the Company has provided Cowen with all substantive written notices, correspondence and summaries of all other communications from the Regulatory Authorities; and (vi) neither the Company nor any of its subsidiaries have received any written notices, correspondence or other communications from the Regulatory Authorities or any other governmental agency requiring or threatening the termination, material modification or suspension of any preclinical studies or clinical trials that are described in the Registration Statement and the Prospectus or the results of which are referred to in the Registration Statement and the Prospectus, other than ordinary course communications with respect to modifications in connection with the design and implementation of such studies or trials, and, to the Company's knowledge, there are no reasonable grounds for the same.

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

(uu) Stamp Taxes. Except as described in the Registration Statement or the Prospectus and except for any net income, or franchise taxes imposed on Cowen by the United Kingdom or any political subdivision or taxing authority thereof or therein as a result of any present or former connection (other than any connection resulting from the transactions contemplated by this Agreement) between Cowen and the jurisdiction imposing such tax, no stamp duty, stamp duty reserve tax, documentary, issuance, transfer, capital, registration or other similar taxes or duties are payable by or on behalf of Cowen in the United Kingdom or the United States (including taxes or duties imposed by any political subdivision or taxing authority thereof) in connection with (A) the execution and delivery, performance or enforcement of this Agreement, (B) the issuance, allotment and delivery of the Placement Shares in the manner contemplated by this Agreement and the Prospectus, or (C) the sale and delivery by Cowen of the Placement Shares as contemplated herein and in the Prospectus.

(vv) No Immunity. Neither the Company nor any of its subsidiaries or their properties or assets has immunity under English, U.S. federal or New York state law from any legal action, suit or proceeding, from the giving of any relief in any such legal action, suit or proceeding, from set-off or counterclaim, from the jurisdiction of any English, U.S. federal or New York state court, from service of process, attachment upon or prior to judgment, or attachment in aid of execution of

judgment, or from execution of a judgment, or other legal process or proceeding for the giving of any relief or for the enforcement of a judgment, in any such court with respect to their respective obligations, liabilities or any other matter under or arising out of or in connection herewith; and, to the extent that the Company or any of its subsidiaries or any of its properties, assets or revenues may have or may hereafter become entitled to any such right of immunity in any such court in which proceedings arising out of, or relating to the transactions contemplated by the Transaction Documents, may at any time be commenced, the Company has, pursuant to Section 16 of this Agreement, waived, and it will waive, or will cause its subsidiaries to waive, such right to the extent permitted by law.

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

(xx) Valid Choice of Law. The choice of laws of the State of New York as the governing law of the Transaction Documents is a valid choice of law under the laws of England and Wales and will be honored by the courts of England and Wales, subject to the restrictions described under the caption "Service of process and enforcement of liabilities" in the Registration Statement and the Prospectus. The Company has the power to submit, and pursuant to Section 16(b) of this Agreement, has legally, validly, effectively and irrevocably submitted, to the personal jurisdiction of each New York state and United States federal court sitting in the City of New York and has validly and irrevocably waived any objection to the laying of venue of any suit, action or proceeding brought in such court.

(yy) Indemnification and Contribution. The indemnification and contribution provisions set forth in Section 9 hereof do not contravene English law or public policy.

(zz) Passive Foreign Investment Company. Subject to the qualifications, limitations, exceptions and assumptions set forth in the Registration Statement and the Prospectus, the Company does not expect it was treated as, for the taxable year ending December 31, 2019, a passive foreign investment company as defined in Section 1297 of the Code.

(aaa) Dividends. Except as disclosed in the Registration Statement and the Prospectus, no approvals are currently required in the United Kingdom in order for the Company to pay dividends or other distributions declared by the Company to the holders of Ordinary Shares. Under current laws and regulations of the United Kingdom and any political subdivision thereof, any amount payable with respect to the Ordinary Shares upon liquidation of the Company or upon redemption thereof and dividends and other distributions declared and payable on the share capital of the Company may be paid by the Company in United States dollars or euros and freely transferred out of the United Kingdom, and no such payments made to the

holders thereof or therein who are non-residents of the United Kingdom will be subject to income, withholding or other taxes under laws and regulations of the United Kingdom or any political subdivision or taxing authority thereof or therein and without the necessity of obtaining any governmental authorization in the United Kingdom or any political subdivision or taxing authority thereof or therein.

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

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

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

(eee) Well-Known Seasoned Issuer. (A) At the time of filing the Registration Statement, (B) at the time of the most recent amendment thereto for the purposes of complying with Section 10(a)(3) of the Securities Act (whether such amendment was by post-effective amendment or incorporated report filed pursuant to Section 13 or 15(d) of the Exchange Act or in the form of a prospectus), (C) at the time the Company or any person acting on its behalf (within the meaning, for this clause only, of Rule 163(c) under the Securities Act) made any offer relating to the Placement Shares in reliance on the exemption of Rule 163 under the Securities Act, and (D) as of the Applicable Time, the Company was and is a "well-known seasoned issuer" (as defined in Rule 405).

Any certificate signed by an officer of the Company and delivered to Cowen or to counsel for Cowen shall be deemed to be a representation and warranty by the Company to Cowen as to the matters set forth therein.

The Company acknowledges that Cowen and, for purposes of the opinions to be delivered pursuant to Section 7 hereof, counsel to the Company and counsel to Cowen, will rely upon the accuracy and truthfulness of the foregoing representations and hereby consents to such reliance.

7. Covenants of the Company. The Company covenants and agrees with Cowen that:

(a) Registration Statement Amendments. After the date of this Agreement and during any period in which a Prospectus relating to any Placement Shares is required to be delivered by Cowen under the Securities Act (including in circumstances where such requirement may be satisfied pursuant to Rule 172 under the Securities Act or similar rule), (i) the Company will notify Cowen promptly of the time when any subsequent amendment to the Registration Statement, other than documents incorporated by reference, has been filed with the Commission and/or has become effective or any subsequent supplement to the Prospectus has been filed and of any request by the Commission for any amendment or supplement to the Registration Statement or Prospectus or for additional information, (ii) the Company will prepare and file with the Commission, promptly upon Cowen's request, any amendments or supplements to the Registration Statement or Prospectus that, in Cowen's reasonable opinion, may be necessary or advisable in connection with the distribution of the Placement Shares by Cowen (*provided, however*, that the failure of Cowen to make such request shall not relieve the Company of any obligation or liability hereunder, or affect Cowen's right to rely on the representations and warranties made by the Company in this Agreement); (iii) the Company will not file any amendment or supplement to the Registration Statement or Prospectus, other than documents incorporated by reference, relating to the Placement Shares or a security convertible into the Placement Shares unless a copy thereof has been submitted to Cowen within a reasonable period of time before the filing and Cowen has not reasonably objected thereto (*provided, however*, that the failure of Cowen to make such objection shall not relieve the Company of any obligation or liability hereunder, or affect Cowen's right to rely on the representations and warranties made by the Company in this Agreement) and the Company will furnish to Cowen at the time of filing thereof a copy of any document that upon filing is deemed to be incorporated by reference into the Registration Statement or Prospectus, except for those documents available via EDGAR; (iv) the Company will cause each amendment or supplement to the Prospectus, other than documents incorporated by reference, to be filed with the Commission as required pursuant to the applicable paragraph of Rule 424(b) of the Securities Act, and (v) prior to the termination of this Agreement, the Company will notify Cowen if at any time the Registration Statement shall no longer be effective as a result of the passage of time pursuant to Rule 415 under the Securities Act or otherwise.

(b) Notice of Commission Stop Orders. The Company will advise Cowen, promptly after it receives notice or obtains knowledge thereof, of the issuance or threatened issuance by the Commission of any stop order suspending the effectiveness of the Registration Statement, of the suspension of the qualification of the Placement Shares for offering or sale in any jurisdiction, or of the initiation or threatening of any proceeding for any such purpose; and it will promptly use its commercially reasonable efforts to prevent the issuance of any stop order or to obtain its withdrawal if such a stop order should be issued.

(c) Delivery of Prospectus; Subsequent Changes. During any period in which a Prospectus relating to the Placement Shares is required to be delivered by Cowen under the Securities Act with respect to a pending sale of the Placement Shares, (including in circumstances where such requirement may be satisfied pursuant to Rule 172 or similar rule under the Securities Act), the Company will comply with all requirements imposed upon it by the Securities Act, as from time to time in force, and to file on or before their respective due dates all reports and any definitive proxy or information statements required to be filed by the Company with the Commission pursuant to Sections 13(a), 13(c), 14, 15(d) or any other provision of or under the Exchange Act. If during such period any event occurs as a result of which the Prospectus as then amended or supplemented would include an untrue statement of a material fact or omit to state a material fact necessary to make the statements therein, in the light of the circumstances then existing, not misleading, or if during such period it is necessary to amend or supplement the Registration Statement or Prospectus to comply with the Securities Act, the Company will promptly notify Cowen to suspend the offering of Placement Shares during such period and the Company will promptly amend or supplement the Registration Statement or Prospectus (at the expense of the Company) so as to correct such statement or omission or effect such compliance; *provided, however*, that the Company may delay the filing of any amendment or supplement if, in the reasonable judgment of the Company, it is in the best interest of the Company to do so.

(d) Listing of Placement Shares. During any period in which the Prospectus relating to the Placement Shares is required to be delivered by Cowen under the Securities Act with respect to a pending sale of the Placement Shares (including in circumstances where such requirement may be satisfied pursuant to Rule 172 under the Securities Act or similar rule), the Company will use its commercially reasonable efforts to cause the Placement Shares to be listed on Nasdaq and to qualify the Placement Shares for sale under the securities laws of such jurisdictions as Cowen reasonably designates and to continue such qualifications in effect so long as required for the distribution of the Placement Shares; *provided, however*, that the Company shall not be required in connection therewith to qualify as a foreign corporation or dealer in securities or file a general consent to service of process in any jurisdiction.

(e) Delivery of Registration Statement and Prospectus. The Company will furnish to Cowen and its counsel (at the expense of the Company) copies of the Registration Statement, the Prospectus (including all documents incorporated by reference therein) and all amendments and supplements to the Registration Statement or Prospectus that are filed with the Commission during any period in which a Prospectus relating to the Placement Shares is required to be delivered under the Securities Act (including all documents filed with the Commission during such period that are deemed to be incorporated by reference therein), in each case as soon as reasonably practicable and in such quantities as Cowen may from time to time reasonably request and, at Cowen's reasonable request, will also furnish copies of the Prospectus to each exchange or market on which sales of the Placement Shares may be made; *provided, however*, that the Company shall not be required to furnish any document (other than the Prospectus) to Cowen to the extent such document is available on EDGAR.

(f) Earnings Statement. The Company will make generally available to its security holders as soon as practicable, but in any event not later than 15 months after the end of the Company's current fiscal quarter, an earnings statement covering a 12-month period that satisfies the provisions of Section 11(a) and Rule 158 of the Securities Act.

(g) Expenses. The Company, whether or not the transactions contemplated hereunder are consummated or this Agreement is terminated, in accordance with the provisions of Section 11 hereunder, will pay the following expenses all incident to the performance of its obligations hereunder, including, but not limited to, expenses relating to (i) the preparation, printing and filing of the Registration Statement and each amendment and supplement thereto, of each Prospectus and of each amendment and supplement thereto, (ii) the preparation, issuance and delivery of the Placement Shares, (iii) the qualification of the Placement Shares under securities laws in accordance with the provisions of Section 7(d) of this Agreement, including filing fees (provided, however, that any fees or disbursements of counsel for Cowen in connection therewith shall be paid by Cowen except as set forth in (vii) below), (iv) the printing and delivery to Cowen of copies of the Prospectus and any amendments or supplements thereto, and of this Agreement, (v) the fees and expenses incurred in connection with the listing or qualification of the Placement Shares for trading on Nasdaq, (vi) the filing fees and expenses, if any, of the Commission, (vii) the filing fees and associated legal expenses of Cowen's outside counsel for filings with the FINRA Corporate Financing Department, such legal expense reimbursement not to exceed \$15,000 and, (viii) the reasonable fees and disbursements of Cowen's counsel in an amount not to exceed \$50,000.

(h) Use of Proceeds. The Company will use the Net Proceeds as described in the Prospectus in the section entitled "Use of Proceeds."

(i) Notice of Other Sales. During the pendency of any Placement Notice given hereunder, and for 5 trading days following the termination of any Placement Notice given hereunder, the Company shall provide Cowen notice as promptly as reasonably possible before it offers to sell, contracts to sell, sells, grants any option to sell or otherwise disposes of any Ordinary Shares or ADSs (other than Placement Shares offered pursuant to the provisions of this Agreement) or securities convertible into or exchangeable for Ordinary Shares or ADSs, warrants or any rights to purchase or acquire Ordinary Shares or ADSs; *provided*, that such notice shall not be required in connection with the (i) issuance, grant or sale of Ordinary Shares or ADSs, options to purchase shares of Ordinary Shares or ADSs or Ordinary Shares or ADSs issuable upon the exercise of options or other equity awards pursuant to any share option, share bonus or other share plan, certain other agreements or arrangement described in the Prospectus or otherwise publicly disclosed, (ii) the issuance of securities in connection with an acquisition, merger or sale or purchase of assets or (iii) the issuance or sale of Ordinary Shares or ADSs

pursuant to any dividend reinvestment plan that the Company may adopt from time to time provided the implementation of such is disclosed to Cowen in advance or (iv) any Ordinary Shares or ADSs issuable upon the exchange, conversion or redemption of securities or the exercise of warrants, options or other rights in effect or outstanding.

(j) Change of Circumstances. The Company will, at any time during a fiscal quarter in which the Company intends to tender a Placement Notice or sell Placement Shares, advise Cowen promptly after it shall have received notice or obtained knowledge thereof, of any information or fact that would alter or affect in any material respect any opinion, certificate, letter or other document provided to Cowen pursuant to this Agreement.

(k) Due Diligence Cooperation. The Company will cooperate with any reasonable due diligence review conducted by Cowen or its agents in connection with the transactions contemplated hereby, including, without limitation, providing information and making available documents and senior corporate officers, during regular business hours and at the Company's principal offices, as Cowen may reasonably request.

(l) Required Filings Relating to Placement of Placement Shares. The Company agrees that on such dates as the Securities Act shall require, the Company will (i) file a prospectus supplement with the Commission under the applicable paragraph of Rule 424(b) under the Securities Act (each and every filing under Rule 424(b), a "**Filing Date**"), which prospectus supplement will set forth, within the relevant period, the amount of Placement Shares sold through Cowen, the Net Proceeds to the Company and the compensation payable by the Company to Cowen with respect to such Placement Shares (provided that the Company may satisfy its obligations under this Section 7(l) (i) by effecting a filing in accordance with the Exchange Act with respect to such information), and (ii) deliver such number of copies of each such prospectus supplement to each exchange or market on which such sales were effected as may be required by the rules or regulations of such exchange or market.

(m) Representation Dates; Certificate. On or prior to the First Delivery Date and each time the Company (i) files the Prospectus relating to the Placement Shares or amends or supplements the Registration Statement or the Prospectus relating to the Placement Shares (other than a prospectus supplement filed in accordance with Section 7(l) of this Agreement) by means of a post-effective amendment, sticker, or supplement but not by means of incorporation of document(s) by reference to the Registration Statement or the Prospectus relating to the Placement Shares; (ii) files an annual report on Form 10-K under the Exchange Act; (iii) files its quarterly reports on Form 10-Q under the Exchange Act; or (iv) files a report on Form 8-K containing amended financial information (other than an earnings release) under the Exchange Act (each date of filing of one or more of the documents referred to in clauses (i) through (iv) shall be a "**Representation Date**"); the Company shall furnish Cowen with a certificate, in the form attached hereto as Exhibit 7(m) within three (3) Trading Days of any Representation Date if requested

by Cowen. The requirement to provide a certificate under this Section 7(m) shall be waived for any Representation Date occurring at a time at which no Placement Notice is pending, which waiver shall continue until the earlier to occur of the date the Company delivers a Placement Notice hereunder (which for such calendar quarter shall be considered a Representation Date) and the next occurring Representation Date; *provided, however*, that such waiver shall not apply for any Representation Date on which the Company files its annual report on Form 10-K. Notwithstanding the foregoing, if the Company subsequently decides to sell Placement Shares following a Representation Date when the Company relied on such waiver and did not provide Cowen with a certificate under this Section 7(m), then before the Company delivers the Placement Notice or Cowen sells any Placement Shares, the Company shall provide Cowen with a certificate, in the form attached hereto as Exhibit 7(m), dated the date of the Placement Notice.

(n) Legal Opinion. On or prior to the First Delivery Date and within three (3) Trading Days of each Representation Date with respect to which the Company is obligated to deliver a certificate in the form attached hereto as Exhibit 7(m) for which no waiver is applicable, the Company shall cause to be furnished to Cowen a written opinion of Goodwin Procter LLP, U.S. counsel to the company (“**Goodwin**”), or other counsel satisfactory to Cowen, in form and substance satisfactory to Cowen and its counsel, dated the date that the opinions are required to be delivered, in form and substance reasonably satisfactory to Cowen and its counsel, respectively, modified, as necessary, to relate to the Registration Statement and the Prospectus as then amended or supplemented. On or prior to the First Delivery Date and within three (3) Trading Days of each Representation Date with respect to which the Company is obligated to deliver a certificate in the form attached hereto as Exhibit 7(m) for which no waiver is applicable, the Company shall cause to be furnished to Cowen the written opinion of Goodwin Procter (UK) LLP, UK counsel to the company (collectively with Goodwin “**Company Counsel**”); *provided, however*, that in lieu of such opinions for subsequent Representation Dates, counsel may furnish Cowen with a letter (a “**Reliance Letter**”) to the effect that Cowen may rely on a prior opinion delivered under this Section 7(n) to the same extent as if it were dated the date of such letter (except that statements in such prior opinion shall be deemed to relate to the Registration Statement and the Prospectus as amended or supplemented at such Representation Date).

(o) Intellectual Property Opinion. On or prior to the First Delivery Date and within three (3) Trading Days of each Representation Date with respect to which the Company is obligated to deliver a certificate in the form attached hereto as Exhibit 7(m) for which no waiver is applicable, the Company shall cause to be furnished to Cowen a written opinion of Clark & Elbing LLP (collectively, the “**Company IP Counsel**”), or other counsel satisfactory to Cowen, in form and substance reasonably satisfactory to Cowen and its counsel, dated the date that the opinion is required to be delivered, with respect to intellectual property matters, modified, as necessary, to relate to the Registration Statement and the Prospectus as then amended or supplemented; *provided, however*, that in lieu of such opinions for

subsequent Representation Dates, counsel may furnish Cowen with a letter (a “**Reliance Letter**”) to the effect that Cowen may rely on a prior opinion delivered under this Section 7(o) to the same extent as if it were dated the date of such letter (except that statements in such prior opinion shall be deemed to relate to the Registration Statement and the Prospectus as amended or supplemented at such Representation Date).

(p) Comfort Letters. On or prior to the First Delivery Date and within three (3) Trading Days of each Representation Date with respect to which the Company is obligated to deliver a certificate in the form attached hereto as Exhibit 7(m) for which no waiver is applicable, the Company shall cause its independent accountants to furnish Cowen letters (the “**Comfort Letters**”), dated the date the Comfort Letter is delivered, in form and substance satisfactory to Cowen, (i) confirming that they are an independent registered public accounting firm within the meaning of the Securities Act and the PCAOB, (ii) stating, as of such date, the conclusions and findings of such firm with respect to the financial information and other matters ordinarily covered by accountants’ “comfort letters” to Cowen in connection with registered public offerings (the first such letter, the “**Initial Comfort Letter**”) and (iii) updating the Initial Comfort Letter with any information that would have been included in the Initial Comfort Letter had it been given on such date and modified as necessary to relate to the Registration Statement and the Prospectus, as amended and supplemented to the date of such letter.

(q) Market Activities. The Company will not, directly or indirectly, (i) take any action designed to cause or result in, or that constitutes or might reasonably be expected to constitute, the stabilization or manipulation of the price of any security of the Company to facilitate the sale or resale of the Placement Shares or (ii) sell, bid for, or purchase the Ordinary Shares or ADSs to be issued and sold pursuant to this Agreement, or pay anyone any compensation for soliciting purchases of the Placement Shares other than Cowen; provided, however, that the Company may bid for and purchase shares of its Ordinary Shares or ADSs in accordance with Rule 10b-18 under the Exchange Act.

(r) Insurance. The Company and its subsidiaries shall maintain, or cause to be maintained, insurance in such amounts and covering such risks as is reasonable and customary for the business for which it is engaged.

(s) Compliance with Laws. The Company and each of its subsidiaries shall maintain, or cause to be maintained, all material environmental permits, licenses and other authorizations required by federal, state and local law in order to conduct their businesses as described in the Prospectus, and the Company and each of its subsidiaries shall conduct their businesses, or cause their businesses to be conducted, in substantial compliance with such permits, licenses and authorizations and with applicable environmental laws, except where the failure to maintain or be in compliance with such permits, licenses and authorizations could not reasonably be expected to result in a Material Adverse Effect.

(t) Investment Company Act. The Company will conduct its affairs in such a manner so as to reasonably ensure that neither it nor its subsidiaries will be or become, at any time prior to the termination of this Agreement, an “investment company,” as such term is defined in the Investment Company Act, assuming no change in the Commission’s current interpretation as to entities that are not considered an investment company.

(u) Securities Act and Exchange Act. The Company will use its best efforts to comply with all requirements imposed upon it by the Securities Act and the Exchange Act as from time to time in force, so far as necessary to permit the continuance of sales of, or dealings in, the Placement Shares as contemplated by the provisions hereof and the Prospectus.

(v) No Offer to Sell. Other than a free writing prospectus (as defined in Rule 405 under the Securities Act) approved in advance by the Company and Cowen in its capacity as principal or agent hereunder, neither Cowen nor the Company (including its agents and representatives, other than Cowen in its capacity as such) will make, use, prepare, authorize, approve or refer to any written communication (as defined in Rule 405 under the Securities Act), required to be filed with the Commission, that constitutes an offer to sell or solicitation of an offer to buy Placement Shares hereunder.

(w) Sarbanes-Oxley Act. The Company and its subsidiaries will use their best efforts to comply with all effective applicable provisions of the Sarbanes-Oxley Act.

8. Conditions to Cowen’s Obligations. The obligations of Cowen hereunder with respect to a Placement will be subject to the continuing accuracy and completeness of the representations and warranties made by the Company herein, to the due performance by the Company of its obligations hereunder, to the completion by Cowen of a due diligence review satisfactory to Cowen in its reasonable judgment, and to the continuing satisfaction (or waiver by Cowen in its sole discretion) of the following additional conditions:

(a) Registration Statement Effective. The Registration Statement and the F-6 Registration Statement shall be effective and shall be available for (i) all sales of Placement Shares issued pursuant to all prior Placement Notices and (ii) the sale of all Placement Shares contemplated to be issued by any Placement Notice.

(b) No Material Notices. None of the following events shall have occurred and be continuing: (i) receipt by the Company or any of its subsidiaries of any request for additional information from the Commission or any other federal or state governmental authority during the period of effectiveness of the Registration Statement or the F-6 Registration Statement, the response to which would require any post-effective amendments or supplements to the Registration Statement, the F-6 Registration Statement or the Prospectus; (ii) the issuance by the Commission or any other federal or state governmental authority of any stop order suspending the effectiveness of the Registration Statement or the F-6 Registration Statement or the initiation of any proceedings for that purpose; (iii) receipt by the Company of any

notification with respect to the suspension of the qualification or exemption from qualification of any of the Placement Shares for sale in any jurisdiction or the initiation or threatening of any proceeding for such purpose; or (iv) the occurrence of any event that makes any material statement made in the Registration Statement, the F-6 Registration Statement or the Prospectus or any material document incorporated or deemed to be incorporated therein by reference untrue in any material respect or that requires the making of any changes in the Registration Statement, the F-6 Registration Statement, related Prospectus or such documents so that, in the case of the Registration Statement or the F-6 Registration Statement, it will not contain any materially untrue statement of a material fact or omit to state any material fact required to be stated therein or necessary to make the statements therein not misleading and, that in the case of the Prospectus, it will not contain any materially untrue statement of a material fact or omit to state any material fact required to be stated therein or necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading.

(c) No Misstatement or Material Omission. Cowen shall not have advised the Company that the Registration Statement, the F-6 Registration Statement or Prospectus, or any amendment or supplement thereto, contains an untrue statement of fact that in Cowen's reasonable opinion is material, or omits to state a fact that in Cowen's opinion is material and is required to be stated therein or is necessary to make the statements therein not misleading.

(d) Material Changes. Except as contemplated in the Prospectus, or disclosed in the Company's reports filed with the Commission, there shall not have been any material adverse change, on a consolidated basis, in the authorized share capital of the Company or any Material Adverse Effect or any development that could reasonably be expected to result in a Material Adverse Effect, or any downgrading in or withdrawal of the rating assigned to any of the Company's securities (other than asset backed securities) by any rating organization or a public announcement by any rating organization that it has under surveillance or review its rating of any of the Company's securities (other than asset backed securities), the effect of which, in the case of any such action by a rating organization described above, in the reasonable judgment of Cowen (without relieving the Company of any obligation or liability it may otherwise have), is so material as to make it impracticable or inadvisable to proceed with the offering of the Placement Shares on the terms and in the manner contemplated in the Prospectus.

(e) Company Counsel Legal Opinions. Cowen shall have received the opinions of Company Counsel and Company IP Counsel required to be delivered pursuant to Section 7(n) and Section 7(o) on or before the date on which such delivery of such opinion is required pursuant to Section 7(n) and Section 7(o).

(f) Cowen Counsel Legal Opinion. Cowen shall have received from Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., counsel for Cowen, such opinion or opinions, on or before the date on which the delivery of the Company Counsel and Company IP Counsel legal opinions are required pursuant to Section 7(n) and Section 7(o), with respect to such matters as Cowen may reasonably require, and the Company shall have furnished to such counsel such documents as they request for enabling them to pass upon such matters.

(g) Comfort Letters. Cowen shall have received the Comfort Letters required to be delivered pursuant to Section 7(p) on or before the date on which such delivery of such Comfort Letters are required pursuant to Section 7(p).

(h) Representation Certificate. Cowen shall have received the certificate required to be delivered pursuant to Section 7(m) on or before the date on which delivery of such certificate is required pursuant to Section 7(m).

(i) Secretary's Certificate. On or prior to the First Delivery Date, Cowen shall have received a certificate, signed on behalf of the Company by its corporate Secretary, in form and substance satisfactory to Cowen and its counsel.

(j) No Suspension. Trading in the ADSs shall not have been suspended on Nasdaq.

(k) Other Materials. On each date on which the Company is required to deliver a certificate pursuant to Section 7(m), the Company shall have furnished to Cowen such appropriate further information, certificates and documents as Cowen may have reasonably requested. All such opinions, certificates, letters and other documents shall have been in compliance with the provisions hereof. The Company will furnish Cowen with such conformed copies of such opinions, certificates, letters and other documents as Cowen shall have reasonably requested.

(l) Securities Act Filings Made. All filings with the Commission required by Rule 424 under the Securities Act to have been filed prior to the issuance of any Placement Notice hereunder shall have been made within the applicable time period prescribed for such filing by Rule 424.

(m) Approval for Listing. The Placement Shares shall either have been (i) approved for listing on Nasdaq, subject only to notice of issuance, or (ii) the Company shall have filed an application for listing of the Placement Shares on Nasdaq at, or prior to, the issuance of any Placement Notice.

(n) No Termination Event. There shall not have occurred any event that would permit Cowen to terminate this Agreement pursuant to Section 11(a).

9. Indemnification and Contribution.

(a) Company Indemnification. The Company agrees to indemnify and hold harmless Cowen, the directors, officers, partners, employees and agents of Cowen and each person, if any, who (i) controls Cowen within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act, or (ii) is controlled by or is under common control with Cowen from and against any and all losses, claims, liabilities, expenses and damages (including, but not limited to, any and all reasonable investigative, legal and other expenses incurred in connection

with, and any and all amounts paid in settlement (in accordance with Section 9(c)) of, any action, suit or proceeding between any of the indemnified parties and any indemnifying parties or between any indemnified party and any third party, or otherwise, or any claim asserted), as and when incurred, to which Cowen, or any such person, may become subject under the Securities Act, the Exchange Act or other federal or state statutory law or regulation, at common law or otherwise, insofar as such losses, claims, liabilities, expenses or damages arise out of or are based, directly or indirectly, on (x) any untrue statement or alleged untrue statement of a material fact contained in the Registration Statement, the F-6 Registration Statement or the Prospectus or any amendment or supplement to the Registration Statement, the F-6 Registration Statement or the Prospectus or in any free writing prospectus or in any application or other document executed by or on behalf of the Company or based on written information furnished by or on behalf of the Company filed in any jurisdiction in order to qualify the Placement Shares under the securities laws thereof or filed with the Commission or (y) the omission or alleged omission to state in any such document a material fact required to be stated in it or necessary to make the statements in it not misleading; provided, however, that this indemnity agreement shall not apply to the extent that such loss, claim, liability, expense or damage arises from the sale of the Placement Shares pursuant to this Agreement and is caused directly or indirectly by an untrue statement or omission made in reliance upon and in conformity with the Agent's Information. This indemnity agreement will be in addition to any liability that the Company might otherwise have.

(b) Cowen Indemnification. Cowen agrees to indemnify and hold harmless the Company and its directors and each officer of the Company that signed the Registration Statement and the F-6 Registration Statement, and each person, if any, who (i) controls the Company within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act or (ii) is controlled by or is under common control with the Company against any and all loss, liability, claim, damage and expense described in the indemnity contained in Section 9(a), as incurred, but only with respect to untrue statements or omissions, or alleged untrue statements or omissions, made in the Registration Statement or the F-6 Registration Statement (or any amendments thereto) or the Prospectus (or any amendment or supplement thereto) in reliance upon and in conformity with the Agent's Information.

(c) Procedure. Any party that proposes to assert the right to be indemnified under this Section 9 will, promptly after receipt of notice of commencement of any action against such party in respect of which a claim is to be made against an indemnifying party or parties under this Section 9, notify each such indemnifying party of the commencement of such action, enclosing a copy of all papers served, but the omission so to notify such indemnifying party will not relieve the indemnifying party from (i) any liability that it might have to any indemnified party otherwise than under this Section 9 and (ii) any liability that it may have to any indemnified party under the foregoing provision of this Section 9 unless, and only to the extent that, such omission results in the forfeiture of substantive rights or defenses by the indemnifying party. If any such action is brought against any indemnified party and it notifies the indemnifying party of its commencement, the

indemnifying party will be entitled to participate in and, to the extent that it elects by delivering written notice to the indemnified party promptly after receiving notice of the commencement of the action from the indemnified party, jointly with any other indemnifying party similarly notified, to assume the defense of the action, with counsel reasonably satisfactory to the indemnified party, and after notice from the indemnifying party to the indemnified party of its election to assume the defense, the indemnifying party will not be liable to the indemnified party for any legal or other expenses except as provided below and except for the reasonable costs of investigation subsequently incurred by the indemnified party in connection with the defense. The indemnified party will have the right to employ its own counsel in any such action, but the fees, expenses and other charges of such counsel will be at the expense of such indemnified party unless (1) the employment of counsel by the indemnified party has been authorized in writing by the indemnifying party, (2) the indemnified party has reasonably concluded (based on advice of counsel) that there may be legal defenses available to it or other indemnified parties that are different from or in addition to those available to the indemnifying party, (3) a conflict or potential conflict exists (based on advice of counsel to the indemnified party) between the indemnified party and the indemnifying party (in which case the indemnifying party will not have the right to direct the defense of such action on behalf of the indemnified party) or (4) the indemnifying party has not in fact employed counsel to assume the defense of such action within a reasonable time after receiving notice of the commencement of the action, in each of which cases the reasonable fees, disbursements and other charges of counsel will be at the expense of the indemnifying party or parties. It is understood that the indemnifying party or parties shall not, in connection with any proceeding or related proceedings in the same jurisdiction, be liable for the reasonable fees, disbursements and other charges of more than one separate firm admitted to practice in such jurisdiction at any one time for all such indemnified party or parties. All such fees, disbursements and other charges will be reimbursed by the indemnifying party promptly as they are incurred. An indemnifying party will not, in any event, be liable for any settlement of any action or claim effected without its written consent. No indemnifying party shall, without the prior written consent of each indemnified party, settle or compromise or consent to the entry of any judgment in any pending or threatened claim, action or proceeding relating to the matters contemplated by this Section 9 (whether or not any indemnified party is a party thereto), unless such settlement, compromise or consent includes an unconditional release of each indemnified party from all liability arising or that may arise out of such claim, action or proceeding.

(d) Contribution. In order to provide for just and equitable contribution in circumstances in which the indemnification provided for in the foregoing paragraphs of this Section 9 is applicable in accordance with its terms but for any reason is held to be unavailable from the Company or Cowen, the Company and Cowen will contribute to the total losses, claims, liabilities, expenses and damages (including any investigative, legal and other expenses reasonably incurred in connection with, and any amount paid in settlement of, any action, suit or proceeding or any claim asserted, but after deducting any contribution received by the Company from persons other than Cowen, such as persons who control the Company within

the meaning of the Securities Act, officers of the Company who signed the Registration Statement or the F-6 Registration Statement and directors of the Company, who also may be liable for contribution) to which the Company and Cowen may be subject in such proportion as shall be appropriate to reflect the relative benefits received by the Company on the one hand and Cowen on the other. The relative benefits received by the Company on the one hand and Cowen on the other hand shall be deemed to be in the same proportion as the total Net Proceeds from the sale of the Placement Shares (before deducting expenses) received by the Company bear to the total compensation received by Cowen from the sale of Placement Shares on behalf of the Company. If, but only if, the allocation provided by the foregoing sentence is not permitted by applicable law, the allocation of contribution shall be made in such proportion as is appropriate to reflect not only the relative benefits referred to in the foregoing sentence but also the relative fault of the Company, on the one hand, and Cowen, on the other, with respect to the statements or omission that resulted in such loss, claim, liability, expense or damage, or action in respect thereof, as well as any other relevant equitable considerations with respect to such offering. Such relative fault shall be determined by reference to, among other things, whether the untrue or alleged untrue statement of a material fact or omission or alleged omission to state a material fact relates to information supplied by the Company or Cowen, the intent of the parties and their relative knowledge, access to information and opportunity to correct or prevent such statement or omission. The Company and Cowen agree that it would not be just and equitable if contributions pursuant to this Section 9(d) were to be determined by pro rata allocation or by any other method of allocation that does not take into account the equitable considerations referred to herein. The amount paid or payable by an indemnified party as a result of the loss, claim, liability, expense, or damage, or action in respect thereof, referred to above in this Section 9(d) shall be deemed to include, for the purpose of this Section 9(d), any legal or other expenses reasonably incurred by such indemnified party in connection with investigating or defending any such action or claim to the extent consistent with Section 9(c) hereof. Notwithstanding the foregoing provisions of this Section 9(d), Cowen shall not be required to contribute any amount in excess of the commissions received by it under this Agreement and no person found guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Securities Act) will be entitled to contribution from any person who was not guilty of such fraudulent misrepresentation. For purposes of this Section 9(d), any person who controls a party to this Agreement within the meaning of the Securities Act, and any officers, directors, partners, employees or agents of Cowen, will have the same rights to contribution as that party, and each officer of the Company who signed the Registration Statement will have the same rights to contribution as the Company, subject in each case to the provisions hereof. Any party entitled to contribution, promptly after receipt of notice of commencement of any action against such party in respect of which a claim for contribution may be made under this Section 9(d), will notify any such party or parties from whom contribution may be sought, but the omission to so notify will not relieve that party or parties from whom contribution may be sought from any other obligation it or they may have under this Section 9(d) except to the extent that the failure to so notify such other party materially prejudiced the substantive rights

or defenses of the party from whom contribution is sought. Except for a settlement entered into pursuant to the last sentence of Section 9(c) hereof, no party will be liable for contribution with respect to any action or claim settled without its written consent if such consent is required pursuant to Section 9(c) hereof.

10. Representations and Agreements to Survive Delivery. The indemnity and contribution agreements contained in Section 9 of this Agreement and all representations and warranties of the Company herein or in certificates delivered pursuant hereto shall survive, as of their respective dates, regardless of (i) any investigation made by or on behalf of Cowen, any controlling persons, or the Company (or any of their respective officers, directors or controlling persons), (ii) delivery and acceptance of the Placement Shares and payment therefor or (iii) any termination of this Agreement.

11. Termination.

(a) Cowen shall have the right by giving notice as hereinafter specified at any time to terminate this Agreement if (i) any Material Adverse Effect, or any development that could reasonably be expected to result in a Material Adverse Effect has occurred that, in the reasonable judgment of Cowen, may materially impair the ability of Cowen to sell the Placement Shares hereunder, (ii) the Company shall have failed, refused or been unable to perform any agreement on its part to be performed hereunder; *provided, however*, in the case of any failure of the Company to deliver (or cause another person to deliver) any certification, opinion, or letter required under Sections 7(m), 7(n), or 7(o), Cowen's right to terminate shall not arise unless such failure to deliver (or cause to be delivered) continues for more than thirty (30) days from the date such delivery was required; or (iii) any other condition of Cowen's obligations hereunder is not fulfilled, or (iv), any suspension or limitation of trading in the Placement Shares or in securities generally on Nasdaq shall have occurred. Any such termination shall be without liability of any party to any other party except that the provisions of Section 7(g) (Expenses), Section 9 (Indemnification and Contribution), Section 10 (Representations and Agreements to Survive Delivery), Section 16 (Applicable Law; Consent to Jurisdiction), Section 17 (Judgement Currency) and Section 18 (Waiver of Jury Trial) hereof shall remain in full force and effect notwithstanding such termination. If Cowen elects to terminate this Agreement as provided in this Section 11(a), Cowen shall provide the required notice as specified in Section 12 (Notices).

(b) The Company shall have the right, by giving five (5) days' notice as hereinafter specified to terminate this Agreement in its sole discretion at any time after the date of this Agreement. Any such termination shall be without liability of any party to any other party except that the provisions of Section 7(g), Section 9, Section 10, Section 16, Section 17 and Section 18 hereof shall remain in full force and effect notwithstanding such termination.

(c) Cowen shall have the right, by giving five (5) days' notice as hereinafter specified to terminate this Agreement in its sole discretion at any time after the date of this Agreement. Any such termination shall be without liability of any party to any other party except that the provisions of Section 7(g), Section 9, Section 10, Section 16, Section 17 and Section 18 hereof shall remain in full force and effect notwithstanding such termination.

(d) Unless earlier terminated pursuant to this Section 11, this Agreement shall automatically terminate upon the issuance and sale of all of the Placement Shares through Cowen on the terms and subject to the conditions set forth herein; *provided* that the provisions of Section 7(g), Section 9, Section 10, Section 16, Section 17 and Section 18 hereof shall remain in full force and effect notwithstanding such termination.

(e) This Agreement shall remain in full force and effect unless terminated pursuant to Sections 11(a), (b), (c), or (d) above or otherwise by mutual agreement of the parties; *provided, however*, that any such termination by mutual agreement shall in all cases be deemed to provide that Section 7(g), Section 9, Section 10, Section 16, Section 17 and Section 18 shall remain in full force and effect.

(f) Any termination of this Agreement shall be effective on the date specified in such notice of termination; *provided, however*, that such termination shall not be effective until the close of business on the date of receipt of such notice by Cowen or the Company, as the case may be. If such termination shall occur prior to the Settlement Date for any sale of Placement Shares, such Placement Shares shall settle in accordance with the provisions of this Agreement.

12. Notices. All notices or other communications required or permitted to be given by any party to any other party pursuant to the terms of this Agreement shall be in writing, unless otherwise specified in this Agreement, and if sent to Cowen, shall be delivered to Cowen at Cowen and Company, LLC, 599 Lexington Avenue, New York, NY 10022, fax no. 646-562-1130, Attention: General Counsel; or if sent to the Company, shall be delivered to Orchard Therapeutics plc, 2 Seaport Lane, 8th Floor East, Boston, MA 02210, Attention: Chief Financial Officer with a copy to Goodwin Procter LLP, 100 Northern Avenue, Boston MA 02210, Attention: Michael Bison. Each party to this Agreement may change such address for notices by sending to the parties to this Agreement written notice of a new address for such purpose. Each such notice or other communication shall be deemed given (i) when delivered personally or by verifiable facsimile transmission (with an original to follow) on or before 4:30 p.m., New York City time, on a Business Day (as defined below), or, if such day is not a Business Day on the next succeeding Business Day, (ii) on the next Business Day after timely delivery to a nationally-recognized overnight courier and (iii) on the Business Day actually received if deposited in the U.S. mail (certified or registered mail, return receipt requested, postage prepaid). For purposes of this Agreement, "**Business Day**" shall mean any day on which the Nasdaq and commercial banks in the City of New York are open for business.

13. Successors and Assigns. This Agreement shall inure to the benefit of and be binding upon the Company and Cowen and their respective successors and the affiliates, controlling persons, officers and directors referred to in Section 9 hereof. References to any of the parties contained in this Agreement shall be deemed to include the successors and permitted assigns of such party. Nothing in this Agreement, express or implied, is intended to confer upon any party other than the parties hereto or their respective successors and permitted assigns any rights,

remedies, obligations or liabilities under or by reason of this Agreement, except as expressly provided in this Agreement. Neither party may assign its rights or obligations under this Agreement without the prior written consent of the other party; *provided, however*, that Cowen may assign its rights and obligations hereunder to an affiliate of Cowen without obtaining the Company's consent.

14. Adjustments for Share Splits. The parties acknowledge and agree that all share-related numbers contained in this Agreement shall be adjusted to take into account any share split, share dividend or similar event effected with respect to the Placement Shares.

15. Entire Agreement; Amendment; Severability. This Agreement (including all schedules and exhibits attached hereto and Placement Notices issued pursuant hereto) constitutes the entire agreement and supersedes all other prior and contemporaneous agreements and undertakings, both written and oral, among the parties hereto with regard to the subject matter hereof. Neither this Agreement nor any term hereof may be amended except pursuant to a written instrument executed by the Company and Cowen. In the event that any one or more of the provisions contained herein, or the application thereof in any circumstance, is held invalid, illegal or unenforceable as written by a court of competent jurisdiction, then such provision shall be given full force and effect to the fullest possible extent that it is valid, legal and enforceable, and the remainder of the terms and provisions herein shall be construed as if such invalid, illegal or unenforceable term or provision was not contained herein, but only to the extent that giving effect to such provision and the remainder of the terms and provisions hereof shall be in accordance with the intent of the parties as reflected in this Agreement.

16. Applicable Law; Consent to Jurisdiction. This Agreement shall be governed by, and construed in accordance with, the internal laws of the State of New York without regard to the principles of conflicts of laws. Each party hereby irrevocably submits to the non-exclusive jurisdiction of the state and federal courts sitting in the City of New York, borough of Manhattan, for the adjudication of any dispute hereunder or in connection with any transaction contemplated hereby, and hereby irrevocably waives, and agrees not to assert in any suit, action or proceeding, any claim that it is not personally subject to the jurisdiction of any such court, that such suit, action or proceeding is brought in an inconvenient forum or that the venue of such suit, action or proceeding is improper. Each party hereby irrevocably waives personal service of process and consents to process being served in any such suit, action or proceeding by mailing a copy thereof (certified or registered mail, return receipt requested) to such party at the address in effect for notices to it under this Agreement and agrees that such service shall constitute good and sufficient service of process and notice thereof. Nothing contained herein shall be deemed to limit in any way any right to serve process in any manner permitted by law.

17. Judgment Currency. The obligations of the Company pursuant to this Agreement in respect of any sum due to Cowen shall, notwithstanding any judgment in a currency other than United States dollars, not be discharged until the first Business Day, following receipt by Cowen of any sum adjudged to be so due in such other currency, on which (and only to the extent that) Cowen may in accordance with normal banking procedures purchase United States dollars with such other currency; if the United States dollars so purchased are less than the sum originally due to Cowen hereunder, the Company agrees, as a separate obligation and notwithstanding any such judgment, to indemnify Cowen against such loss.

18. Waiver of Jury Trial. The Company and Cowen each hereby irrevocably waives any right it may have to a trial by jury in respect of any claim based upon or arising out of this Agreement or any transaction contemplated hereby.

19. Recognition of the U.S. Special Resolution Regimes. In the event that Cowen is a Covered Entity becomes subject to a proceeding under a U.S. Special Resolution Regime, the transfer from Cowen of this Agreement, and any interest and obligation in or under this Agreement, will be effective to the same extent as the transfer would be effective under the U.S. Special Resolution Regime if this Agreement, and any such interest and obligation, were governed by the laws of the United States or a state of the United States. In the event that Cowen is a Covered Entity or a BHC Act Affiliate of Cowen becomes subject to a proceeding under a U.S. Special Resolution Regime, Default Rights under this Agreement that may be exercised against Cowen are permitted to be exercised to no greater extent than such Default Rights could be exercised under the U.S. Special Resolution Regime if this Agreement were governed by the laws of the United States or a state of the United States.

For purposes of this Section 8(h), a “**BHC Act Affiliate**” has the meaning assigned to the term “affiliate” in, and shall be interpreted in accordance with, 12 U.S.C. § 1841(k). “**Covered Entity**” means any of the following: (i) a “covered entity” as that term is defined in, and interpreted in accordance with, 12 C.F.R. § 252.82(b); (ii) a “covered bank” as that term is defined in, and interpreted in accordance with, 12 C.F.R. § 47.3(b); or (iii) a “covered FSI” as that term is defined in, and interpreted in accordance with, 12 C.F.R. § 382.2(b). “**Default Right**” has the meaning assigned to that term in, and shall be interpreted in accordance with, 12 C.F.R. §§ 252.81, 47.2 or 382.1, as applicable. “**U.S. Special Resolution Regime**” means each of (i) the Federal Deposit Insurance Act and the regulations promulgated thereunder and (ii) Title II of the Dodd-Frank Wall Street Reform and Consumer Protection Act and the regulations promulgated thereunder.

20. Absence of Fiduciary Relationship. The Company acknowledges and agrees that:

(a) Cowen has been retained solely to act as sales agent in connection with the sale of the Placement Shares and that no fiduciary, advisory or agency relationship between the Company and Cowen has been created in respect of any of the transactions contemplated by this Agreement, irrespective of whether Cowen has advised or is advising the Company on other matters;

(b) the Company is capable of evaluating and understanding and understands and accepts the terms, risks and conditions of the transactions contemplated by this Agreement;

(c) the Company has been advised that Cowen and its affiliates are engaged in a broad range of transactions which may involve interests that differ from those of the Company and that Cowen has no obligation to disclose such interests and transactions to the Company by virtue of any fiduciary, advisory or agency relationship; and

(d) the Company waives, to the fullest extent permitted by law, any claims it may have against Cowen, for breach of fiduciary duty or alleged breach of fiduciary duty and agrees that Cowen shall have no liability (whether direct or

indirect) to the Company in respect of such a fiduciary claim or to any person asserting a fiduciary duty claim on behalf of or in right of the Company, including stockholders, partners, employees or creditors of the Company.

21. Counterparts. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. Delivery of an executed Agreement by one party to the other may be made by facsimile transmission.

22. Definitions. As used in this Agreement, the following term has the meaning set forth below:

(a) “*Applicable Time*” means the date of this Agreement, each Representation Date, the date on which a Placement Notice is given, and any date on which Placement Shares are sold hereunder.

(b) “*Agent’s Information*” means, solely the following information in the Prospectus: the third sentence in the eighth paragraph under the caption “Plan of Distribution” in the Prospectus.

[Remainder of Page Intentionally Blank]

If the foregoing correctly sets forth the understanding between the Company and Cowen, please so indicate in the space provided below for that purpose, whereupon this letter shall constitute a binding agreement between the Company and Cowen.

Very truly yours,

COWEN AND COMPANY, LLC

By: /s/ Jeff Urlich

Name: Jeff Urlich

Title: Managing Director

ACCEPTED as of the date first-above written:

ORCHARD THERAPEUTICS PLC

By: /s/ Mark Rothera

Name: Mark Rothera

Title: Chief Executive Officer

FORM OF PLACEMENT NOTICE

From: []
Cc: []
To: []
Subject: Cowen at the Market Offering—Placement Notice

Ladies and Gentlemen:

Pursuant to the terms and subject to the conditions contained in the Sales Agreement between Orchard Therapeutics plc (the "Company"), and Cowen and Company, LLC ("Cowen") dated February 27, 2020 (the "Agreement"), I hereby request on behalf of the Company that Cowen sell up to [] shares of the Company's American Depositary Shares ("ADSs"), at a minimum market price of \$ per ADS. Sales should begin on the date of this Notice and shall continue until [DATE] [all ADSs are sold].

Notice Parties

Company:

John Ilett
Frank Thomas

Cowen:

Jeff Urlich
Michael Murphy
William Follis

Compensation

Cowen shall be paid compensation up to 3% of the gross proceeds from the sales of Placement Shares pursuant to the terms of this Agreement.

OFFICER CERTIFICATE

The undersigned, the duly qualified and elected _____, of Orchard Therapeutics plc, a public limited company incorporated under the laws of England and Wales (“**Company**”), does hereby certify in such capacity and on behalf of the Company, pursuant to Section 7(m) of the Sales Agreement dated February 27, 2020 (the “**Sales Agreement**”) between the Company and Cowen and Company, LLC, that to the best of the knowledge of the undersigned.

(i) The representations and warranties of the Company in Section 6 of the Sales Agreement (A) to the extent such representations and warranties are subject to qualifications and exceptions contained therein relating to materiality or Material Adverse Effect, are true and correct on and as of the date hereof with the same force and effect as if expressly made on and as of the date hereof, except for those representations and warranties that speak solely as of a specific date and which were true and correct as of such date, and (B) to the extent such representations and warranties are not subject to any qualifications or exceptions, are true and correct in all material respects as of the date hereof as if made on and as of the date hereof with the same force and effect as if expressly made on and as of the date hereof except for those representations and warranties that speak solely as of a specific date and which were true and correct as of such date; and

(ii) The Company has complied with all agreements and satisfied all conditions on its part to be performed or satisfied pursuant to the Sales Agreement at or prior to the date hereof.

By: _____
Name:
Title:

Date: _____



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

goodwinlaw.com
+44 (0) 20 7447 4200

27 February 2020

Orchard Therapeutics plc
108 Cannon Street
London, EC4N 6EU

Ladies and Gentlemen:

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 prospectus supplement (the “**Prospectus Supplement**”) to the Company’s prospectus dated November 1, 2019 (the “**Prospectus**”), pursuant to the U.S. Securities Act of 1933, as amended (the “**Securities Act**”).

The Prospectus Supplement relates to the registration for the issue and sale by the Company of American depositary shares (“**ADSs**”), each ADS representing one ordinary share at a nominal value of £0.10 per share (the “**Ordinary Shares**” and together with the ADSs, the “**Shares**”). The Company has entered into a sales agreement with Cowen and Company LLC (“**Cowen**”) dated 27 February 2020 (the “**Sales Agreement**”), pursuant to which the Company may offer and sell its ADSs having an aggregate offering price of up to \$100,000,000 from time to time through Cowen acting as its sales agent.

The sale of any ADSs by the Company pursuant to the Prospectus Supplement will constitute an “at the market offering” as defined in Rule 415(a)4 promulgated under the Securities Act. The Company’s ADSs are listed on The Nasdaq Global Select Market under the symbol “**ORTX**”.

1. INTRODUCTION

1.1 Purpose

In connection with the preparation and filing of the Prospectus Supplement, 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 27 February 2020 at 10:41 am (London time);
- (b) an enquiry of the Central Index of Winding Up Petitions, London on 27 February 2020 at 10:41 am (London time) ((a) and (b) together, the "**Searches**");
- (c) a PDF copy of the resolutions passed by the shareholders of the Company at the Company's annual general meeting on 26 June 2019;
- (d) minutes of a meeting of the board of directors of the Company (the "**Board**") held on 30 January 2020 (the "**Board Meeting**") at which it was resolved, inter alia, that the Company be authorised to issue for sale the ADSs in accordance with the offer terms set out in the Prospectus Supplement.
- (e) a PDF copy of the current articles of association of the Company filed at the Companies House on 18 December 2018 (the "**Articles**") and certificate of incorporation of the Company dated 1 August 2018; and
- (f) a copy of the Prospectus Supplement filed with the SEC on 27 February 2020.

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; and
- (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.

1.5 Assumptions and reservations

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

2. 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 Prospectus Supplement, the Prospectus and any related Prospectus supplement(s), will be duly and validly authorised and issued, fully paid or credited as fully paid and will not be subject to any call for payment of further capital.

3. EXTENT OF OPINIONS

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

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

4. DISCLOSURE AND RELIANCE

This letter is addressed to you in connection with the Prospectus Supplement. We consent to the filing of this letter as an exhibit to the Prospectus Supplement. 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.

Orchard Therapeutics plc
27 February 2020
Page 4

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 Prospectus Supplement;
- (g) that the Prospectus Supplement, as finally amended, has become effective under the Securities Act;
- (h) that the Board Meeting was duly constituted and convened and all constitutional, statutory and other formalities were duly observed, the requisite majority of directors voted in favour of approving the resolutions and the resolutions passed thereby were duly adopted, have not been revoked or varied and remain in full force and effect;
- (i) an appropriate prospectus supplement with respect to the Shares has been prepared, delivered and filed in compliance with the Securities Act and the rules and regulations thereunder;
- (j) the Shares will be sold or issued in accordance with a duly authorised, executed and delivered purchase, underwriting or similar agreement as may be required from time to time by Cowen acting as the Company's sales agent;
- (k) that the Shares when issued will be accurately and properly completed, duly authorised, executed and delivered on behalf of the Company and authenticated, issued and paid for and registered in the register of holders of Shares maintained for this purpose, in accordance with the then operative Articles and all applicable laws (for the avoidance of doubt, as in force at all relevant times);

- (l) the directors of the Company, including any 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;
- (m) 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 resolutions recorded in the Board Minutes and that all actions to be carried out by the Company are or will be in its commercial interests;
- (n) 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;
- (o) 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, as amended, 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);
- (p) that the resolutions set out in the Board Minutes were validly passed and have not been and will not be revoked or varied and remain in full force and effect and will remain so as at the date of this letter;
- (q) following the date of this letter and prior to the issue of the Shares, the Company will validly enter into the Sales Agreement (as defined above);
- (r) that no Shares or rights to subscribe for Shares have been or shall be offered to the public in the United Kingdom in breach of the Financial Services and Markets Act 2000, as amended (“**FSMA**”) or of any other United Kingdom laws or regulations concerning offers of securities to the public, and no communication has been or shall be made in relation to the Shares in breach of section 21 of FSMA or any other United Kingdom laws or regulations relating to offers or invitations to subscribe for, or to acquire rights to subscribe for or otherwise acquire, shares or other securities; and
- (s) 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) we have made no enquiries of any individual connected with the Company;
- (e) a certificate, documentation, notification, opinion or the like might be held by the English courts not to be conclusive if it can be shown to have an unreasonable or arbitrary basis or in the event of a manifest error; and
- (f) it should be understood that we have not been responsible for investigating or verifying (i) the accuracy of the facts, including statements of foreign law, or the reasonableness of any statements of opinion, contained in the Prospectus Supplement; or (ii) that no material facts have been omitted from it.

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in this Registration Statement on Form S-3 of Orchard Therapeutics plc of our report dated February 27, 2020 relating to the financial statements and the effectiveness of internal control over financial reporting, which appears in Orchard Therapeutics plc's Annual Report on Form 10-K for the year ended December 31, 2019. We also consent to the references to us under the headings "Experts" in such registration statement.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
February 27, 2020

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 22, 2019 relating to the financial statements, which appears in Orchard Therapeutics plc's Annual Report on Form 10-K for the year ended December 31, 2019. We also consent to the references to us under the headings "Experts" in such registration statement.

/s/ PricewaterhouseCoopers LLP

Reading, United Kingdom
February 27, 2020