

PROSPECTUS SUPPLEMENT

(To prospectus dated April 29, 2022)



\$30,000,000

American Depositary Shares representing Ordinary Shares

We have entered into a sales agreement with Guggenheim Securities, LLC, or Guggenheim Securities, relating to the sale of American Depositary Shares, or ADSs, offered by this prospectus supplement and the accompanying prospectus. 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 \$30,000,000 from time to time through Guggenheim Securities acting as our sales agent.

Our ADSs are listed on The Nasdaq Capital Market under the symbol "ORTX". On October 5, 2022, the last reported sale price of our ADSs was \$0.52 per ADS.

Sales of our ADSs, if any, under this prospectus supplement and the accompanying prospectus 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. Guggenheim Securities 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 Guggenheim Securities and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

The compensation to Guggenheim Securities 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, Guggenheim Securities will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Guggenheim Securities will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Guggenheim Securities 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 and the accompanying prospectus. Any representation to the contrary is a criminal offense.

Guggenheim Securities

The date of this prospectus supplement is October 6, 2022.

TABLE OF CONTENTS

Prospectus Supplement

PRESENTATION OF FINANCIAL INFORMATION	S-1
ABOUT THIS PROSPECTUS SUPPLEMENT	S-2
SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS	S-4
PROSPECTUS SUPPLEMENT SUMMARY	S-6
THE OFFERING	S-7
RISK FACTORS	S-9
USE OF PROCEEDS	S-12
DIVIDEND POLICY	S-13
DILUTION	S-14
PLAN OF DISTRIBUTION	S-15
LEGAL MATTERS	S-17
EXPERTS	S-17
SERVICE OF PROCESS AND ENFORCEMENT OF LIABILITIES	S-17
WHERE YOU CAN FIND MORE INFORMATION	S-17
INCORPORATION BY REFERENCE	S-18

Accompanying Prospectus

	Page
ABOUT THIS PROSPECTUS	1
PRESENTATION OF FINANCIAL INFORMATION	3
PROSPECTUS SUMMARY	4
RISK FACTORS	6
SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS	7
CAPITALIZATION	9
SECURITIES WE MAY OFFER	10
DESCRIPTION OF SHARE CAPITAL AND ARTICLES OF ASSOCIATION	11
DESCRIPTION OF AMERICAN DEPOSITARY SHARES	25
DESCRIPTION OF DEBT SECURITIES	36
DESCRIPTION OF WARRANTS	50
DESCRIPTION OF UNITS	51
TAXATION	52
USE OF PROCEEDS	53
PLAN OF DISTRIBUTION	54
LEGAL MATTERS	57
EXPERTS	57
SERVICE OF PROCESS AND ENFORCEMENT OF LIABILITIES	57
WHERE YOU CAN FIND MORE INFORMATION	59
INCORPORATION BY REFERENCE	60

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 a shelf registration statement that we filed with the Securities Exchange Commission, or SEC. We may from time to time sell our ADSs representing our ordinary shares having an aggregate offering price of up to \$30,000,000 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 the accompanying prospectus, 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 the accompanying prospectus or 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 Guggenheim Securities 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, the accompanying prospectus and any related free writing prospectus filed by us with the SEC. We and Guggenheim Securities 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, the accompanying prospectus 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, the accompanying prospectus 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 and accompanying prospectus contain 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.

[Table of Contents](#)

We own various U.S. federal trademark registrations and applications and unregistered trademarks, including our corporate logo. This prospectus supplement, the accompanying prospectus 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, the accompanying prospectus or any related free writing prospectus are the property of their respective owners.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying 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 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 initiation, timing, progress and results of our preclinical studies and clinical trials, 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 market opportunity for and size of the patient populations for Libmeldy (OTL-200) and our product candidates, if approved, for commercial use;
- the implementation of our business model and our strategic plans for our business;
- our plans and ability to build out our commercial infrastructure, including our ability to successfully identify patients and market and sell Libmeldy in Europe and any of our product candidates for which we receive marketing approval;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the pricing and reimbursement of Libmeldy and any of our product candidates, if approved, including reimbursement for patients treated in a country where they are not resident;
- the adequacy, scalability and commercial viability of our manufacturing capacity, methods and processes, including those of our manufacturing partners, and plans for future development;
- the rate and degree of market acceptance and clinical utility of our commercial products and product candidates, in particular, and gene therapy, in general;
- our ability to establish or maintain collaborations or strategic relationships;
- our ability to obtain additional funding for our operations;
- the impact of the COVID-19 global pandemic on our business operations, including clinical trials, regulatory strategy, and the operations of our third-party manufacturers, suppliers and partners;
- the scope of protection we and our licensors are able to establish and maintain for intellectual property rights covering our commercial products and product candidates;
- developments and projections relating to our competitors and our industry;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- the impact of laws and regulations;

Table of Contents

- our ability to attract and retain qualified employees and key personnel;
- our ability to contract with third party suppliers, clinical sites and manufacturers and their ability to perform adequately;
- our projected financial condition, including the sufficiency of our cash, cash equivalents and investments to fund operations in future periods and future liquidity, working capital and capital requirements;
- our ability to comply with the listing requirements of The Nasdaq Stock Market;
- the impact of inflation on our business, results of operations or financial condition;
- the impact of geopolitical events, including the ongoing conflict between Russia and Ukraine; 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 and the accompanying 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 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, the accompanying prospectus or incorporated by reference in this prospectus supplement and the accompanying prospectus. It may not contain all of the information that is important to you. You should carefully read the entire prospectus supplement, the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and accompanying prospectus before deciding whether to invest in our securities.

We are a global gene therapy company dedicated to transforming the lives of people affected by rare diseases through the development of innovative, potentially curative gene therapies. Our *ex vivo* autologous hematopoietic stem cell, or HSC, gene therapy approach harnesses the power of genetically modified blood stem cells and seeks to correct the underlying cause of disease in a single administration. We seek to achieve this outcome by utilizing a lentiviral vector to introduce a functional copy of a missing or faulty gene into the patient's own, or autologous, HSCs through an *ex vivo* process, resulting in a gene-modified cellular drug product that can then be administered to the patient at the bedside.

To date, over 160 patients have been treated with our current and former product candidates across seven different diseases, with follow-up periods of more than 11 years following a single administration. We believe the data observed across these development programs, in combination with our expertise in the development, manufacturing and commercialization of gene and cell therapies, position us to provide potentially curative therapies to people suffering from a broad range of diseases.

We are currently focusing our *ex vivo* autologous HSC gene therapy approach on severe neurometabolic diseases and early research programs. Our lead program is OTL-200, which was approved in the European Union, the United Kingdom, Iceland, Liechtenstein and Norway under the brand name Libmeldy for eligible patients with early-onset metachromatic leukodystrophy, or MLD. Our planned BLA submission timeline for OTL-200 with the U.S. Food and Drug Administration is late 2022 to early 2023.

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

Corporate Information

We were originally incorporated under the laws of England and Wales in August 2018 as Orchard Rx Limited (now known as Orchard Therapeutics plc) to become a holding company for Orchard Therapeutics (Europe) Limited (previously known as Orchard Therapeutics Limited). Orchard Rx Limited subsequently re-registered as a public limited company and its name was changed from Orchard Rx Limited to Orchard Therapeutics plc in October 2018. Orchard Therapeutics (Europe) Limited was originally incorporated under the laws of England and Wales in September 2015 as Newincco 1387 Limited and subsequently changed its name to Orchard Therapeutics Limited in November 2015 and to Orchard Therapeutics (Europe) Limited in October 2018. Our registered office is located at 245 Hammersmith Road, 3rd Floor, London, England, W6 8PW, 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 \$30,000,000.
Shares to be outstanding after this offering	Up to 184,128,520 ordinary shares (including ordinary shares represented by ADSs), assuming sales of 57,692,307 ordinary shares represented by ADSs in this offering at an offering price of \$0.52 per ADS, which was the last reported sale price of our ADSs on The Nasdaq Capital Market on October 5, 2022. The actual number of ADSs issued will vary depending on the sales price under this offering.
Manner of offering	“At the market offering” that may be made from time to time through our sales agent, Guggenheim Securities. 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	We currently anticipate using such proceeds primarily for general corporate purposes and to fund ongoing commercialization of Libmeldy, 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. See “Use of Proceeds” on page S-12 of this prospectus supplement.
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 into this prospectus supplement and the accompanying prospectus, for a discussion of factors to consider carefully before deciding to invest in our securities.
The Nasdaq Capital Market symbol	“ORTX”
The total number of our ordinary shares (including ordinary shares represented by one ADS) to be outstanding after this offering is based on 126,436,213 of our ordinary shares outstanding as of June 30, 2022, and excludes:	
	<ul style="list-style-type: none">• 17,223,698 ordinary shares issuable upon the exercise of options for ordinary shares outstanding as of June 30, 2022, at a weighted-average exercise price of \$5.52 per share;• 2,352,708 ordinary shares issuable upon the vesting of time-based and performance-based restricted stock units, or RSUs, outstanding as of June 30, 2022;• 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;

[Table of Contents](#)

- 4,576,090 ordinary shares available for future issuance under our 2018 Share Option and Incentive Plan as of June 30, 2022;
- 823,497 ordinary shares available for future issuance under our 2018 Employee Share Purchase Plan as of June 30, 2022; and
- 721,500 ordinary shares available for future issuance under our 2020 Inducement Equity Plan as of June 30, 2022.

Unless otherwise stated, all information contained in this prospectus supplement assumes no issuance or exercise of options after June 30, 2022 and reflects an assumed public offering price of \$0.52, which was the last reported sale price of our common stock on The Nasdaq Capital Market on October 5, 2022.

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 and accompanying prospectus 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, 2021, and our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2022 and June 30, 2022, each of 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 Quarterly Report on Form 10-Q for the quarter ended June 30, 2022, 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 our current or future collaborators to successfully develop and commercialize product candidates for which we are eligible to receive milestone and royalty payments;
- failure by us to adequately scale our manufacturing capabilities and commercial and sales organization to succeed in our commercialization efforts of Libmeldy;
- 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;

Table of Contents

- 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;
- 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;
- general economic, geopolitical and market conditions, including the significant disruptions to the U.S. and global economies and the related significant volatility and negative pressure in financial markets caused by the COVID-19 global pandemic, supply chain issues, inflationary pressures and the ongoing conflict in the Ukraine;
- 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 Capital 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 may experience immediate dilution of your investment.

The ADSs sold in this offering, if any, will be sold from time to time at various prices and may exceed the net tangible book value per share of our ADSs. After giving effect to the assumed sales of our ADSs in the aggregate amount of \$30,000,000 in this offering at an assumed public offering price of \$0.52 per ADS, the last reported sale price of our ADSs on The Nasdaq Capital Market on October 5, 2022, and after deducting estimated discounts and commissions and estimated offering expenses payable by us, you would experience immediate accretion of \$0.40 per ADS as of June 30, 2022, 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. However, in the future, the price per ADS being offered may be higher than the net tangible book value per ordinary share and ADS prior to this offering, in which case new investors would suffer immediate dilution to the extent the public offering price per ADS in the offering exceeds the net tangible book value per ordinary share and ADS after this offering. You may also incur dilution to the extent outstanding options are exercised. 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 \$30,000,000 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 Libmeldy, 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 June 30, 2022, was \$142.5 million, or \$1.13 per ordinary share (equivalent to \$1.13 per ADS). Net tangible book value per ADS is determined by dividing our total tangible assets, less total liabilities, by 126,436,213, the total number of our ordinary shares outstanding as of June 30, 2022.

After giving effect to the assumed sale by us of our ADSs in the aggregate amount of \$30,000,000 in this offering at an assumed public offering price of \$0.52 per ADS, the last reported sale price of our ADSs on The Nasdaq Capital Market on October 5, 2022 and after deducting estimated discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of June 30, 2022, would have been \$168.5 million, or \$0.92 per ordinary share (equivalent to \$0.92 per ADS). This represents an immediate decrease in net tangible book value of \$0.21 per ordinary share and ADS to our existing shareholders and immediate accretion in net tangible book value of \$(0.40) per ADS to new investors purchasing our ADSs in this offering. 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 \$0.40 less than the as adjusted net tangible book value per ADS after this offering. The following table illustrates this accretion on a per ADS basis.

Assumed public offering price per ADS		\$ 0.52
Net tangible book value per ADS as of June 30, 2022	\$ 1.13	
Decrease in net tangible book value per ADS attributable to the offering	<u>(0.21)</u>	
As adjusted net tangible book value per ADS after giving effect to the offering		<u>0.92</u>
Dilution (accretion) per ADS to new investors participating in the offering		<u><u>\$(0.40)</u></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 126,436,213 of our ordinary shares outstanding as of June 30, 2022, and exclude:

- 17,223,698 ordinary shares issuable upon the exercise of options for ordinary shares outstanding as of June 30, 2022, at a weighted-average exercise price of \$5.52 per share;
- 2,352,708 ordinary shares issuable upon the vesting of time-based and performance-based restricted stock units, or RSUs, outstanding as of June 30, 2022;
- 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;
- 4,576,090 ordinary shares available for future issuance under our 2018 Share Option and Incentive Plan as of June 30, 2022;
- 823,497 ordinary shares available for future issuance under our 2018 Employee Share Purchase Plan as of June 30, 2022; and
- 721,500 ordinary shares available for future issuance under our 2020 Inducement Equity Plan as of June 30, 2022.

PLAN OF DISTRIBUTION

We have entered into a sales agreement with Guggenheim Securities, under which we may issue and sell from time to time up to an aggregate of \$30,000,000 of our ADSs, each representing one ordinary share, through Guggenheim Securities 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 Capital Market or any other trading market for our ADSs. If authorized by us in writing, Guggenheim Securities may purchase our ADSs as principal.

Guggenheim Securities 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 Guggenheim Securities. We will designate the maximum amount of ADSs to be sold through Guggenheim Securities on a daily basis or otherwise determine such maximum amount together with Guggenheim Securities. Subject to the terms and conditions of the sales agreement, Guggenheim Securities will use its commercially reasonable efforts to sell on our behalf all of the ADSs requested to be sold by us. We may instruct Guggenheim Securities not to sell ADSs if the sales cannot be effected at or above the price designated by us in any such instruction. Guggenheim Securities or we may suspend the offering of our ADSs being made through Guggenheim Securities under the sales agreement upon proper notice to the other party. Guggenheim Securities 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 Guggenheim Securities 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 Guggenheim Securities up to \$50,000 of Guggenheim Securities’ actual outside legal expenses incurred by Guggenheim Securities in connection with this offering, as well as Guggenheim Securities’ 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 Guggenheim Securities under the sales agreement, will be approximately \$0.3 million.

The remaining sales proceeds, after deducting any expenses payable by us and any other transaction fees, including those 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.

Guggenheim Securities will provide written confirmation to us following the close of trading on The Nasdaq Capital 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 Guggenheim Securities under the sales agreement, the net proceeds to us and the compensation paid by us to Guggenheim Securities 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, Guggenheim Securities will be deemed to be an “underwriter” within the meaning of the Securities Act, and the compensation paid to Guggenheim Securities will be deemed to be underwriting commissions or discounts. We have agreed in the sales agreement to provide indemnification and contribution to Guggenheim Securities against certain liabilities, including liabilities under the Securities Act. As sales agent, Guggenheim Securities will not engage in any transactions that stabilizes our ADSs.

[Table of Contents](#)

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

Guggenheim Securities 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 Guggenheim Securities is 330 Madison Avenue, New York, NY 10017.

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. Guggenheim Securities, 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 incorporated in this prospectus supplement by reference to the Annual Report on Form 10-K for the year ended December 31, 2021 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

SERVICE OF PROCESS AND ENFORCEMENT OF LIABILITIES

We are 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 and the accompanying prospectus are part of the Registration Statement we filed with the SEC. This prospectus supplement and the accompanying prospectus omit 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 and the accompanying 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 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 and the accompanying prospectus is considered to be part of this prospectus supplement and the accompanying prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus supplement and the accompanying prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus supplement and the accompanying prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus supplement, the accompanying prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus supplement and the accompanying prospectus 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, 2021, filed on March 30, 2022;
- The information specifically incorporated by reference into our Annual Report on [Form 10-K](#) for the year ended December 31, 2021 from our [definitive proxy statement](#) on Schedule 14A (other than information furnished rather than filed), which was filed with the SEC on April 27, 2022
- Quarterly Reports on Form 10-Q filed with the SEC for the quarters ended [March 31, 2022](#) and [June 30, 2022](#), filed with the SEC on May 12, 2022 and August 4, 2022, respectively;
- Current Reports on Form 8-K filed with the SEC on [January 10, 2022](#), [January 21, 2022](#), [February 4, 2022](#), April 8, 2022 and June 10, 2022; 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. 333-263967) 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
245 Hammersmith Road, 3rd Floor
London, England, W6 8PW
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.

[Table of Contents](#)

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.

PROSPECTUS



\$200,000,000

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

We may offer and sell from time to time up to \$200,000,000 in the aggregate of our: ordinary shares, each of which may be represented by one American Depositary Share; senior or subordinated debt securities; warrants to purchase any securities that may be sold under this prospectus; units or any combination of these securities as described in this prospectus. We will describe in a prospectus supplement the securities we are offering and selling, as well as the specific terms of the securities. We may also authorize one or more free writing prospectuses to be provided to you in connection with each offering of the securities. Any prospectus supplement and related free writing prospectuses may also add, update or change information contained in this prospectus. For more detailed information, see "Plan of Distribution" on page 54.

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

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

Investing in our securities involves certain risks. See "[Risk Factors](#)" beginning on page 6 of this prospectus and in the applicable prospectus supplement and any related free writing prospectus and in the documents that are incorporated by reference into this prospectus or the applicable prospectus supplement for certain risks you should consider. You should read the entire prospectus carefully before you make your investment decision.

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

The date of this prospectus is April 29, 2022

Table of Contents

	Page
ABOUT THIS PROSPECTUS	1
PRESENTATION OF FINANCIAL INFORMATION	3
PROSPECTUS SUMMARY	4
RISK FACTORS	6
SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS	7
CAPITALIZATION	9
SECURITIES WE MAY OFFER	10
DESCRIPTION OF SHARE CAPITAL AND ARTICLES OF ASSOCIATION	11
DESCRIPTION OF AMERICAN DEPOSITARY SHARES	25
DESCRIPTION OF DEBT SECURITIES	36
DESCRIPTION OF WARRANTS	50
DESCRIPTION OF UNITS	51
TAXATION	52
USE OF PROCEEDS	53
PLAN OF DISTRIBUTION	54
LEGAL MATTERS	57
EXPERTS	57
SERVICE OF PROCESS AND ENFORCEMENT OF LIABILITIES	57
WHERE YOU CAN FIND MORE INFORMATION	59
INCORPORATION BY REFERENCE	60

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement, as amended, that we filed with the U.S. Securities and Exchange Commission, or SEC, under the Securities Act of 1933, as amended.

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

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

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

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

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

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

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

We own various trademark registrations and applications, and unregistered trademarks, including Orchard Therapeutics plc and our corporate logo. All other trade names, trademarks and service marks of other companies

[Table of Contents](#)

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

PRESENTATION OF FINANCIAL INFORMATION

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

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

PROSPECTUS SUMMARY

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

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

We are a global gene therapy company dedicated to transforming the lives of people affected by rare diseases through the development of innovative, potentially curative gene therapies. Our *ex vivo* autologous hematopoietic stem cell, or HSC, gene therapy approach harnesses the power of genetically modified blood stem cells and seeks to correct the underlying cause of disease in a single administration. We seek to achieve this outcome by utilizing a lentiviral vector to introduce a functional copy of a missing or faulty gene into the patient’s own, or autologous, HSCs through an *ex vivo* process, resulting in a gene-modified cellular drug product that can then be administered to the patient at the bedside.

To date, over 160 patients have been treated with our current and former product candidates across seven different diseases, with follow-up periods of more than 11 years following a single administration. We believe the data observed across these development programs, in combination with our expertise in the development, manufacturing and commercialization of gene and cell therapies, position us to provide potentially curative therapies to people suffering from a broad range of diseases.

We are currently focusing our *ex vivo* autologous HSC gene therapy approach on severe neurometabolic diseases and early research programs. Our lead program is OTL-200, which was approved in the European Union, the United Kingdom, Iceland, Liechtenstein and Norway under the brand name Libmeldy for eligible patients with early-onset metachromatic leukodystrophy, or MLD. Three eligible patients have been treated in a commercial setting to date. Our planned BLA submission timeline for OTL-200 with the U.S. Food and Drug Administration is late 2022 to early 2023.

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

Corporate Information

We were originally incorporated under the laws of England and Wales in August 2018 as Orchard Rx Limited (now known as Orchard Therapeutics plc) to become a holding company for Orchard Therapeutics (Europe) Limited (previously known as Orchard Therapeutics Limited). Orchard Rx Limited subsequently re-registered as a public limited company and its name was changed from Orchard Rx Limited to Orchard Therapeutics plc in October 2018. Orchard Therapeutics (Europe) Limited was originally incorporated under the laws of England and Wales in September 2015 as Newincco 1387 Limited and subsequently changed its name to Orchard

[Table of Contents](#)

Therapeutics Limited in November 2015 and to Orchard Therapeutics (Europe) Limited in October 2018. Our registered office is located at 108 Cannon Street, London EC4N 6EU, United Kingdom, and our telephone number is +44 (0) 203 808 8286. Our website address is www.orchard-tx.com. We do not incorporate the information on or accessible through our website into this prospectus, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus.

RISK FACTORS

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

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference into it contain forward-looking statements. Forward-looking statements relate to future events or our future financial performance. We generally identify forward-looking statements by terminology such as “may,” “would,” “should,” “expects,” “plans,” “anticipates,” “could,” “intends,” “target,” “projects,” “contemplates,” “believes,” “estimates,” “predicts,” “assume,” “intend,” “potential,” “continue” or other similar words or the negative of these terms. These statements are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. The outcome of the events described in these forward-looking statements is subject to risks, uncertainties and other factors referenced under in “Risk Factors” in this prospectus and described in any prospectus supplement and our periodic filings with the SEC incorporated by reference in this prospectus or any prospectus supplement. Accordingly, you should not place undue reliance upon these forward-looking statements. We cannot assure you that the events and circumstances reflected in the forward-looking statements will be achieved or occur, the timing of events and circumstances and actual results could differ materially from those projected in the forward looking statements. Forward-looking statements contained in this prospectus include, but are not limited to, statements about:

- the timing, progress and results of clinical trials and preclinical studies for our programs and product candidates, including statements regarding the timing of initiation and completion of trials or studies and related preparatory work and the period during which the results of the trials or studies will become available;
- the timing, scope and likelihood of regulatory submissions, filings and approvals;
- our ability to develop and advance product candidates into, and successfully complete, clinical trials;
- our expectations regarding the market opportunity for and size of the patient populations for Libmeldy (OTL-200) and our product candidates, if approved for commercial use;
- the implementation of our business model and our strategic plans for our business, commercial products, product candidates and technology;
- our plans and ability to build out our commercial infrastructure and successfully identify eligible patients for Libmeldy in Europe and our product candidates, if approved for commercial use;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the pricing and reimbursement of Libmeldy and any of our product candidates, if approved, including reimbursement for patients treated in a country where they are not a resident;
- the adequacy, scalability and commercial viability of our manufacturing capacity, methods and processes, including those of our manufacturing partners, and our plans for future development;
- the rate and degree of market acceptance and clinical utility of our commercial products and product candidates and gene therapy in general;
- our ability to establish or maintain collaborations or strategic relationships or obtain additional funding;
- the impact of the COVID-19 global pandemic on our business operations;
- our competitive position;
- the scope of protection we and our licensors are able to establish and maintain for intellectual property rights covering our commercial products and product candidates;
- developments and projections relating to our competitors and our industry;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;

Table of Contents

- the impact of laws and regulations;
- our ability to attract and retain qualified employees and key personnel;
- our ability to contract with third-party suppliers, clinical sites and manufacturers and their ability to perform adequately;
- our projected financial condition, including the sufficiency of our cash, cash equivalents and investments to fund operations in future periods and future liquidity, working capital and capital requirements; and
- other risks and uncertainties, including those listed under the caption “Risk factors” in this prospectus as well as those risk factors that are incorporated by reference in this prospectus.

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

CAPITALIZATION

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

SECURITIES WE MAY OFFER

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

DESCRIPTION OF SHARE CAPITAL AND ARTICLES OF ASSOCIATION

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

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

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

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

- general authorization of our directors for purposes of Section 551 of the Companies Act 2006 to allot shares in the company or grant rights to subscribe for or convert any securities into shares in the company up to a maximum aggregate nominal amount of £13,023,851.50 for a period of five years from the date of the 2021 annual general meeting; and
- empowering of our directors pursuant to Section 570 of Companies Act 2006 to allot equity securities for cash pursuant to the Section 551 authority referred to above as if the statutory preemption rights under Section 561(1) of the Companies Act 2006 did not apply to such allotments.

Issued share capital

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

Ordinary shares

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

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

Registered shares

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

[Table of Contents](#)

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

Under the Companies Act 2006, we must enter an allotment of shares in our share register as soon as practicable and in any event within two months of the allotment. We will perform all procedures necessary to update the share register to reflect the ordinary shares being sold in any offering, including updating the share register with the number of ordinary shares to be issued to the depositary upon the closing of any offering. We are also required by the Companies Act 2006 to register a transfer of shares (or, if applicable, give the transferee notice of and reasons for refusal as the transferee may reasonably request) as soon as practicable and in any event within two months of receiving notice of the transfer.

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

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

Preemptive rights

English law generally provides shareholders with preemptive rights when new shares are issued for cash; however, it is possible for the articles of association, or shareholders in general meeting, to exclude preemptive rights. Such an exclusion of preemptive rights may be for a maximum period of up to five years from the date of adoption of the articles of association, if the exclusion is contained in the articles of association, or from the date of the shareholder resolution, if the exclusion is by shareholder resolution. In either case, this exclusion would need to be renewed by our shareholders upon its expiration (i.e., at least every five years). At our annual general meeting in June 2021 our shareholders approved the exclusion of preemptive rights for a period of five years from the date of approval, which exclusion will need to be renewed upon expiration (i.e., at least every five years) to remain effective, but may be sought more frequently for additional five-year terms (or any shorter period).

Registration rights

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

Demand registration rights

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

Short-form registration rights

Pursuant to the investment and shareholders’ agreement, for so long as we are eligible to file a registration statement on Form F-3 or Form S-3, upon the written request of holders of a majority of these securities at an

[Table of Contents](#)

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

Piggyback registration rights

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

Indemnification

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

Expiration of registration rights

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

Articles of association

Our current Articles of Association, or the Articles, were adopted by our shareholders at our 2020 annual general shareholder meeting. A summary of the terms of the Articles is set out below. The summary below is not a complete copy of the terms of the Articles.

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

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

Share capital

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

Voting

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

Table of Contents

Variation of rights

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

Dividends

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

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

Liquidation Preference

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

Transfer of ordinary shares

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

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

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

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

Allotment of shares and preemption rights

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

[Table of Contents](#)

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

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

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

Alteration of share capital

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

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

Board of directors

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

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

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

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

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

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

Table of Contents

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

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

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

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

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

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

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

General meetings

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

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

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;

Table of Contents

- (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.

	England and Wales	Delaware
Number of Directors	Under the Companies Act 2006, a public limited company must have at least two directors and the number of directors may be fixed by or in the manner provided in a company's articles of association.	Under Delaware law, a corporation must have at least one director and the number of directors shall be fixed by or in the manner provided in the bylaws.
Removal of Directors	Under the Companies Act 2006, shareholders may remove a director without cause by an ordinary resolution (which is passed by a	Under Delaware law, any director or the entire board of directors may be removed, with or without cause, by the holders of a majority of the shares

	England and Wales	Delaware
	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.	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. Shareholders holding at least 5% of the paid-up capital of the company carrying voting rights at general meetings (excluding any paid up capital held as treasury shares) can	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.

	England and Wales	Delaware
Notice of General Meetings	<p>require the directors to call a general meeting and, if the directors fail to do so within a certain period, may themselves convene a general meeting.</p> <p>Under the Companies Act 2006, at least 21 days' notice must be given for an annual general meeting and any resolutions to be proposed at the meeting. Subject to a company's articles of association providing for a longer period, at least 14 days' notice is required for any other general meeting of a public limited company. In addition, certain matters, such as the removal of directors or auditors, require special notice, which is 28 days' notice. The shareholders of a company may in all cases consent to a shorter notice period, the proportion of shareholders' consent required being 100% of those entitled to attend and vote in the case of an annual general meeting and, in the case of any other general meeting, a majority in number of the members having a right to attend and vote at the meeting, being a majority who together hold not less than 95% in nominal value of the shares giving a right to attend and vote at the meeting.</p>	<p>Under Delaware law, unless otherwise provided in the certificate of incorporation or bylaws, written notice of any meeting of the stockholders must be given to each stockholder entitled to vote at the meeting not less than ten nor more than 60 days before the date of the meeting and shall specify the place, date, hour and purpose or purposes of the meeting.</p>
Proxy	<p>Under the Companies Act 2006, at any meeting of shareholders, a shareholder may designate another person to attend, speak and vote at the meeting on their behalf by proxy.</p>	<p>Under Delaware law, at any meeting of stockholders, a stockholder may designate another person to act for such stockholder by proxy, but no such proxy shall be voted or acted upon after three years from its date, unless the proxy provides for a longer period. A director of a Delaware corporation may not issue a proxy representing the director's voting rights as a director.</p>
Preemptive Rights	<p>Under the Companies Act 2006, "equity securities," being (i) shares in the company other than shares that, with respect to dividends and capital, carry a right to participate only up to a specified amount in a distribution, referred to as "ordinary shares," or</p>	<p>Under Delaware law, shareholders have no preemptive rights to subscribe to additional issues of stock or to any security convertible into such stock unless, and except to the extent that, such rights are expressly provided for in the certificate of incorporation.</p>

	England and Wales	Delaware
Authority to Allot	<p>(ii) rights to subscribe for, or to convert securities into, ordinary shares, proposed to be allotted for cash must be offered first to the existing equity shareholders in the company in proportion to the respective nominal value of their holdings, unless an exception applies or a special resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise in each case in accordance with the provisions of the Companies Act. See “Description of Share Capital and Articles of Association—Preemptive Rights” in this prospectus.</p> <p>Under the Companies Act 2006, the directors of a company must not allot shares or grant rights to subscribe for or convert any security into shares unless an exception applies or an ordinary resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise, in each case in accordance with the provisions of the Companies Act.</p>	<p>Under Delaware law, if the corporation’s charter or certificate of incorporation so provides, the board of directors has the power to authorize the issuance of stock. The board may authorize capital stock to be issued for consideration consisting of cash, any tangible or intangible property or any benefit to the corporation or any combination thereof. It may determine the amount of such consideration by approving a formula. In the absence of actual fraud in the transaction, the judgment of the directors as to the value of such consideration is conclusive.</p>
Liability of Directors and Officers	<p>Under the Companies Act 2006, any provision, whether contained in a company’s articles of association or any contract or otherwise, that purports to exempt a director of a company, to any extent, from any liability that would otherwise attach to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company, is void. Any provision by which a company directly or indirectly provides an indemnity, to any extent, for a director of the company or of an associated company against any liability attaching to him in connection with any negligence, default, breach</p>	<p>Under Delaware law, a corporation’s certificate of incorporation may include a provision eliminating or limiting the personal liability of a director to the corporation and its stockholders for damages arising from a breach of fiduciary duty as a director. However, no provision can limit the liability of a director for:</p> <ul style="list-style-type: none">• any breach of the director’s duty of loyalty to the corporation or its stockholders;• acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;

	England and Wales	Delaware
	<p>of duty or breach of trust in relation to the company of which he is a director is also void except as permitted by the Companies Act, which provides exceptions for the company to company against any liability attaching to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company of which he is a director is also void except as permitted by the Companies Act 2006, which provides exceptions for the company to (i) purchase and maintain insurance against such liability; (ii) provide a “qualifying third party indemnity,” or an indemnity against liability incurred by the director to a person other than the company or an associated company or criminal proceedings in which he is convicted; and (iii) provide a “qualifying pension scheme indemnity,” or an indemnity against liability incurred in connection with the company’s activities as trustee of an occupational pension plan.</p>	<ul style="list-style-type: none">• intentional or negligent payment of unlawful dividends or stock purchases or redemptions; or• any transaction from which the director derives an improper personal benefit.
Voting Rights	<p>Under English law, unless a poll is demanded by the shareholders of a company or is required by the chairman of the meeting or the company’s articles of association, shareholders shall vote on all resolutions on a show of hands. Under the Companies Act, a poll may be demanded by (i) not fewer than five 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</p>	<p>Delaware law provides that, unless otherwise provided in the certificate of incorporation, each stockholder is entitled to one vote for each share of capital stock held by such stockholder.</p>

	England and Wales	Delaware
Shareholder Vote on Certain Transactions	<p>10% of the total sum paid up on all the shares conferring that right. A company's articles of association may provide more extensive rights for shareholders to call a poll.</p> <p>Under English law, an ordinary resolution is passed on a show of hands if it is approved by a simple majority (more than 50%) of the votes cast by shareholders present (in person or by proxy) and entitled to vote. If a poll is demanded, an ordinary resolution is passed if it is approved by holders representing a simple majority of the total voting rights of shareholders present, in person or by proxy, who, being entitled to vote on the resolution. Special resolutions require the affirmative vote of not less than 75% of the votes cast by shareholders present, in person or by proxy, at the meeting.</p> <p>The Companies Act 2006 provides for schemes of arrangement, which are arrangements or compromises between a company and any class of shareholders or creditors and used in certain types of reconstructions, amalgamations, capital reorganizations or takeovers.</p> <p>These arrangements require:</p> <ul style="list-style-type: none">• the approval at a shareholders' or creditors' meeting convened by order of the court, of a majority in number representing 75% in value of the shareholders or creditors or class thereof present and voting, either in person or by proxy; and• the approval of the court.	<p>Generally, under Delaware law, unless the certificate of incorporation provides for the vote of a larger portion of the stock, completion of a merger, consolidation, sale, lease or exchange of all or substantially all of a corporation's assets or dissolution requires:</p> <ul style="list-style-type: none">• the approval of the board of directors; and• the approval by the vote of the holders of a majority of the outstanding stock or, if the certificate of incorporation provides for more or less than one vote per share, a majority of the votes of the outstanding stock of the corporation entitled to vote on the matter.
Standard of Conduct for Directors	<p>Under English law, a director owes various statutory and fiduciary duties to the company, including:</p> <ul style="list-style-type: none">• to act in the way he considers, in good faith, would be most likely to promote the success of the company for the benefit of its members as a whole;	<p>Delaware law does not contain specific provisions setting forth the standard of conduct of a director. The scope of the fiduciary duties of directors is generally determined by the courts of the State of Delaware. In general, directors have a duty to act without self-interest, on a well-informed basis and in a manner they</p>

England and Wales

- to avoid a situation in which he has, or can have, a direct or indirect interest that conflicts, or possibly conflicts, with the interests of the company;
- to act in accordance with the company's constitution and only exercise his powers for the purposes for which they are conferred;
- to exercise independent judgment;
- to exercise reasonable care, skill and diligence;
- not to accept benefits from a third party conferred by reason of his being a director or doing, or not doing, anything as a director; and
- to declare any interest that he has, whether directly or indirectly, in a proposed or existing transaction or arrangement with the company.

Delaware

reasonably believe to be in the best interest of the stockholders.

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

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

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

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

England and Wales

2006 provides that (i) a court may allow a shareholder to bring a derivative claim (that is, an action in respect of and on behalf of the company) in respect of a cause of action arising from a director's negligence, default, breach of duty or breach of trust and (ii) a shareholder may bring a claim for a court order where the company's affairs have been or are being conducted in a manner that is unfairly prejudicial to some of its shareholders.

Delaware

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 our registrar, Equiniti Limited. The share register reflects only record owners of our ordinary shares. Holders of our ADSs are not treated as our shareholders and their names are therefore not entered in our share register. The 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

Citibank, N.A., or Citibank, is the depository for the ADSs. Citibank's depository offices are located at, 388 Greenwich Street, New York, New York 10013. ADSs represent ownership interests in securities that are on deposit with the depository. ADSs may be represented by certificates that are commonly known as American Depositary Receipts, or ADRs. The depository typically appoints a custodian to safekeep the securities on deposit. In this case, the custodian is Citibank, N.A., London Branch, located at 25 Canada Square, Canary Wharf, London, E14 5LB, United Kingdom.

We have appointed Citibank as depository pursuant to a deposit agreement. A copy of the deposit agreement is on file with the SEC under cover of a registration statement on Form F-6. You may obtain a copy of the deposit agreement from the SEC's website (www.sec.gov). Please refer to Registration No. 333-227905 when retrieving such copy.

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

Each ADS represents the right to receive, and to exercise the beneficial ownership interests in, one ordinary share that is on deposit with the depository and/or custodian. An ADS also represents the right to receive, and to exercise the beneficial interests in, any other property received by the depository or the custodian on behalf of the owner of the ADS but that has not been distributed to the owners of ADSs because of legal restrictions or practical considerations. We and the depository may agree to change the ADS-to-ordinary share ratio by amending the deposit agreement. This amendment may give rise to, or change, the depository fees payable by ADS owners. The custodian, the depository and their respective nominees will hold all deposited property for the benefit of the holders and beneficial owners of ADSs. The deposited property does not constitute the proprietary assets of the depository, the custodian or their nominees. Beneficial ownership in the deposited property will under the terms of the deposit agreement be vested in the beneficial owners of the ADSs. The depository, the custodian and their respective nominees will be the record holders of the deposited property represented by the ADSs for the benefit of the holders and beneficial owners of the corresponding ADSs. A beneficial owner of ADSs may or may not be the holder of ADSs. Beneficial owners of ADSs will be able to receive, and to exercise beneficial ownership interests in, the deposited property only through the registered holders of the ADSs, the registered holders of the ADSs (on behalf of the applicable ADS owners) only through the depository, and the depository (on behalf of the owners of the corresponding ADSs) directly, or indirectly, through the custodian or their respective nominees, in each case upon the terms of the deposit agreement.

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

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

Table of Contents

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

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

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

Dividends and Distributions

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

Distributions of Cash

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

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

[Table of Contents](#)

The distribution of cash will be made net of the fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. The depository will hold any cash amounts it is unable to distribute in a non-interest bearing account for the benefit of the applicable holders and beneficial owners of ADSs until the distribution can be effected or the funds that the depository holds must be escheated as unclaimed property in accordance with the laws of the relevant states of the United States.

Distributions of Shares

Whenever we make a free distribution of ordinary shares for the securities on deposit with the custodian, we will deposit the applicable number of ordinary shares with the custodian. Upon receipt of confirmation of such deposit, the depository will either distribute to holders new ADSs representing the ordinary shares deposited or modify the ADS-to-ordinary shares ratio, in which case each ADS you hold will represent rights and interests in the additional ordinary shares so deposited. Only whole new ADSs will be distributed. Fractional entitlements will be sold and the proceeds of such sale will be distributed as in the case of a cash distribution.

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

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

Distributions of Rights

Whenever we intend to distribute rights to subscribe for additional ordinary shares, we will give prior notice to the depository and we will assist the depository in determining whether it is lawful and reasonably practicable to distribute rights to subscribe for additional ADSs to holders.

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

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

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

The depository will sell the rights that are not exercised or not distributed if such sale is lawful and reasonably practicable. The proceeds of such sale will be distributed to holders as in the case of a cash distribution. If the depository is unable to sell the rights, it will allow the rights to lapse.

Elective Distributions

Whenever we intend to distribute a dividend payable at the election of shareholders either in cash or in additional shares, we will give prior notice thereof to the depository and will indicate whether we wish the elective

[Table of Contents](#)

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

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

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

Other Distributions

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

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

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

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

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

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

Redemption

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

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

Changes Affecting Ordinary Shares

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

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

Issuance of ADSs upon Deposit of Ordinary Shares

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

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

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

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

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

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

Transfer, Combination and Split Up of ADRs

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

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

Table of Contents

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

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

Withdrawal of Ordinary Shares upon Cancellation of ADSs

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

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

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

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

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

Voting rights

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

At our request, the depository will distribute to you any notice of shareholders' meeting received from us together with information explaining how to instruct the depository to exercise the voting rights of the ordinary shares represented by ADSs. In lieu of distributing such materials, the depository bank may distribute to holders of ADSs instructions on how to retrieve such materials upon request.

Table of Contents

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

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

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

Fees and charges

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

<u>Service</u>	<u>Fee</u>
(1) Issuance of ADSs (e.g., an issuance of ADS upon a deposit of ordinary shares or upon a change in the ADS(s)-to-ordinary shares ratio, or for any other reason), excluding ADS issuances as a result of distributions of ordinary shares as described in paragraph (4) below.	Up to \$0.05 per ADS issued
(2) Cancellation of ADSs (e.g., a cancellation of ADSs for delivery of deposited property or upon a change in the ADS(s)-to-ordinary shares ratio, or for any other reason).	Up to \$0.05 per ADS cancelled
(3) Distribution of cash dividends or other cash distributions (e.g., upon a sale of rights and other entitlements).	Up to \$0.05 per ADS held
(4) Distribution of ADSs pursuant to (i) ordinary share dividends or other free ordinary share distributions, or (ii) exercise of rights to purchase additional ADSs.	Up to \$0.05 per ADS held
(5) Distribution of securities other than ADSs or rights to purchase additional ADSs (e.g., upon a spin-off).	Up to \$0.05 per ADS held
(6) ADS Services.	Up to \$0.05 per ADS held on the applicable record date(s) established by the depositary

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

- taxes (including applicable interest and penalties) and other governmental charges;
- the registration fees as may from time to time be in effect for the registration of ordinary shares on the share register and applicable to transfers of ordinary shares to or from the name of the custodian, the depositary, or any nominees upon the making of deposits and withdrawals, respectively;

Table of Contents

- certain cable, telex and facsimile transmission and delivery expenses;
- the expenses and charges incurred by the depositary in the conversion of foreign currency;
- the fees and expenses incurred by the depositary in connection with compliance with exchange control regulations and other regulatory requirements applicable to ordinary shares, ADSs and ADRs; and
- the fees and expenses incurred by the depositary, the custodian or any nominee in connection with the servicing or delivery of deposited property.

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

In the event of refusal to pay the depositary fees, the depositary may, under the terms of the deposit agreement, refuse the requested service until payment is received or may set off the amount of the depositary fees from any distribution to be made to the ADS holder. Certain depositary fees and charges (such as the ADS services fee) may become payable shortly after the closing of 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

[Table of Contents](#)

give notice to the holders at least 30 days before termination. Until termination, your rights under the deposit agreement will be unaffected.

Termination

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

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

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

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

Transmission of notices, reports and proxy soliciting material

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

Limitations on obligations and liabilities

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

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

Table of Contents

- We and the depository disclaim any liability if we or the depository are prevented or forbidden from or subject to any civil or criminal penalty or restraint on account of, or delayed in, doing or performing any act or thing required by the terms of the deposit agreement, by reason of any provision, present or future of any law or regulation, or by reason of present or future provision of any provision of our Articles of Association or any provision of or governing the securities on deposit, or by reason of any act of God or war or other circumstances beyond our control.
- We and the depository 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 depository 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 depository 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 depository 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 depository 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 depository bank and you as ADS holder.
- Nothing in the deposit agreement precludes Citibank (or its affiliates) from engaging in transactions in which parties adverse to us or the ADS owners have interests, and nothing in the deposit agreement obligates Citibank to disclose those transactions, or any information obtained in the course of those transactions, to us or to the ADS owners, or to account for any payment received as part of those transactions.

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

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

Taxes

You will be responsible for the taxes and other governmental charges payable on the ADSs and the ordinary shares represented by the ADSs. We, the depository and the custodian may deduct from any distribution the taxes

[Table of Contents](#)

and governmental charges payable by holders and may sell any and all property on deposit to pay the taxes and governmental charges payable by holders. You will be liable for any deficiency if the sale proceeds do not cover the taxes that are due.

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

Foreign currency conversion

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

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

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

Governing Law/Waiver of Jury Trial

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

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

The deposit agreement provides that, to the extent permitted by law, ADS holders waive the right to a jury trial of any claim they may have against us or the depositary arising out of or relating to our ordinary shares, the ADSs or the deposit agreement, including any claim under U.S. federal securities laws. If we or the 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 may offer under this prospectus. When we offer to sell a particular series of debt securities, we will describe the specific terms of the securities in a supplement to this prospectus, including any additional covenants or changes to existing covenants relating to such series. The prospectus supplement also will indicate whether any of the general terms and provisions described in this prospectus apply to a particular series of debt securities. You should read the applicable indenture if you do not fully understand a term or the way we use it in this prospectus.

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

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

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

General

We expect that the indentures will:

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

Table of Contents

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;

Table of Contents

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

Table of Contents

- 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

Table of Contents

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.

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;

Table of Contents

- 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;

Table of Contents

- 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 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.

Table of Contents

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 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;

Table of Contents

- 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.

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;

Table of Contents

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

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

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

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

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

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

Subordination

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

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

[Table of Contents](#)

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

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

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

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

Defeasance and Discharge

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

Defeasance of Certain Covenants

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

Conversion Rights

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

Global Securities

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

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

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

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

Table of Contents

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

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

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

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

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

No Recourse

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

[Table of Contents](#)

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

DESCRIPTION OF WARRANTS

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

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

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

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

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

DESCRIPTION OF UNITS

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

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

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

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

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

TAXATION

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

Our most recent Annual Report on Form 10-K for the year ended December 31, 2021, 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, 2021, as updated by other reports and documents we file with the SEC after the date of this prospectus and that are incorporated by reference herein, provides a discussion of the material U.K. tax consequences that may be relevant to prospective investors in our ordinary shares. The applicable prospectus supplement may also contain information about any U.K. tax considerations relating to the securities covered by such prospectus supplement.

USE OF PROCEEDS

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

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

PLAN OF DISTRIBUTION

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

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

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

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

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

We may use a dealer to sell our securities.

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

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

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

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

Table of Contents

We may enter into derivative or hedging transactions with third parties or sell securities not covered by this prospectus to third parties in privately negotiated transactions. In connection with such a transaction, the third parties may sell securities covered by and pursuant to this prospectus and any accompanying prospectus supplement. If so, the third party may use securities borrowed from us or others to settle such sales and may use securities received from us to close out any related short positions. We may also loan or pledge securities covered by this prospectus and any accompanying prospectus supplement to third parties, who may sell the loaned securities or, in an event of default in the case of a pledge, sell the pledged securities pursuant to this prospectus and any accompanying prospectus supplement.

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

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

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

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

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

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

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

[Table of Contents](#)

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

LEGAL MATTERS

Certain legal matters of English law and U.S. federal law will be passed upon for us by Goodwin Procter (UK) LLP and Goodwin Procter LLP, respectively. Any underwriters will be advised about other issues relating to any offering by their own legal counsel.

EXPERTS

The financial statements incorporated in this Prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2021 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

SERVICE OF PROCESS AND ENFORCEMENT OF LIABILITIES

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

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

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

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

[Table of Contents](#)

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

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

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

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

WHERE YOU CAN FIND MORE INFORMATION

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

This prospectus is part of the registration statement we filed with the SEC. This prospectus omits some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the registration statement for further information about us and our consolidated subsidiaries and the securities we are offering. Statements in this prospectus concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements. You can obtain a copy of the registration statement from the SEC's website.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus the information contained in other documents we file with the SEC, which means that we can disclose important information to you by referring you to those documents. Any statement contained in any document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded, for purposes of this prospectus, to the extent that a statement contained in or omitted from this prospectus, or in any other subsequently filed document that also is or is deemed to be incorporated by reference herein, modifies or supersedes such statement. Any such statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus. We incorporate by reference the documents listed below which have been filed by us:

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

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

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

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

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

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.



\$30,000,000

American Depositary Shares representing Ordinary Shares

PROSPECTUS SUPPLEMENT

Guggenheim Securities

October 6, 2022
