UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

SCHEDULE 14A

Proxy Statement Pursuant to Section 14(a) of the Securities Exchange Act of 1934 (Amendment No.

)

Filed by the Registrant \boxtimes

Filed by a Party other than the Registrant \Box

Check the appropriate box:

Preliminary Proxy Statement

□ Confidential, for Use of the Commission Only (as permitted by Rule 14a-6(e)(2))

□ Definitive Proxy Statement

Definitive Additional Materials

□ Soliciting Material under §240.14a-12

ORCHARD THERAPEUTICS PLC

(Name of Registrant as Specified In Its Charter)

N/A

(Name of Person(s) Filing Proxy Statement, if other than the Registrant)

Payment of Filing Fee (Check all boxes that apply):

No fee required.

□ Fee paid previously with preliminary materials.

Fee computed on table in exhibit required by Item 25(b) per Exchange Act Rules 14a-6(i)(1) and 0-11



April [], 2023

Re: 2023 Annual General Meeting of Orchard Therapeutics plc

Dear Shareholders,

On behalf of our Board of Directors and employees, thank you for your investment in, and continued support of, Orchard Therapeutics plc (the "**Company**").

This letter, the notice of the Annual General Meeting of Shareholders (the "AGM") set out in this document (the "Notice"), and associated materials for the AGM are being sent to you because, as of April [], 2023 (being the latest practicable date before the circulation of this document), you are registered as a holder of ordinary shares in the register of members of the Company. This letter, the Notice and associated materials will also be available to holders of American Depositary Shares ("ADS") and contains information relevant to holders of ADSs.

Our AGM will take place at [] at []. The Notice is set out in this document, and it contains the resolutions to be proposed at the AGM (the "**Resolutions**").

For the purposes of the AGM, a quorum will be formed by one or more qualifying persons present at a meeting and between them holding at least $33 \frac{1}{3}$ percent in number of the issued shares. A "qualifying person" is an individual who is a member, a person authorized to act as the representative of a member (being a corporation) in relation to the meeting, or a person appointed as proxy of a member in relation to the meeting.

ACTION TO BE TAKEN BY HOLDERS OF ORDINARY SHARES

If you are a holder of ADSs, please ignore this section and refer instead to the section below titled—"Action to be taken by Holders of American Depositary Shares".

If you are a holder of ordinary shares in the Company, please vote on the Resolutions by appointing a proxy. A form of proxy (the "Ordinary Shareholder Proxy Form") for use at the AGM is enclosed. You are encouraged to appoint the Chair of the AGM as your proxy.

You are advised to complete and return the Ordinary Shareholder Proxy Form in accordance with the instructions printed on it. Your completed Ordinary Shareholder Proxy Form must arrive at the Company's registrar, Equiniti, Aspect House, Spencer Road, Lancing, West Sussex, BN99 6DA, England as soon as possible but in any event by no later than [1].

In order to attend and vote at the AGM as an ordinary shareholder, you must continue to be registered as a holder of ordinary shares in the Company's register of members as of [].

Therefore, if you sell or transfer your ordinary shares in the Company on or prior to [, 2023], your Ordinary Shareholder Proxy Form can no longer be used and, if submitted (whether before or after you sell or transfer your ordinary shares), will be treated as invalid. Please pass this document to the person who arranged the sale or transfer for delivery to the purchaser or transferee. The purchaser or transferee should contact Christopher York, Company Secretary, by telephone at +44 (0) 203 808 8286 to request a new Ordinary Shareholder Proxy Form.

Should you elect to convert your holding of ordinary shares in the capital of the Company into an interest in the capital of the Company represented by ADSs before the AGM, you will cease to be a holder of ordinary shares in your own name and will not be entitled to vote at the AGM as an ordinary shareholder. You will also not be able to use the enclosed Ordinary Shareholder Proxy Form. However, you may be able to exercise your vote as a holder of an interest in the capital of the Company represented by American Depositary Shares. Please refer to the next section titled —"*Action to be taken by Holders of American Depositary Shares*".

ACTION TO BE TAKEN BY HOLDERS OF AMERICAN DEPOSITARY SHARES

In order to exercise your vote as a holder of an interest in the capital of the Company represented by ADSs, you or your bank, broker or nominee must be registered as a holder of ADSs in the ADS register maintained by our depositary, Citibank, N.A., at [] on [] (the record date for ADS holders).

If you held ADSs through a bank, broker or nominee on April [], 2023, the AGM documentation, including the ADS proxy card, will be sent to that organization which should forward the materials to you. Please reach out to your bank, broker or nominee to provide your voting instructions.

Please note that ADS proxy cards submitted by ADS holders must be received by Citibank, N.A. no later than [].

CONTACTS FOR ADS HOLDERS

If you have queries about how you can deliver voting instructions, please contact Citibank, N.A. —ADR Shareholder Services by telephone: +1-877-248-4237 (toll free within the United States) or +1-781-575-4555 (for international callers) or by email: citibank@shareholders-online.com or at Citibank, N.A. — Shareholder Services, P.O. Box 505050, Louisville, KY 40233-9724.

CONTACTS AT THE COMPANY

If at any point you require guidance, please contact Christopher York, Company Secretary, by telephone at +44 (0) 203 808 8286.

RECOMMENDATION

The Board of Directors believe that each Resolution is in the best interest of the Company and its shareholders as a whole and is likely to promote the success of the Company. Accordingly, the Board of Directors unanimously recommends that you vote in favor of each of the Resolutions. Each director with personal holdings of equity interests in the Company intends to do so in respect of his or her own beneficial holdings. You will find an explanatory note in relation to each of the Resolutions in the attached proxy statement.

Thank you for your ongoing support of Orchard Therapeutics.

Sincerely,

James Geraghty Chairman



Orchard Therapeutics plc 245 Hammersmith Road London W6 8PW United Kingdom Registered Company No. 11494381

NOTICE OF 2023 ANNUAL GENERAL MEETING OF SHAREHOLDERS TO BE HELD ON []

NOTICE is hereby given that the Annual General Meeting of Orchard Therapeutics plc, a public limited company incorporated under the laws of England and Wales (referred to herein as the "Company," "we," "us" and "our"), will be held on [] at [], for transaction of the following business:

Ordinary Resolutions

1. To re-elect James Geraghty as a director, who retires by rotation in accordance with the Company's Articles of Association.

2. To re-elect Steven M. Altschuler as a director, who retires by rotation in accordance with the Company's Articles of Association.

3. To re-elect Marc Dunoyer as a director, who retires by rotation in accordance with the Company's Articles of Association.

4. To re-appoint PricewaterhouseCoopers LLP, a United Kingdom entity, as U.K. statutory auditors of the Company, to hold office until the conclusion of the next annual general meeting of shareholders.

5. To ratify the appointment of PricewaterhouseCoopers LLP, a Delaware limited liability partnership, as the Company's independent registered public accounting firm, for the fiscal year ending December 31, 2023.

6. To authorize the Audit Committee to determine the Company's auditors' remuneration for the fiscal year ending December 31, 2023.

7. To receive the U.K. statutory annual accounts and reports for the fiscal year ended December 31, 2022 and to note that the Company's directors do not recommend the payment of any dividend for the year ended December 31, 2022.

8. To approve the compensation of the Company's named executive officers for the year ended December 31, 2022 on a non-binding, advisory basis.

9. To receive and approve the Company's U.K. statutory directors' remuneration report for the year ended December 31, 2022 on a non-binding, advisory basis, which is set forth as *Annex A* to the attached proxy statement.

10. To authorize the Board of Directors, generally and unconditionally for the purpose of s551 of the U.K. Companies Act 2006, to allot shares in the Company or to grant rights to subscribe for or to convert any security into shares in the Company ("Rights") up to a maximum aggregate nominal amount of £18,398,450.

The authority referred to in this resolution shall expire (unless previously renewed, varied or revoked) on [], 2028, but the Company may at any time before the expiration of this authority make an offer or agreement which would or might require shares to be allotted, or Rights to be granted, pursuant to this authority after its expiration, and the Board of Directors may allot shares or grant Rights in pursuance of that offer or agreement as if the authority conferred by this resolution had not expired.

The authority referred to in this resolution is in addition to all subsisting authorities conferred on the Board of Directors in accordance with s551 of the U.K. Companies Act 2006 (including without limitation the authority conferred at the Company's annual general meeting held on 16 June 2021), but the Board of Directors may allot shares or grant Rights pursuant to an offer made or agreement entered into by the Company before the expiry of the authority pursuant to which that offer was made or agreement entered into.

11. To authorize the Board of Directors, generally and unconditionally for the purpose of s551 of the U.K. Companies Act 2006, to allot non-voting ordinary shares of the Company, nominal value £0.10 each, and voting ordinary shares of the Company, nominal value £0.10 each (together, "Ordinary Shares"), and/or to grant rights to subscribe for or to convert any security into Ordinary Shares ("Warrant Rights") up to a maximum nominal amount of £15,158,359, pursuant to the securities purchase agreement between the Company and the purchasers named therein, dated March 6, 2023, as it may be amended from time to time (the "Securities Purchase Agreement") (including, upon exercise of any Warrant Rights granted and/or to be granted in accordance with the Securities Purchase Agreement, the allotment and issue of any resulting Ordinary Shares).

The authority referred to in this resolution shall expire (unless previously renewed, varied or revoked) on March 10, 2026, but the Company may at any time before the expiration of this authority make an offer or agreement which would or might require shares to be allotted, or Warrant Rights to be granted, pursuant to this authority after its expiration, and the Board of Directors may allot shares or grant Warrant Rights in pursuance of that offer or agreement as if the authority conferred by this resolution had not expired.

The authority referred to in this resolution is in addition to all subsisting authorities conferred on the Board of Directors in accordance with s551 of the U.K. Companies Act 2006 (including without limitation the authority conferred at the Company's annual general meeting held on 16 June 2021) and would be in addition to the authority sought in Resolution 10 (if approved), but the Board of Directors may allot shares or grant Warrant Rights pursuant to an offer made or agreement entered into by the Company before the expiry of the authority pursuant to which that offer was made or agreement entered into.

Special resolutions

12. To empower the Board of Directors, generally pursuant to s570(1) of the U.K. Companies Act 2006, to allot equity securities (as defined in s560 of the U.K. Companies Act 2006) for cash pursuant to the general authority conferred on them by Resolution 10 as if s561(1) of the U.K. Companies Act 2006 did not apply to that allotment. This power:

- a. shall be limited to the allotment of equity securities up to a maximum aggregate nominal amount of £18,398,450;
- b. expires (unless previously renewed, varied or revoked), on [], 2028, but the Company may at any time before the expiration of this authority make an offer or agreement which would or might require equity securities to be allotted after that expiry and the Board of Directors may allot equity securities pursuant to any of those offers or agreements as if this power had not expired; and
- c. applies in relation to a sale of shares which is an allotment of equity securities by virtue of s560(3) of the U.K. Companies Act 2006 as if in the first paragraph of this resolution the words "pursuant to the general authority conferred on them by Resolution 10" were omitted.

13. To empower the Board of Directors, generally pursuant to s570(1) of the U.K. Companies Act 2006, to allot equity securities (as defined in s560 of the U.K. Companies Act 2006) for cash pursuant to the general

authority conferred on them by Resolution 11 as if s561(1) of the U.K. Companies Act 2006 did not apply to that allotment. This power:

- a. shall be limited to the allotment of equity securities up to a maximum aggregate nominal amount of £15,158,359; and
- b. expires (unless previously renewed, varied or revoked), on March 10, 2028, but the Company may at any time before the expiration of this authority make an offer or agreement which would or might require equity securities to be allotted after that expiry and the Board of Directors may allot equity securities pursuant to any of those offers or agreements as if this power had not expired.

Proposals 1 through 11 will be proposed as ordinary resolutions under English law. Assuming that a quorum is present, 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) at the meeting and entitled to vote. On a poll, an ordinary resolution is passed if it is approved by holders representing a simple majority (more than 50%) of the total voting rights of shareholders present (in person or by proxy) who (being entitled to vote) vote on the resolution.

Proposals 12 and 13 will be proposed as special resolutions under English law. A special resolution is passed on a show of hands if it is approved by a majority of not less than 75% of the votes cast by shareholders present (in person or by proxy) at the meeting and entitled to vote. On a poll, a special resolution is passed if it is approved by holders representing not less than 75% of the total voting rights of shareholders present (in person or by proxy) who (being entitled to vote) vote on the resolution.

The result of the shareholder votes on the ordinary resolutions in proposals 4 (*appointment of PricewaterhouseCoopers LLP as our U.K. statutory auditors*), 5 (*ratification of the appointment of PricewaterhouseCoopers LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2023*), 7 (*receipt of our U.K. statutory annual accounts and reports for the year ended December 31, 2022*), 8 (*approval of the compensation of our named executive officers for the year ended December 31, 2022*) and 9 (*approval of our U.K. statutory directors' annual report on remuneration for the year ended December 31, 2022*) are advisory in nature and as a result will not require our Board of Directors or any committee thereof to take any action. However, our Board of Directors values the opinions of our shareholders and will carefully consider the outcome of the votes on such proposals.

The results of any polls taken on the resolutions at the Annual General Meeting and any other information required by the U.K. Companies Act 2006 will be made available on our website (*www.orchard-tx.com*) as soon as reasonably practicable following the Annual General Meeting and for the required period thereafter.

BY ORDER OF THE BOARD

/s/

Christopher York Company Secretary April [], 2023

Notes

(a) Only those members registered in the register of members of the Company at [] will be entitled to attend and vote at the Annual General Meeting ("**AGM**") in respect of the number of ordinary shares registered in their name at the time. Changes to entries on the relevant register after that deadline will be disregarded in determining the rights of any person to attend and vote at the AGM. Should the AGM be adjourned or postponed to a time not more than 48 hours after the deadline, the same deadline will also apply for the purpose of determining the entitlement of members to attend and vote (and for the purpose of determining the number of votes they may

Registered Office 245 Hammersmith Road London W6 8PW United Kingdom Registered in England and Wales No. 11494381

cast) at the adjourned or postponed AGM. Should the AGM be adjourned or postponed for a longer period, then to be so entitled, members must be entered on the register of members at the time which is 48 hours before the time fixed for the adjourned or postponed AGM or, if the Company gives notice of the adjourned or postponed AGM, at the time specified in the notice.

(b) Any member may appoint a proxy to attend, speak and vote on his or her behalf. A member may appoint more than one proxy in relation to the AGM provided that each proxy is appointed to exercise the rights attached to a different share or shares of the member. A proxy need not be a member but must attend the meeting in person. If a member wishes his or her proxy to speak on his or her behalf at the AGM, he or she will need to appoint his or her own choice of proxy and give his or her instructions directly to them. Completion and return of Ordinary Shareholder Proxy Form will not preclude a member from attending, speaking and voting at the AGM or any adjournment or postponement thereof in person. If a proxy is appointed and the member attends the AGM in person, the proxy appointment will automatically be terminated. A validly appointed proxy shall be authorized (at his or her discretion) to consent to any adjournment or postponement of the AGM and, unless otherwise terminated or amended in accordance with these notes or the notes to the Ordinary Shareholder Proxy Form, the submitted Ordinary Shareholder Proxy Form shall remain effective at any such adjourned or postponed AGM. The Ordinary Shareholder Proxy Form, used by the holders of ordinary shares to vote, should be lodged with the Company's Registrar (Equiniti Limited) not later than [__] on [__], 2023. The attached proxy statement explains proxy voting and the matters to be voted on in more detail. Please read the proxy statement carefully. For specific information regarding the voting of your ordinary shares, please refer to the proxy statement under the section entitled "*Questions and Answers About Voting*."

(c) Any corporation that is a member can appoint one or more corporate representatives who may exercise on its behalf all of its powers as a member provided that, if it is appointing more than one corporate representative, it does not do so in relation to the same shares.

(d) In the case of joint holders, the vote of the senior holder who tenders the vote whether in person or by proxy will be accepted to the exclusion of the votes of any other joint holders. For these purposes, seniority shall be determined by the order in which the names stand in the Company's relevant register or members for the certificated or uncertificated shares of the Company (as the case may be) in respect of the joint holding.

(e) Certificateless Registry for Electronic Share Transfer ("**CREST**") members who wish to appoint a proxy or proxies through the CREST electronic proxy appointment service may do so for the AGM and any adjournments or postponements of it by using the procedures described in the CREST Manual (available via *www.euroclear.com*). CREST personal members or other CREST sponsored members, and those CREST members who have appointed voting service providers, should refer to their sponsors or voting service providers, who will be able to take the appropriate action on their behalf.

For a proxy appointment or instruction made using the CREST service to be valid, the appropriate CREST message (a "**CREST Proxy Instruction**") must be properly authenticated in accordance with Euroclear's specifications and must contain the information required for those instructions as described in the CREST Manual (available via *www.euroclear.com*). The message, regardless of whether it relates to the appointment of a proxy or to an amendment to the instruction given to the previously appointed proxy, must, to be valid, be transmitted so as to be received by the Company's agent (ID:RA19) by [_] on [_]. For this purpose, the time of receipt will be taken to be the time (as determined by the timestamp applied to the message by the CREST Applications Host) from which the Company's agent is able to retrieve the message by enquiry to CREST in the manner prescribed by CREST. After this time, any change of instructions to proxies appointed through CREST should be communicated to the appointee through other means.

CREST members and, where applicable, their CREST sponsors or voting service providers should note that Euroclear UK does not make available special procedures in CREST for any particular messages. Normal system timings and limitations will, therefore, apply in relation to the input of CREST Proxy Instructions. It is the responsibility of the CREST member concerned to take (or, if the CREST member is a CREST personal member or sponsored member or has appointed voting service providers, to procure that its CREST sponsors or voting service providers take) such action as shall be necessary to ensure that a message is transmitted by means of the

CREST system by any particular time. In this connection, CREST members and, where applicable, their CREST sponsors or voting service providers are referred, in particular, to those sections of the CREST Manual concerning practical limitations of the CREST system and timings.

The Company may treat as invalid a CREST Proxy Instruction in the circumstances set out in Regulation 35(5)(a) of the Uncertificated Securities Regulations 2001.

(f) If you are an institutional investor you may be able to appoint a proxy electronically via the Proxymity platform, a process which has been agreed by the Company and approved by the Registrar. For further information regarding Proxymity, please go to *www.proxymity.io*. Your proxy must be lodged by [] on [] in order to be considered valid. Before you can appoint a proxy via this process you will need to have agreed to Proxymity's associated terms and conditions. It is important that you read these carefully as you will be bound by them and they will govern the electronic appointment of your proxy.

(g) As of April [], 2023 (being the last practicable date before circulation of this Notice), the Company's issued ordinary share capital consisted of [] ordinary shares, carrying one vote each, and [] non-voting ordinary shares, with no voting rights. Therefore, the total voting rights in the Company as of that date are []. Each ADS of the Company represents ten ordinary shares.

(h) Under s527 of the U.K. Companies Act 2006, members meeting the threshold requirement set out in that section have the right to require the Company to publish on a website a statement setting out any matter relating to: (i) the audit of the Company's accounts (including the auditor's report and the conduct of the audit) that are to be laid before the AGM; or (ii) any circumstance connected with an auditor of the Company ceasing to hold office since the previous meeting at which annual accounts and reports were laid in accordance with s437 of the U.K. Companies Act 2006. The Company may not require the shareholders requesting any such website publication to pay its expenses in complying with ss527 or 528 of the U.K. Companies Act 2006. Where the Company is required to place a statement on a website under s527 of the U.K. Companies Act 2006, it must forward the statement to the Company's auditor not later than the time when it makes the statement available on the website. The business which may be dealt with at the AGM includes any statement that the Company has been required, under s527 of the U.K. Companies Act 2006, to publish on a website.

(i) Except as set out in the notes to this Notice, any communication with the Company in relation to the AGM, including in relation to proxies, should be sent to the Company's Registrar, Equiniti Limited, Aspect House, Spencer Road, Lancing, West Sussex, BN99 6DA, England. No other means of communication will be accepted. In particular, you may not use any electronic address provided either in this notice or in any related documents to communicate with the Company for any purpose other than those expressly stated.

(j) Copies of the service agreement for our executive director and of the letters of appointment for our non-executive directors will be available for inspection at the registered office of the Company during normal business hours on any weekday (public holidays excepted) and at the place of the AGM for one hour before the meeting and at the meeting itself.

(k) Any ordinary shareholder attending the meeting has the right to ask questions. The Company must cause to be answered any such question relating to the business being dealt with at the meeting but no such answer need be given if: (i) to do so would interfere unduly with the preparation for the meeting or involve the disclosure of confidential information; (ii) the answer has already been given on a website in the form of an answer to a question; or (iii) it is undesirable in the interests of the Company or the good order of the meeting that the question be answered.

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Orchard Therapeutics plc 245 Hammersmith Road London W6 8PW United Kingdom Registered Company No. 11494381

PROXY STATEMENT FOR THE 2023 ANNUAL GENERAL MEETING OF SHAREHOLDERS TO BE HELD ON []

INFORMATION CONCERNING PROXY SOLICITATION AND VOTING

We have sent you this proxy statement and the enclosed form of proxy (the "Ordinary Shareholder Proxy Form") because the Board of Directors (the "Board" or "Board of Directors") of Orchard Therapeutics plc (referred to herein as the "Company", "we", "us" or "our") is soliciting your proxy to vote at our annual general meeting of shareholders (referred to herein as the "Meeting" or the "AGM") to be held on [1], 2023, at [1], at [1].

- This proxy statement summarizes information about the proposals to be considered at the Meeting and other information you may find
 useful in determining how to vote.
- The Ordinary Shareholder Proxy Form is the means by which ordinary shareholders actually authorize another person to vote their shares in accordance with their instructions.

In addition to solicitations by mail, our directors, officers and regular employees, without additional remuneration, may solicit proxies by telephone, e-mail and personal interviews. All costs of solicitation of proxies will be covered by us.

We are mailing the Notice of 2023 AGM (the "Notice"), this proxy statement and the Ordinary Shareholder Proxy Form to our ordinary shareholders of record as of April [], 2023 (being the latest practicable date before the circulation of this document) for the first time on or about April [], 2023. In this mailing, we are also including our U.K. statutory annual accounts and reports for the year ended December 31, 2022 ("2022 U.K. Annual Report") and our annual report on Form 10-K for the year ended December 31, 2022 ("Annual Report on Form 10-K"). In addition, we have provided brokers, dealers, bankers, and their nominees, at our expense, with additional copies of our proxy materials, the 2022 U.K. Annual Report on Form 10-K so that our record holders can supply these materials to the beneficial owners of our ordinary shares.

While this document is being sent to our ordinary shareholders of record, this document will also be sent to holders of American Depositary Shares ("ADSs") and contains information relevant to holders of ADSs.

Important Notice Regarding the Availability of Proxy Materials for the Shareholder Meeting to be held on [1], 2023:

The Notice, this proxy statement, the Annual Report on Form 10-K, the 2022 U.K. Annual Report, and the Ordinary Shareholder Proxy Form are available on the Investors & Media section of our website at *https://ir.orchard-tx.com/financial-information/sec-filings*.

QUESTIONS AND ANSWERS ABOUT VOTING

1) Why am I receiving these materials?

Ordinary shareholders

We have sent you this proxy statement, the enclosed Ordinary Shareholder Proxy Form and related materials because you are an ordinary shareholder of record and our Board of Directors is soliciting your proxy to vote at the Meeting, including at any adjournments or postponements of the Meeting. You do not need to attend the Meeting to vote your shares. Instead, please simply complete, sign and return the enclosed Ordinary Shareholder Proxy Form. The duly completed Ordinary Shareholder Proxy Form must be lodged with our registrar, Equiniti, by no later than [1] on [1], 2023.

CREST members may appoint a proxy by using the CREST electronic proxy appointment service. CREST members who wish to appoint a proxy or give an instruction through the CREST electronic proxy appointment service may do so by using the procedures described in the CREST manual.

You are encouraged to appoint the Chair of the Meeting as your proxy.

Materials for ordinary shareholders will be mailed on or about [], 2023 to all ordinary shareholders of record entitled to vote at the Meeting.

ADS holders

Materials for ADS holders of record, including this proxy statement, the Annual Report on Form 10-K and an ADS proxy card (the "ADS Proxy Card"), will be mailed on or about [], 2023 to all ADS holders, including banks, brokers and nominees, who are registered as holders of ADSs in the ADS register at [] (the record date for ADS holders).

The duly completed ADS Proxy Cards submitted by the ADS holders of record must be received by Citibank N.A. no later than [] on [], 2023 (the record date for ADS holders).

2) Who can vote at the Meeting?

Ordinary shareholders

Only ordinary shareholders of record registered in the register of members at [] on [], 2023 will be entitled to vote at the Meeting. The holders of ordinary shares are entitled to one vote per share on all matters that are subject to a shareholder vote.

As of [], 2023 (being the last practicable date before the circulation of this proxy statement) there were [] ordinary shares issued and outstanding, which are entitled to vote. There were also [] non-voting ordinary shares outstanding.

Whether or not you plan to attend the Meeting, we urge you to fill out and return the enclosed Ordinary Shareholder Proxy Form to ensure your vote is counted. All proxies, however submitted, must be lodged with Equiniti by no later than [] on [], 2023 for holders of ordinary shares.

You are encouraged to appoint the Chair of the Meeting as your proxy.

If you sell or transfer your ordinary shares in the Company on or prior to [], 2023, your Ordinary Shareholder Proxy Form can no longer be used and if submitted (whether before or after you sell or transfer your ordinary shares) will be treated as invalid. Please pass this document to the person who arranged the sale or

transfer for delivery to the purchaser or transferee. The purchaser or transferee should contact Christopher York, Company Secretary, to request a new Ordinary Shareholder Proxy Form.

Beneficial owners of ordinary shares which are registered in the name of a broker, bank or nominee

If, on [], 2023, your ordinary shares were held in an account at a brokerage firm, bank or other similar organization and you are the beneficial owner of shares, these proxy materials should be forwarded to you by that organization. The organization holding your account is considered the shareholder of record for purposes of voting at the Meeting. You are encouraged to provide voting instructions to your broker, bank or nominee so that they may submit a proxy.

ADS holders

You are entitled to exercise your vote as a holder of an interest in the capital of the Company represented by ADSs if you or your brokerage firm, bank or nominee is registered as a holder of ADSs in the ADS register maintained by Citibank, N.A. as of [] on [], 2023 (the record date for ADS holders).

If you hold ADSs through a brokerage firm, bank or nominee as of the record date, the materials for ADS holders, including the ADS Proxy Card, will be sent to that organization. The organization holding your account is considered the ADS holder of record. Please reach out to that organization to provide your voting instructions.

Please note that ADS Proxy Cards submitted by ADS holders must be received by Citibank, N.A. no later than [] on [], 2023.

Citibank, N.A. will collate all votes properly submitted by ADS holders and submit a vote on behalf of all ADS holders. Each ADS represents ten voting ordinary shares.

Contacts for ADS holders

If you have queries about how you can deliver voting instructions, please contact Citibank, N.A. —ADR Shareholder Services by telephone: +1-877-248-4237 (toll free within the United States) or +1-781-575-4555 (for international callers) or by email: citibank@shareholders-online.com or at Citibank, N.A. — Shareholder Services, P.O. Box 505050, Louisville, KY 40233-9724.

Contacts at the Company

If at any point you require guidance, please contact Christopher York, Company Secretary, by telephone at +44 (0) 203 808 8286.

3) What is the difference between an ordinary shareholder of record and a beneficial owner?

These terms describe how your ordinary shares are held. If your ordinary shares are registered directly in our register of members maintained by Equiniti, our registrar, you are a shareholder of record and the proxy materials are being sent directly, or otherwise being made available, to you. If your ordinary shares are held in the name of a broker, bank or other nominee, you are a beneficial owner of the shares held by your broker, bank or nominee and the proxy materials are being made available or forwarded to you by your broker, bank or other nominee, who is treated as the shareholder of record. As the beneficial owner, you have the right to direct your broker, bank or other nominee on how to vote your ordinary shares by following the voting instructions provided to you by such broker, bank or other nominee.

4) What are the requirements to elect the directors and approve each of the proposals?

You may cast your vote for or against each of the proposals or abstain from voting your shares on one or more of these proposals.

Proposals 1 through 11 will be proposed as ordinary resolutions under English law. Assuming that a quorum is present, 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) at the meeting and entitled to vote. On a poll, an ordinary resolution is passed if it is approved by holders representing a simple majority (more than 50%) of the total voting rights of shareholders present (in person or by proxy) who (being entitled to vote) vote on the resolution.

Proposals 12 and 13 will be proposed as special resolutions under English law. Assuming that a quorum is present, a special resolution is passed on a show of hands if it is approved by the holders of not less than 75% of the votes cast by shareholders present (in person or by proxy) at the meeting and entitled to vote. On a poll, a special resolution is passed if it is approved by holders representing not less than 75% of the total voting rights of shareholders present (in person or by proxy) who (being entitled to vote) vote on the resolution.

The result of the shareholder votes on the ordinary resolutions in proposals 4 (*appointment of PricewaterhouseCoopers LLP as our U.K. statutory auditors*), 5 (*ratification of the appointment of PricewaterhouseCoopers LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2023*), 7 (*receipt of our U.K. statutory annual accounts and reports for the year ended December 31, 2022*), 8 (*approval of the compensation of our named executive officers for the year ended December 31, 2022*) and 9 (*approval of our U.K. statutory directors' annual report on remuneration for the year ended December 31, 2022*) are advisory in nature and as a result will not require our Board of Directors or any committee thereof to take any action. However, our Board of Directors values the opinions of our shareholders and will carefully consider the outcome of the votes on such proposals.

5) What are the voting recommendations of our Board regarding the election of directors and other proposals?

The following table summarizes the items that will be brought for a vote of our shareholders at the Meeting, along with the Board's voting recommendations.

Proposal	Description of Proposal	Board's Recommendation
1	Re-election of James Geraghty to the Board of Directors	FOR
2	Re-election of Steven M. Altschuler to the Board of Directors	FOR
3	Re-election of Marc Dunoyer to the Board of Directors	FOR
4	Re-appointment of PricewaterhouseCoopers LLP, a United Kingdom entity, as U.K. statutory auditors of the Company, to hold office until the conclusion of the next annual general meeting of shareholders*	FOR
5	Ratification of the appointment of PricewaterhouseCoopers LLP, a Delaware limited liability partnership, as the Company's independent registered public accounting firm for the fiscal year ending December 31, 2023*	FOR
6	Authorization for the Audit Committee to determine the Company's auditors' remuneration for the fiscal year ending December 31, 2023	FOR
7	Receipt of the U.K. statutory annual accounts and reports for the fiscal year ended December 31, 2022*	FOR

Proposal	Description of Proposal	Board's Recommendation	
8	Approval of the compensation of the Company's named executive officers for the year-ended December 31, 2022, on a non-binding, advisory basis*	FOR	
9	Approval of our U.K. statutory directors' annual report on remuneration for the year ended December 31, 2022*	report on remuneration for the year ended December 31, 2022* FOR	
10	Authorization for the Board of Directors to allot shares or to grant rights to subscribe for or convert any security into shares up to a maximum aggregate nominal amount of £18,398,450	FOR	
11	Authorization for the Board of Directors to allot non-voting ordinary shares and/or voting ordinary shares (together, the "Ordinary Shares") or to grant rights to subscribe for or convert any security into Ordinary Shares (the "Warrant Rights") up to a maximum aggregate nominal amount of £15,158,359 pursuant to the securities purchase agreement between the Company and purchasers named therein, dated March 6, 2023, as it may be amended from time to time (the "Securities Purchase Agreement") (including, upon exercise of any Warrant Rights granted and/or to be granted in accordance with the Securities Purchase Agreement, the allotment and issue of any resulting Ordinary Shares)	FOR	
12	Empowering the Board of Directors to allot equity securities for cash up to a maximum aggregate nominal amount of £18,398,450 pursuant to the authorization in Resolution 10 as if U.K. statutory pre-emption rights did not apply	FOR	
13	Empowering the Board of Directors to allot equity securities for cash up to a maximum aggregate nominal amount of £15,158,359 pursuant to the authorization in Resolution 11 as if U.K. statutory pre-emption rights did not apply	FOR	

* Denotes an advisory vote.

6) What constitutes a quorum?

In accordance with our Articles of Association and The Nasdaq Stock Market LLC ("Nasdaq") rules, we require 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 vote on the business to be transacted at the Meeting.

If you are an ordinary shareholder of record, your shares will be counted towards the quorum only if you are present in person or represented by proxy at the Meeting. If you are a beneficial owner of ordinary shares held in an account at a brokerage firm, bank or other similar organization your shares will be counted towards the quorum if your broker or nominee submits a proxy for those shares and the proxy represents the holder at the Meeting. If you are an ADS holder you will not count towards the quorum of the Meeting. An ordinary shareholder, including Citibank N.A., represented by a proxy at the Meeting will be counted towards the quorum requirement even where the proxy abstains from voting. If an Ordinary Shareholder Proxy Form does not instruct the proxy how to vote, the proxy may vote as he or she sees fit or abstain in relation to any business of the Meeting, but the member represented by that proxy at the Meeting will be counted towards the quorum requirement.

If there is no quorum, the Meeting will stand adjourned to such time, date and place as may be fixed by the Chair of the Meeting (being not less than 10 clear days after the date of the original meeting). Under our Articles of Association, if a quorum is not present at the adjourned meeting within 15 minutes (or such longer interval as the Chair in his or her absolute discretion thinks fit) from the time appointed for holding the meeting, or if a

quorum ceases to be present during a meeting, the meeting shall be dissolved if convened on the requisition of members and in all other cases shall stand adjourned to another time, date and place as may be fixed by the chairperson of the Meeting (being not less than 10 clear days after the date of the original meeting).

7) How do I vote my shares?

Ordinary shareholders

If you are an ordinary shareholder of record, you may vote in person at the Meeting or if you do not wish to vote in person or will not be attending the Meeting, you may vote by proxy. You may appoint a proxy to vote on your behalf by completing and signing the Ordinary Shareholder Proxy Form and returning it in the envelope provided. If you properly give instructions as to your proxy appointment by executing and returning a form of proxy and your proxy appointment is not subsequently revoked, your shares will be voted in accordance with your instructions. If your ordinary shares are held in an account at a brokerage firm, bank or similar organization, you should follow directions provided by your broker, bank or other nominee.

All proxies must be lodged with our registrar (Equiniti) by no later than [] on [], 2023.

You are encouraged to appoint the Chair of the Meeting as your proxy.

ADS holders

If you are a holder of ADSs, you may exercise your right to vote by completing and submitting the ADS Proxy Card which will be sent to you by Citibank N.A. If your ADSs are held in an account at a brokerage firm, bank or similar organization, you should follow the directions provided by your broker, bank or other nominee. All ADS Proxy Cards, however submitted, must be received by Citibank, N.A. no later than [] on [], 2023.

Citibank N.A. will collate all votes properly submitted by ADS holders and submit a vote to the Company on behalf of all ADS holders.

8) How will my shares be voted if I do not specify how they should be voted?

If you sign and send your Ordinary Shareholder Proxy Form or ADS Proxy Card but do not indicate how you want your shares to be voted, your shares may be voted by the person that you appoint as your proxy as he or she deems fit or your proxy may abstain in relation to any business of the Meeting.

In accordance with the terms of the deposit agreement by and among the Company, Citibank, N.A. as depositary and holders and beneficial owners of ADSs issued thereunder dated as of November 2, 2018 (the "Deposit Agreement") and as amended to date, holders of ADSs as of [] on [], 2023 (the record date for ADS holders) who do not provide the depositary with voting instructions on or before [] on [], 2023 will be deemed to have instructed the depositary to give a discretionary proxy to a person designated by the Company to vote the underlying ordinary shares at the Meeting, and such shares, if such discretionary proxy is given, will be voted in accordance with the Board of Directors' recommendations; provided, however, that no such discretionary proxy shall be given by the depositary with respect to any matter to be voted upon as to which the Company informs the depositary that (a) the Company does not wish such proxy to be given, (b) substantial opposition exists, or (c) the rights of holders of deposited securities under the Deposit Agreement may be adversely affected.

If you are a beneficial owner of ordinary shares or ADSs and your broker, bank or nominee does not receive instructions from you about how your shares are to be voted, such broker, bank or nominee may be permitted to vote your shares on your behalf, depending on the rules applicable to such broker, bank or nominee and the type of proposal. Under rules of the New York Stock Exchange, which are also applicable to Nasdaq-listed

companies, brokers, banks and other securities intermediaries that are subject to New York Stock Exchange rules may use their discretion to vote your "uninstructed" shares on matters considered to be "routine" under New York Stock Exchange rules, but they do not have discretionary power to vote your shares on "non-routine" matters.

A "broker non-vote" refers to a share represented at the meeting held by an ordinary shareholder as to which instructions have not been received from the beneficial owner or person entitled to vote such shares and with respect to which, on one or more, but not all matters, the broker does not have discretionary voting power to vote such share because such matter is considered "non-routine" under New York Stock Exchange rules.

We encourage you to submit your proxy with instructions and exercise your right to vote as a shareholder.

9) Can I change my vote or revoke a proxy?

An ordinary shareholder of record can revoke his or her proxy before the time of voting at the Meeting by:

(1) mailing a revised form of the Ordinary Shareholder Proxy Form dated later than the prior Ordinary Shareholder Proxy Form. The revised Ordinary Shareholder Proxy Form must be lodged with our registrar, Equiniti, by no later than [] on [], 2023;

(2) notifying our Company Secretary in writing that you are revoking your proxy. Your revocation must be received at our registered office before the Meeting to be effective; or

(3) attending the Meeting and entering a new vote at the Meeting.

If your ordinary shares are held in an account at a brokerage firm, bank or similar organization, you may change or revoke your voting instructions by contacting the broker, bank or other nominee holding the shares or by your broker, bank or other nominee validly appointing you as proxy to attend at the Meeting. See also "*What if I plan to attend the Meeting*?"

If you hold ADSs, directly or through a broker, bank or other nominee, you must follow the instructions provided by Citibank, N.A. or such broker, bank or other nominee if you wish to change your vote. The last instructions you submit prior to the deadline indicated by Citibank, N.A. or the broker, bank or other nominee, as applicable, will be used to instruct Citibank N.A. how to vote your ADSs.

10) Who counts the votes?

Equiniti has been engaged as our independent agent to tabulate shareholder votes. If you are an ordinary shareholder of record, you can return your executed Ordinary Shareholder Proxy Form to Equiniti for tabulation (see instructions on the Ordinary Shareholder Proxy Form). If you hold your ordinary shares through a broker, your broker will return the Ordinary Shareholder Proxy Form to Equiniti.

If you are a registered holder of ADSs, you can return your executed ADS Proxy Card to Citibank, N.A. for tabulation. If you hold your ADSs through a broker, bank or other organization, that organization can return the ADS Proxy Card to Citibank, N.A. following your instruction. Citibank, N.A. will submit your votes to Equiniti for tabulation.

11) How are votes counted?

Votes will be counted by Equiniti, who will separately count "for" and "against" votes, and "votes withheld" or abstentions. A "vote withheld" or abstention is not a vote in law and will not be counted in the calculation of the votes "for" and "against" a resolution. Broker non-votes will have no effect on any proposal.

12) How many votes do I have?

On a show of hands, each ordinary shareholder of record present in person, and each duly authorized representative present in person of a shareholder that is a corporation, has one vote. On a show of hands, each proxy present in person who has been duly appointed by one or more shareholders has one vote, except that a proxy may vote one vote for and one vote against a resolution if, in certain circumstances, the proxy is instructed by more than one shareholder to vote in different ways on a resolution. On a poll, each shareholder present in person or by proxy or in the case of a corporation, by a duly authorized representative, has one vote for each voting ordinary share held by the ordinary shareholder. Each ADS of the Company represents ten voting ordinary shares.

13) What if I plan to attend the Meeting?

Ordinary shareholders can attend the Meeting, but attendance will be limited to ordinary shareholders of record as of [] on [], 2023. In order to obtain admittance to the Meeting each ordinary shareholder may be asked to present valid picture identification, such as a driver's license or passport. If your ordinary shares are held through brokerage accounts or by a bank or other nominee you may be able to attend at the discretion of the Chair.

If you are an ADS holder, please note that you will not be able to cast votes at the Meeting. In order to vote your ADSs, you should complete and submit the ADS Proxy Card in accordance with the instructions set out above.

If the arrangements for our AGM change materially, we will issue a further communication via a Form 8-K filing with the U.S. Securities and Exchange Commission (the "SEC") and on the Investors & Media section of our website at www.orchard-tx.com.

14) How do you solicit proxies?

We have engaged MacKenzie Partners, Inc., a proxy solicitation firm, to assist in soliciting votes of shareholders. The estimated fees anticipated to be paid to MacKenzie Partners, Inc. are approximately \$21,500 and those costs will be borne by us (in addition to our paying the cost of mailing proxy materials). We have agreed to customary indemnification obligations with regard to MacKenzie's solicitation of votes. The initial solicitation of proxies may be supplemented by additional mail communications and by telephone, fax, e-mail, internet and personal solicitation by our directors, officers or other employees. No additional compensation for soliciting proxies will be paid to our directors, officers or other employees for their proxy solicitation efforts. We also reimburse Citibank, N.A. for their expenses in sending materials, including ADS Proxy Cards, to ADS holders of record.

15) What do I do if I receive more than one notice or form of proxy?

If you hold your ordinary shares in more than one account, you will receive an Ordinary Shareholder Proxy Form and related proxy materials for each account. If you hold ADSs in more than one account, you will receive an ADS Proxy Card and related proxy materials for each account. To ensure that all of your shares are voted, please sign, date and return all forms of proxy. Please be sure to vote all of your shares.

16) Will there be any other business conducted at the Meeting?

No. In accordance with our Articles of Association, no matters other than proposals 1 through 13 may be presented at the Meeting. We have not been notified of, and our Board is not aware of, any other matters to be presented for action at the Meeting.

17) What is Equiniti's role?

Equiniti is our registrar. All communications concerning ordinary shareholder of record accounts, including address changes, name changes, ordinary share transfer requirements and similar issues can be handled by contacting Equiniti by telephone: 0371-384-2030 or +44 (0) 121-415-7047 (overseas) or by writing to Equiniti, Aspect House, Spencer Road, Lancing, West Sussex, BN99 6DA, England.

18) What is Citibank's role?

Citibank N.A. serves as our ADS depositary bank. Communications concerning ADS holder of record accounts can be handled by contacting Citibank, N.A. —ADR Shareholder Services by telephone: +1-877-248-4237 (toll free within the United States) or +1-781-575-4555 (for international callers) or by email: citibank@shareholders-online.com or at Citibank, N.A. — Shareholder Services, P.O. Box 505050, Louisville, KY 40233-9724.

19) How can I find out the results of the voting at the Meeting?

Voting results will be announced by the filing of a current report on Form 8-K with the SEC within four business days after the Meeting. If final voting results are unavailable at that time, we will file an amended current report on Form 8-K within four business days of the day the final results are available.

The results of any polls taken on the resolutions at the Meeting and any other information required by the U.K. Companies Act 2006 will be made available on our website (*www.orchard-tx.com*) as soon as reasonably practicable following the Meeting and for the required period thereafter.

ELECTION OF DIRECTORS

Our Board of Directors currently consists of eight members. In accordance with the terms of our Articles of Association, our Board of Directors is divided into three classes (Class I, Class II and Class III) with members of each class serving staggered three-year terms. The members of the classes are divided as follows:

Class I	Class II	Class III
(Terms expiring at	(Terms expiring at	(Terms expiring at
2025 Annual General Meeting)	2023 Annual General Meeting)	2024 Annual General Meeting)
John T Curnutte	James Geraghty	Joanne T. Beck
Bobby Gaspar	Steven M. Altschuler	Charles A. Rowland, Jr.
Alicia Secor	Marc Dunoyer	

Upon the expiration of the term of a class of directors, each director in that class will be eligible to be elected for a new three-year term at the annual general meeting in the year in which his or her term expires.

Our Board of Directors has nominated James Geraghty, Steven M. Altschuler and Marc Dunoyer for election as the Class II directors at the Meeting. The nominees are presently directors and have indicated a willingness to continue to serve as directors, if elected. If the nominees become unable or unwilling to serve, however, the proxies may be voted for a substitute nominee selected by our Board of Directors.

In connection with the proposals to elect James Geraghty, Steven M. Altschuler and Marc Dunoyer, we have set forth each nominee's biographical information in proposals 1, 2 and 3, respectively. For biographical information for the other directors, see the section titled "*Board of Directors and Corporate Governance*."

Proposal 1: RE-ELECTION OF JAMES GERAGHTY TO THE BOARD OF DIRECTORS

James Geraghty is currently the Chairman of our Board of Directors and has been nominated for re-election as a director. If elected, he will hold office from the date of his election until the 2026 annual general meeting of shareholders where he must retire by rotation and offer himself for re-election, or until his earlier death, resignation or removal. Mr. Geraghty has agreed to serve if elected, and the Board has no reason to believe that he will be unable to serve.

James Geraghty has been chairman of our Board of Directors since May 2018. He has also served as chairman of publicly traded biopharmaceutical company Pieris Pharmaceuticals, Inc. since December 2017, and as a member of the boards of directors of Fulcrum Therapeutics, Inc. since May 2016 and Voyager Therapeutics, Inc. since January 2014, each of which is a publicly traded biotechnology company. He previously served on the Board of Aceragen, Inc (formerly Idera Pharmaceuticals) from May 2013 until March 2023. He served as an Entrepreneur in Residence at Third Rock Ventures, a biotech venture capital firm, from May 2013 to August 2017. Prior to that, Mr. Geraghty served as Senior Vice President, North America Strategy and Business Development at Sanofi S.A., a publicly traded pharmaceutical company, from February 2011 to October 2013. Earlier, he held many roles at Genzyme Corporation from 1992 to 2011, most recently as Senior Vice President of International Development. While at Genzyme, his roles included President of Genzyme Europe and General Manager of Genzyme's cardiovascular business. Mr. Geraghty was formerly chairman of the board of Juniper Pharmaceuticals, Inc. from June 2015 until it was acquired in August 2018. Mr. Geraghty holds a B.A. from Georgetown University, an M.S. from the University of Pennsylvania, and a J.D. from Yale Law School. We believe Mr. Geraghty's experience as a senior executive and on the boards of other life sciences companies qualifies him to serve on our Board.

The Board of Directors recommends a vote FOR the re-election of James Geraghty to our Board of Directors.

Proposal 2: RE-ELECTION OF STEVEN M. ALTSCHULER TO THE BOARD OF DIRECTORS

Steven M. Altschuler, M.D. is currently a member of our Board of Directors and has been nominated for re-election as a director. If elected, he will hold office from the date of his election until the 2026 annual general meeting of shareholders where he must retire by rotation and offer himself for re-election, or until his earlier death, resignation or removal. Dr. Altschuler has agreed to serve if elected, and the Board has no reason to believe that he will be unable to serve.

Steven M. Altschuler, M.D. has been a member of our Board of Directors since January 2020. Dr. Altschuler has served as a Managing Director at Ziff Capital Partners since May 2018 and as an academic healthcare consultant working with multiple health systems since October 2017. He previously served as the Executive Vice President of Health Affairs at the University of Miami and Chief Executive Officer of UHealth-University of Miami Health System from January 2016 to October 2017. From April 2000 to November 2015, he was Chief Executive Officer of Children's Hospital of Philadelphia ("CHOP") and The Children's Hospital of Philadelphia Foundation. Prior to serving as the Chief Executive Officer of CHOP, Dr. Altschuler served in many leadership roles at CHOP, including: Division Chief of Gastroenterology, Physician-in-Chief, inaugural holder of the Leonard and Madlyn Abramson Endowed Chair in Pediatrics, and Professor and Chair of the Department of Pediatrics at the Perelman School of Medicine at the University of Pennsylvania, where he was a faculty member from 1985 to 2000. Dr. Altschuler previously served on the board of directors for Kead Johnson Nutrition Company from 2009 through 2017, and on the board of directors of Spark Therapeutics, Inc. from March 2013 until its acquisition by Roche Holding AG in December 2019. Dr. Altschuler has served on the boards of directors of WW International, Inc. since 2012 and is currently a member of its audit committee and compensation and benefits committee, and 89bio, Inc. since March 2020 as its chairman and member of its compensation committee. Dr. Altschuler holds a B.A. in mathematics and an M.D., both from Case Western Reserve University. He completed his pediatric internship and residency at Children's Hospital Center-Boston and fellowship training in gastroenterology and nutrition at CHOP and the University of Pennsylvania School of Medicine. We believe that Dr. Altschuler is qualified to serve on our Board because of his extensive experience in the medical indust

The Board of Directors recommends a vote <u>FOR</u> the re-election of Steven M. Altschuler to our Board of Directors.

Proposal 3: RE-ELECTION OF MARC DUNOYER TO THE BOARD OF DIRECTORS

Marc Dunoyer is currently a member of our Board of Directors and has been nominated for re-election as a director. If elected, he will hold office from the date of his election until the 2026 annual general meeting of shareholders where he must retire by rotation and offer himself for re-election, or until his earlier death, resignation or removal. Mr. Dunoyer has agreed to serve if elected, and the Board has no reason to believe that he will be unable to serve.

Marc Dunoyer has been a member of our Board of Directors since June 2018. Since August 2021, he has served as chief executive officer of Alexion, AstraZeneca's Rare Disease group, following its acquisition in July 2021. Mr. Dunoyer previously served as the Chief Financial Officer of AstraZeneca from November 2013 through August 2021 and as Executive Vice President, Global Portfolio & Product Strategy from June 2013 to October 2013. Mr. Dunoyer also served on the board of directors of AstraZeneca until August 2021. Prior to joining AstraZeneca, from February 2010 to March 2013, Mr. Dunoyer served as the Foundational Global Head of the Rare Diseases unit at GlaxoSmithKline plc, a publicly traded pharmaceutical company. At GlaxoSmithKline, Mr. Dunoyer also served on the company's corporate executive team and previously held the position of President for Asia-Pacific and Japan. Mr. Dunoyer has previously held international positions in operations and general management at Hoechst Marion Roussel, a wholly owned subsidiary of Sanofi S.A., a publicly traded pharmaceutical company, and holds an M.B.A. degree from the Hautes Etudes Commerciales and a Bachelor of Law degree from Paris University. We believe Mr. Dunoyer is qualified to serve on our Board because of his executive experience in our industry.

The Board of Directors recommends a vote <u>FOR</u> the re-election of Marc Dunoyer to our Board of Directors.

Proposal 4:

RE-APPOINTMENT OF PRICEWATERHOUSECOOPERS LLP, A UNITED KINGDOM ENTITY, AS U.K. STATUTORY AUDITORS OF THE COMPANY, TO HOLD OFFICE UNTIL THE CONCLUSION OF THE NEXT ANNUAL GENERAL MEETING OF SHAREHOLDERS

At each meeting at which the accounts are laid before shareholders, the Company is required to appoint U.K. statutory auditors to serve until the next such meeting. Proposal 4 seeks your approval of the re-appointment of PricewaterhouseCoopers LLP, a United Kingdom entity ("PwC UK"), to serve as our U.K. statutory auditor, to hold office until the conclusion of the next annual general meeting of shareholders. In the event this proposal does not receive the affirmative vote of the holders of a majority of the shares entitled to vote and who are present in person or represented by proxy at the Meeting, the Board of Directors may appoint an auditor to fill the vacancy. If the re-appointment of PwC UK is approved, the Audit Committee, at its discretion, may nonetheless direct the appointment of a different U.K. statutory auditor at any time it decides that such a change would be in the best interest of the Company and its shareholders.

The Board of Directors recommends a vote <u>FOR</u> the re-appointment of PricewaterhouseCoopers LLP, a United Kingdom entity, as our U.K. statutory auditors.

Proposal 5:

RATIFICATION OF THE APPOINTMENT OF PRICEWATERHOUSECOOPERS LLP, A DELAWARE LIMITED LIABILITY PARTNERSHIP, AS THE COMPANY'S INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM FOR THE FISCAL YEAR ENDING DECEMBER 31, 2023

Proposal 5 seeks your ratification of the appointment of PricewaterhouseCoopers LLP, a Delaware limited liability partnership ("PwC USA"), as the Company's independent registered public accounting firm for the fiscal year ending December 31, 2023.

Background to Proposal 5

The Audit Committee is solely responsible for selecting the Company's independent registered public accounting firm for the fiscal year ending December 31, 2023. The Audit Committee has selected PwC USA as our independent registered public accounting firm for the fiscal year ending December 31, 2023, and has further directed that we submit the selection of PwC USA for ratification by our shareholders at the Meeting. In the event this proposal does not receive the affirmative vote of the holders of a majority of the shares entitled to vote and who are present in person or represented by proxy at the Meeting, the Board of Directors may appoint an auditor to fill the vacancy. If the appointment of PwC USA is ratified, the Audit Committee, at its discretion, may nonetheless direct the appointment of a different independent registered public accounting firm at any time it decides that such a change would be in the best interest of the Company and its shareholders.

PwC USA has indicated its willingness to act as the Company's auditors. A representative of PwC USA is expected to be present at the Meeting and will have an opportunity to make a statement if he or she desires to do so and to respond to appropriate questions from our shareholders.

PwC USA commenced auditing our annual financial statements in 2019. Previously when the Company reported as a foreign private issuer, PwC UK served as principal auditor for the Company's consolidated financial statements as reported on Form 20-F.

Fees for Independent Registered Public Accounting Firm—PwC USA and PwC UK

The table below sets forth a summary of the fees billed to the Company by PwC USA and PwC UK for professional services rendered during the fiscal years ended December 31, 2022 and December 31, 2021, respectively. All such services and fees were pre-approved by the Audit Committee, which concluded that the provision of such services was compatible with the maintenance of each firm's independence in the conduct of its auditing functions.

Fees	December 31, 2022 (\$) (in thousands)	December 31, 2021 (\$) (in thousands)
Audit Fees(1)	1,446	1,349
Audit-related fees		
Tax fees(2)	—	3
All Other Fees(3)	3	5
Total	1,449	1,357

(1) "Audit Fees" consist of fees billed for the audit of our annual consolidated financial statements, statutory audits, review of interim condensed consolidated financial statements included in quarterly reports, assistance with review of documents filed with the SEC, fees normally provided in connection with registration statements, and services that are normally provided by PwC in connection with statutory and regulatory filings or engagements, attest services.

- (2) "Tax Fees" represents tax preparation assistance for a Board member, which was reimbursed by the Company consistent with our Directors' Remuneration Policy.
- (3) "All Other Fees" consist of non-audit fees paid to PwC USA for access to its proprietary accounting research database and financial statement disclosure checklist.

The Board of Directors recommends a vote

<u>FOR</u> the ratification of the appointment of PricewaterhouseCoopers LLP, a Delaware Limited Liability Partnership, as the Company's independent registered public accounting firm.

Proposal 6: AUTHORIZATION FOR THE AUDIT COMMITTEE TO DETERMINE THE AUDITORS' REMUNERATION FOR THE FISCAL YEAR ENDING DECEMBER 31, 2023

Proposal 6 authorizes the Audit Committee to determine our auditors' remuneration for the fiscal year ending December 31, 2023. Fees for PwC USA, our independent registered public accounting firm, and PwC UK, our statutory auditor, in respect of the years ended December 31, 2022 and December 31, 2021, are set forth in Proposal 5 above.

The Board of Directors recommends a vote <u>FOR</u> the authorization of our Audit Committee to determine our Auditors' remuneration.

Proposal 7:

RESOLUTION TO RECEIVE THE COMPANY'S U.K. STATUTORY ANNUAL ACCOUNTS AND REPORTS

At the Meeting, our Board of Directors will present our U.K. statutory annual accounts and reports for the period January 1, 2022 through December 31, 2022, which includes the audited portion of the directors' annual report on remuneration. We will provide our shareholders with an opportunity to receive the U.K. statutory annual accounts and reports and to raise questions in relation to them.

The Board of Directors recommends a vote <u>FOR</u> the resolution to receive the Company's U.K. statutory annual accounts and reports.

Proposal 8: ADVISORY VOTE TO APPROVE THE COMPANY'S EXECUTIVE COMPENSATION

The Dodd-Frank Wall Street Reform and Consumer Protection Act, as amended, and Section 14A of the Securities Exchange Act of 1934, as amended (the "Exchange Act") enable our shareholders to approve, on an advisory, non-binding basis, the compensation of our named executive officers as disclosed under the "Named Executive Officer Compensation" section, the 2022 Summary Compensation Table and the related compensation tables, notes and narratives in this proxy statement.

This proposal, known as a "Say-on-Pay" proposal, gives our shareholders the opportunity to express their views on our named executive officers' compensation as a whole. Our shareholders previously voted to hold advisory votes each year to approve the compensation paid to our named executive officers, and we have adopted that approach. This vote is not intended to address any specific item of compensation or any specific named executive officer, but rather the overall compensation of all of our named executive officers and the philosophy, policies and practices described in this proxy statement.

Our compensation programs are designed to support our business goals and promote our long-term profitable growth. We urge shareholders to read the "*Named Executive Officer Compensation*" section in this proxy statement, which describes in more detail how our executive compensation policies and procedures operate and are designed to achieve our compensation objectives. We also encourage you to review the 2022 Summary Compensation Table and other related compensation tables and narratives, which provide detailed information on the compensation of our named executive officers. The Board and the Compensation Committee believe that the policies and procedures described and explained in the "Named Executive Officer Compensation" section are effective in achieving our goals.

The vote under this Proposal 8 is advisory, and therefore not binding on the Company, the Board or our Compensation Committee. However, the Board and our Compensation Committee value the opinions of our shareholders and will review and consider the voting results when making future decisions regarding our executive compensation program.

Shareholders will be asked at the Meeting to approve the following resolution pursuant to this Proposal 8:

"**RESOLVED**, that the shareholders of the Company approve, on a non-binding, advisory basis, the compensation of the Company's 'named executive officers,' as disclosed in this proxy statement under the 'Named Executive Officer Compensation' section, the compensation tables and the narrative disclosures that accompany the compensation tables."

The Board of Directors recommends you vote FOR approval of the compensation to our named executive officers as set forth in this Proxy Statement.

Proposal 9:

ADVISORY VOTE TO APPROVE OUR U.K. STATUTORY DIRECTORS' ANNUAL REPORT ON REMUNERATION

Our U.K. statutory directors' remuneration report is set forth in Annex A to this proxy statement. The directors' remuneration report includes the annual report on remuneration. This document describes in detail our remuneration policies and procedures and explains how these policies and procedures help to achieve our compensation objectives with regard to our directors and the retention of high-quality directors. Our Board of Directors and the Compensation Committee believe that the policies and procedures as articulated in the directors' remuneration report are effective and that as a result of these policies and procedures we have and will continue to have high-quality directors. Our Board of Directors has approved and signed the report in accordance with English law.

At the Meeting, the shareholders will vote on the annual report on remuneration. This vote is advisory and non-binding. Although non-binding, our Board of Directors and Compensation Committee will review and consider the voting results when making future decisions regarding our director remuneration program. Following the Meeting, and as required under English law, the directors' annual report on remuneration will be delivered to the U.K. Registrar of Companies.

The Board of Directors recommends you vote

FOR approval of our U.K. statutory Directors' Annual Report on Remuneration set forth in Annex A.

BACKGROUND ON PROPOSALS 10 AND 12

Pursuant to the U.K. Companies Act 2006 (the "Companies Act"), our Board of Directors may only allot shares or grant rights over shares if authorized to do so by our shareholders. If shareholders authorize our Board to allot shares or grant rights over shares, the Companies Act requires us, where the allotment is for cash, to offer them first to our existing shareholders in proportion to their holdings, unless the shareholders have sanctioned the disapplication of their statutory rights of pre-emption in respect of such allotment or grant of rights.

In practice, the operation of such pre-emption rights is onerous and can result in significant delay and additional expense to the cost of an equity fundraising. It is customary for similarly-situated companies to seek authority from their shareholders to dis-apply statutory pre-emption rights for cash issues of up to a limit approved by the Company's shareholders.

Companies incorporated in the United States are not subject to these same restrictions. Since the Company is solely listed on the Nasdaq Capital Market and most of the Company's peers are incorporated in the United States, the Board believes the Company will be at a competitive disadvantage if Proposals 10 and 12 are not approved.

The Board anticipates that there may be occasions where it needs flexibility to finance business opportunities and growth without a pre-emptive offer to existing shareholders. To ensure the Company's continued ability to respond to market conditions and address business needs, the Board considers it appropriate that it be authorized to allot shares up to an aggregate nominal amount of £18,398,450 on a non-pre-emptive basis.

This authority to allot shares on a non-pre-emptive basis will not replace the existing authority granted by shareholders at the annual general meeting of shareholders held on June 16, 2021 (but instead be in addition to any such existing shareholder authority).

Proposals 10 and 12, are, in the Board's view, appropriate to avoid us potentially being at a competitive disadvantage as compared to our peer companies, many of whom are incorporated in the United States. In particular, the requirement to first offer shares that we propose to issue for cash to all of our existing shareholders in time-consuming pro-rata rights offerings would considerably reduce the speed at which we could complete capital-raising activities undertaken in furtherance of our growth strategy and would potentially make it difficult for us to complete such transactions. Many of our strategic competitors are incorporated in the United States where they are not subject to restrictions on their ability to issue shares.

Further, approval of Proposals 10 and 12 by shareholders will not exempt the Company from any Nasdaq corporate governance or other requirements, including those limiting the issuance of shares. For these reasons, we, therefore, consider that the Proposals 10 and 12 are appropriate to the needs of the Company and in the interests of shareholders.

We are asking you to approve these proposals, which the Board believes are in the best interests of its shareholders and the Company as a whole.

The full details of the proposals are set forth below.

BACKGROUND ON PROPOSALS 11 AND 13

On March 6, 2023, the Company entered into a Securities Purchase Agreement (the "Securities Purchase Agreement") with the purchasers named therein, pursuant to which the Company agreed to sell to the purchasers, in an unregistered offering, ordinary shares, non-voting ordinary shares and warrants to purchase ordinary shares and non-voting ordinary shares (the "Private Placement").

The Private Placement consisted of two closings. The first closing occurred on March 10, 2023. The second closing is contingent on (x) the Company's announcement of its intention to file a biologics license application submission following receipt of the minutes from the U.S. Food and Drug Administration in connection with the Company's pre-BLA (Type B) meeting for OTL-200, provided that such minutes do not expressly advise the Company not to proceed with a BLA submission, and (y) receipt of shareholder approval of these Proposals 11 and 13.

Upon the second closing, if approved by shareholders, the Company will issue and sell (i) 42,500,000 shares (both voting and non-voting ordinary shares) (which would be represented by 4,250,000 ADSs) and (ii) warrants to purchase an aggregate of 46,750,000 shares (both voting and non-voting ordinary shares) (which would be represented by 4,675,000 ADSs upon exercise of the warrants), at a purchase price of \$8.00 per ten shares and accompanying warrant.

Proposals 11 and 13 would permit the Company to issue and sell the shares and warrants described above on a non-pre-emptive basis. Pursuant to the Securities Purchase Agreement, each of the purchasers named therein have agreed to vote all ordinary shares (including ordinary shares represented by ADSs) held of record by such purchasers or with respect to which such purchasers are entitled to vote in favor of Proposals 11 and 13.

We are asking you to approve these proposals, which the Board believes are in the best interests of its shareholders and the Company as a whole.

The Company has disclosed further information about the Securities Purchase Agreement and Private Placement in its filings with the United States Securities and Exchange Commission.

The full details of the proposals are set forth below.

Proposal 10: AUTHORIZATION OF ALLOTMENT OF SHARES

Under the U.K. Companies Act 2006, our Board of Directors cannot allot shares in the Company (other than pursuant to an employee share scheme) unless they are authorized to do so by the Company in general meeting. The Board of Directors currently have an existing authority to allot shares in the Company and to grant rights to subscribe for or convert securities into shares in the Company. This authority was granted to the Board of Directors on June 16, 2021 and was in respect of a maximum aggregate nominal amount of £13,023,851.50. Under the current authority, the Company has the right to grant rights to subscribe for or convert securities into shares in the Company in respect of a maximum aggregate nominal amount of £5,599,595.70. This Proposal 10 is an ordinary resolution to seek a new authority, in addition to such subsisting amounts under the existing authority.

Proposal 10 proposes that the Board of Directors are granted authority to allot new shares or to grant rights to subscribe for or to convert any security into shares in the Company up to a maximum aggregate nominal amount of £18,398,450.

If approved by shareholders, this authority will run for five years and will expire on [], 2028. If shareholders do not approve Proposal 10, the subsisting amounts under the existing authorization granted at the time of the general meeting of the Company held June 16, 2021 will continue to apply until June 15, 2026 or until such earlier time as it has been fully utilized. However, the Board considers that it would be significantly constrained in its ability to fund the development of the Company's business, including to grant incentives pursuant to the Company's share incentive schemes, absent a further shareholder authorization.

The Board of Directors has no present intention of exercising this authority, except in relation to the Company's share incentive schemes or, in the event that the authority pursuant to Proposal 11 is not approved by shareholders, in connection with the Securities Purchase Agreement. The Board believes it is in the interests of shareholders for the Board to have this flexibility to allot shares otherwise than just in relation to such transactions should circumstances and its intentions change.

The Board of Directors recommends you vote <u>FOR</u> the authorization of allotment of shares.

Proposal 11: AUTHORIZATION OF ALLOTMENT OF SHARES IN CONNECTION WITH THE SECURITIES PURCHASE AGREEMENT

As noted above, under the U.K. Companies Act 2006, our Board of Directors cannot allot shares in the Company (other than pursuant to an employee share scheme) unless they are authorized to do so by the Company in general meeting. The purpose of this Proposal 11 is to seek authority to enable the Company to grant shares and warrants in connection with the Securities Purchase Agreement (including the issue of the associated underlying shares upon the future exercise of the warrants).

Proposal 11 proposes that the Board of Directors is granted authority to allot new Ordinary Shares, both voting and non-voting, and to grant warrants in respect of such shares, in connection with the Private Placement (and subject to the terms of the Securities Purchase Agreement) up to a maximum aggregate nominal amount of $\pounds 15,158,359$.

If approved by shareholders, this authority will expire on March 10, 2026. This authority is in addition to any existing authority obtained (to the extent unused) at the Company's general meeting held June 16, 2021 and would be in addition to the authority sought in Proposal 10 (if approved).

As set out in further detail on page 22 of this proxy statement, the Board of Directors believes that the Private Placement is in the best interests of the Company as a whole and its shareholders. Accordingly, the Board of Directors asks shareholders to approve Proposal 11.

The Board of Directors recommends you vote

FOR the authorization of allotment of shares in connection with the Securities Purchase Agreement.

Proposal 12: DISAPPLICATION OF PRE-EMPTION RIGHTS

Proposal 12 seeks a disapplication of pre-emption rights for cash issues of up to a certain proportion of the Company's issued ordinary share capital. Our Board of Directors currently has a power to allot shares as if the rights of pre-emption applicable under the U.K. Companies Act did not apply for cash issues. This power was granted to the Directors pursuant to shareholder resolutions passed on June 16, 2021 and was in respect of a maximum aggregate nominal amount of £13,023,851.50.

Proposal 12 will, if passed, give the Board of Directors power, pursuant to the authority to allot granted by Proposal 10, to allot shares for cash or to grant rights to subscribe for or to convert any security into shares without first offering them to existing shareholders in proportion to their existing holdings up to an aggregate maximum nominal amount of £18,398,450. This authority is in addition to any existing authority obtained (to the extent unused) at the Company's general meeting held June 16, 2021.

Proposal 12 will be required to be passed as a special resolution and, if passed, this authority will run for five years and will expire on [], 2028. If shareholders do not approve Proposal 12, the subsisting amounts under the existing authorization granted at the time of the general meeting of the Company held June 16, 2021 will continue to apply until June 15, 2026 or until such earlier time as it has been fully utilized. However, the Board considers that it would be significantly constrained in its ability to fund the development of the Company's business absent a shareholder authorization to allot the equity securities granted by Proposal 10 free from applicable rights of pre-emption.

The Board of Directors has no present intention of exercising this power, except in relation to the Company's share incentive schemes or, in the event that the authority pursuant to Proposal 11 is not approved by shareholders, in connection with the Securities Purchase Agreement. However, the Board believes it is in the interests of the Company as a whole and its shareholders for the Directors to have the ability to allot shares for cash otherwise than just in relation to such transactions should circumstances and their intentions change.

The Board of Directors recommends you vote <u>FOR</u> the disapplication of pre-emption rights.

Proposal 13: DISAPPLICATION OF PRE-EMPTION RIGHTS IN CONNECTION WITH THE SECURITIES PURCHASE AGREEMENT

Proposal 13 seeks a disapplication of pre-emption rights in connection with the Private Placement. The purpose of this Proposal 13 is to enable the Company to grant shares and warrants in connection with the Private Placement (in accordance and subject to the terms of the Securities Purchase Agreement) as if the rights of pre-emption applicable under the U.K. Companies Act for cash issues did not apply.

Proposal 13 will, if passed, give the Board of Directors power, pursuant to the authority to allot granted by Proposal 11, to allot shares for cash or to grant rights to subscribe for or to convert any security into shares without first offering them to existing shareholders in proportion to their existing holdings up to an aggregate maximum nominal amount of £15,158,359 in connection with the Private Placement. This authority is in addition to any existing authority obtained (to the extent unused) at the Company's general meeting held June 16, 2021 and would be in addition to the authority sought in Proposal 12.

Proposal 13 will be required to be passed as a special resolution and, if passed, this authority will expire on March 10, 2026.

As set out in further detail on page 22 of this proxy statement, the Board of Directors believes that the Private Placement is in the best interests of the Company as a whole and its shareholders. Accordingly, the Board of Directors asks shareholders to approve Proposal 13.

The Board of Directors recommends you vote

FOR the disapplication of pre-emption rights in connection with the Securities Purchase Agreement.

BOARD OF DIRECTORS AND CORPORATE GOVERNANCE

BOARD OF DIRECTORS

Directors

Below is a list of our Directors and their positions and ages as of the date of this proxy statement.

Name	Age	Position
James Geraghty	68	Chairman of the Board of Directors
Steven M. Altschuler, M.D.	69	Non-Executive Director
Joanne T. Beck, Ph.D.	62	Non-Executive Director
John T. Curnutte, M.D., Ph.D.	71	Non-Executive Director
Marc Dunoyer	70	Non-Executive Director
Bobby Gaspar, M.D., Ph.D.	59	Chief Executive Officer and Director
Charles A. Rowland, Jr.	64	Non-Executive Director
Alicia Secor	60	Non-Executive Director

During the year ended December 31, 2021, there were four full meetings of our Board of Directors. All of our Directors attended a minimum of 75% of the aggregate of the meetings of the Board of Directors and meetings of the committees of which he or she was a member during 2022.

Director Nominees

The biographical information for each of James Geraghty, Steven M. Altschuler, M.D. and Marc Dunoyer, the nominees to our Board of Directors, is provided in Proposals 1, 2 and 3, respectively.

Continuing Directors

Below is biographical information for those directors who are not standing for re-election at this Meeting and who will remain seated following the Meeting.

Joanne T. Beck, Ph.D. has been a member of our Board of Directors since July 2018. Dr. Beck has served as Chief Technology Officer of Aerium Therapeutics since November 2022. From December 2019 until November 2022, Dr. Beck served as Chief Operating Officer at Boston Pharmaceuticals, Inc., where she also served as Chief Executive Officer (ad interim) from December 2021 through May 2022. Dr. Beck previously served as the Executive Vice President, Pharmaceutical Development & Operations at Celgene from April 2016 to December 2019. Prior to joining Celgene, Dr. Beck was the Senior Vice President, Pharmaceutical Development at Shire from January 2012 to April 2016. From May 2004 to January 2012, Dr. Beck held leadership roles in both pharmaceutical and vascular operations at Abbott, most recently as Head of Global Business Excellence and Strategic Program Management. Earlier in her career she had technical leadership roles at Amgen and Genentech. From January to December 2019, Dr. Beck served on the board of directors for Catabasis Pharmaceuticals, Inc., a public pharmaceutical company. Dr. Beck holds a B.A. in chemistry from Lewis and Clark College and a Ph.D. in biochemistry and molecular biology from Oregon Health and Science University. We believe Dr. Beck's experience as a senior executive and as a director at a publicly traded life sciences company qualifies her to serve on our Board.

John Curnutte M.D., Ph.D. has been a member of our Board of Directors since August 2019. Since June 2020, Dr. Curnutte has served as a senior advisor to Samsara BioCapital. Dr. Curnutte previously served as Executive Vice President of Research and Development at Portola Pharmaceuticals, Inc. ("Portola"), a publicly traded biotechnology company, from February 2011 to May 2019, as Interim Co-President of Portola from June 2018 to August 2018, and has been engaged by Portola as a consultant since May 2019. Since August 2017,

Dr. Curnutte has served as a member of the board of directors of Pliant Therapeutics, Inc., a clinical stage biopharmaceutical company. From February 2015 to June 2016, Dr. Curnutte served as a member of the board of directors of Diadexus, Inc., a medical diagnostics company. Previously, Dr. Curnutte held positions at 3-V Biosciences, Inc., where he was Chief Executive Officer from May 2008 to March 2010 and was an independence consultant from April 2010 to January 2011. From September 2000 to May 2008, he served as President of Schering-Plough Biopharma, a biopharmaceutical subsidiary of Schering-Plough Corporation, and Senior Vice President of Discovery Research at Schering Plough Research Institute, a pharmaceutical and healthcare company. From August 1993 to September 2000, Dr. Curnutte held various senior management positions at Genentech, Inc. Dr. Curnutte was an adjunct clinical professor of pediatrics at the Stanford University School of Medicine and a member of the medical staff from 1994 to 2013. Dr. Curnutte holds an A.B. in biochemistry and molecular biology from Harvard University and an M.D. and a Ph.D. in biological chemistry from Harvard Medical School.

Bobby Gaspar, M.D., Ph.D. has served as our Chief Executive Officer since March 2020 and as a member of our Board of Directors since February 2016. Prior to serving as our Chief Executive Officer, Dr. Gaspar served as our President of Research, Chief Scientific Officer from January 2020 to March 2020 and as our Chief Scientific Officer since February 2016. Since March 2020, he has been an honorary professor of pediatrics and immunology at the UCL Great Ormond Street Institute of Child Health after serving as a professor from October 2007 to March 2020. Dr. Gaspar holds an M.B.B.S. from Kings College London and a Ph.D. from UCL.

Charles A. Rowland, Jr. has been a member of our Board of Directors since July 2018. From April 2016 to February 2017, Mr. Rowland served as President and Chief Executive Officer of Aurinia Pharmaceuticals Inc., where he also served as a member of the board of directors from July 2014 through February 2017. Mr. Rowland previously served as Vice President and Chief Financial Officer of ViroPharma Incorporated, an international biopharmaceutical company, from October 2008 until it was acquired by Shire plc, in January 2014. Prior to that, Mr. Rowland held positions of increasing responsibility at Biovail Pharmaceuticals, Inc., Breakaway Technologies, Inc., Endo Pharmaceuticals Inc., Pharmacia Corporation, Novartis AG, and Bristol-Myers Squibb Co. Mr. Rowland also serves on the boards of other publicly traded life sciences companies, including Generation Bio, where he also serves as the chairman of the audit committee (since July 2018), Viking Therapeutics, where he is also the chairman of the compensation committee and a member of the audit committee (since July 2017), and Nabriva Therapeutics, AG, based in Dublin, Ireland, where he also serves as a chairman of the compensation committee (since January 2015). Mr. Rowland previously served on the boards of several life sciences companies, including Blueprint Medicines, where he also served as chairman of the audit committee and member of the compensation committee (from March 2015 through June 2022), Vitae Pharmaceuticals, Inc., where is also served as chairman of the audit committee (from September 2014 until it was acquired by Allergan in September 2016), BIND Therapeutics, Inc., where he also served as chairman of the audit Committee (from May 2014 until July 2016), and Idenix Pharmaceuticals, Inc., where he also served as a member of the audit committee (from June 2013 until it was acquired by Merck & Co. in August 2014). Mr. Rowland holds a B.S. in accounting from Saint Joseph's University and an M.B.A. with a finance concentration from Rutgers University. We believe that Mr. Rowland's extensive professional experience as a chief financial executive in the biotechnology and pharmaceutical industries and his experience serving as a director of various publicly traded biotechnology companies qualifies him to serve as a member of our Board of Directors.

Alicia Secor has been a member of our Board of Directors since November 2018. Ms. Secor currently serves as President, Chief Executive Officer of Atalanta Therapeutics, Inc., where she also serves on the board of directors. Previously, from August 2016 until its sale to Catalent in August 2018, Ms. Secor served as President and Chief Executive Officer at Juniper Pharmaceuticals, Inc., a diversified public healthcare company. Prior to her role at Juniper, Ms. Secor held several leadership positions in the life sciences industry, including Chief Commercial Officer at Zafgen Inc. from January 2014 to July 2016, Senior Vice President and Chief Operating Officer at Synageva BioPharma Corp, and roles of increasing responsibility at Genzyme, including serving as Vice President and General Manager of the metabolic disease division. Ms. Secor is also a member of the board

of directors at G1 Therapeutics Inc. Ms. Secor was previously a member of the board of the Foundation for Prader-Willi Research until June 2022 and GW Pharmaceuticals, plc, from January 2018 until its acquisition by Jazz Pharmaceuticals in May 2021. She received her B.S. in health administration from the University of New Hampshire and an M.B.A. from Northeastern University. We believe Ms. Secor is qualified to serve on our board because of her experience serving as an officer and director of various publicly traded biotechnology companies.

CORPORATE GOVERNANCE

Structure of our Board of Directors

The leadership structure of our Board of Directors separates the positions of Chief Executive Officer and Chair of the Board in order to ensure independent leadership of the Board. Our Board believes that this separation is appropriate for the Company at this time because it allows for a division of responsibilities, with our Chief Executive Officer focused on leading the day to day operations at the Company while the Chair may focus on leading the Board in overseeing management.

Independence of our Board of Directors

Our Board of Directors has determined that all of our directors, other than Bobby Gaspar, our Chief Executive Officer, qualify as "independent" directors in accordance with the independence requirements under the applicable Nasdaq rules as well as applicable rules promulgated by the SEC. Dr. Gaspar is not considered independent because he is an employee of the Company.

Our Board of Directors has made a subjective determination as to each independent director that no relationships exist that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In making these determinations, our Board of Directors reviewed and discussed information provided by the directors and us with regard to each director's business and personal activities and relationships as they may relate to us and our management. There are no family relationships among any of our directors or executive officers.

Our independent directors meet in regularly scheduled executive sessions at which only independent directors are present. All of the committees of our Board of Directors are comprised entirely of directors determined by the Board of Directors to be independent.

Board Oversight of Risk Management

Our management is primarily responsible for assessing and managing risk, while our Board of Directors is responsible for overseeing management's execution of its responsibilities. Our Board of Directors is supported by its committees in fulfillment of this responsibility. For example, our Audit Committee focuses on our overall financial risk by evaluating our internal controls and disclosure policies as well as ensuring the integrity of our financial statements and periodic reports. The Audit Committee also monitors compliance with legal and regulatory requirements. Our Compensation Committee strives to create incentives that encourage an appropriate level of risk-taking consistent with our business strategy. Our Nominating and Corporate Governance Committee ensures that our governance policies and procedures are appropriate in light of the risks we face. Finally, our Science and Technology Committee reviews our research and development pipeline to ensure that we make well-informed choices and to evaluate our progress in achieving our long-term strategic goals and objectives.

COMMITTEES OF OUR BOARD OF DIRECTORS

Our Board of Directors has four standing committees: the Audit Committee, the Compensation Committee, the Nominating and Corporate Governance Committee and the Science and Technology Committee. The charters

for each of these committees can be found on our website at www.orchard-tx.com. Each committee reviews its respective charter at least annually.

Name Steven M. Altschuler, M.D.	Audit	Compensation	Nominating and Corporate Governance	Science and <u>Technology</u> X
Joanne T. Beck, Ph.D.		Х		X
John T. Curnutte, M.D., Ph.D.			Х	Chair
Marc Dunoyer	Х		Х	
James Geraghty			Chair	
Charles A. Rowland, Jr.	Chair	Chair		
Alicia Secor	Х	Х	Х	

Audit Committee

Our Audit Committee is currently comprised of Mr. Dunoyer, Mr. Rowland and Ms. Secor, with Mr. Rowland serving as chair of the committee. Our Board of Directors has determined that each member of the Audit Committee meets the independence requirements of Rule 10A-3 under the Exchange Act and the applicable Nasdaq rules. Our Board of Directors has determined that Mr. Rowland is an "audit committee financial expert" within the meaning of SEC regulations and the applicable Nasdaq rules. The Audit Committee held six meetings during 2022. The Audit Committee's responsibilities include:

- · recommending the appointment of the independent registered public accounting firm to the general meeting of shareholders;
- the appointment, compensation, retention and oversight of any accounting firm engaged for the purpose of preparing or issuing an audit report or performing other audit services;
- pre-approving the audit services and non-audit services to be provided by our independent auditor before the auditor is engaged to render such services;
- evaluating the independent auditor's qualifications, performance and independence, and presenting its conclusions to the full Board of Directors on at least an annual basis;
- monitoring the company's internal controls over financial reporting, disclosure controls and any remediation plan associated with any significant control deficiencies or material weaknesses and discussing with management;
- reviewing and discussing with management and our independent registered public accounting firm our financial statements and our financial reporting process; and
- reviewing, approving or ratifying any related party transactions.

Compensation Committee

Our Compensation Committee is currently comprised of Dr. Beck, Mr. Rowland and Ms. Secor, with Mr. Rowland serving as chair of the committee. Our Board of Directors has determined that each member of the Compensation Committee is "independent" as defined under the applicable Nasdaq rules. The Compensation Committee held five meetings during 2022. The Compensation Committee's responsibilities include:

- identifying, reviewing and proposing policies relevant to the compensation and benefits of our directors and executive officers;
- evaluating each executive officer's performance in light of such policies and reporting to the board;
- overseeing and administering our employee share option scheme or equity incentive plans in operation from time to time; and

overseeing the Company's policies and strategies relating to culture and human capital management, including diversity and inclusion.

Compensation Committee Interlocks and Insider Participation

None of the members of our Compensation Committee has at any time during the prior three years been one of our officers or employees. None of our executive officers currently serves, or in the past fiscal year has served, as a member of our Compensation Committee or the compensation committee of any entity that has one or more executive officers serving on our Board of Directors.

Our Board of Directors has delegated to the Compensation Committee the authority to determine the compensation for our executive officers. Non-executive director compensation is recommended by our Compensation Committee to the Board of Directors for approval. Our Chief Executive Officer may participate in general discussions with our Compensation Committee and Board of Directors about these compensation matters but he does not participate in discussions during which his individual compensation is being considered and approved.

In 2022, the Compensation Committee retained the services of Radford, which is part of the Rewards Solutions practice at Aon plc, an independent compensation consultant, to assist the Compensation Committee with respect to compensation actions in 2022 with the goal of ensuring that our compensation arrangements for our Chief Executive Officer, our other senior executive officers and our non-executive directors were appropriate and competitive. Radford provided data from comparable publicly traded biopharmaceutical companies and otherwise assisted the Compensation Committee in its design of competitive compensation for our Chief Executive Officer, senior executives and non-executive directors. The Compensation Committee expects to continue to use compensation consultants to assist the Compensation program and non-executive directors' compensation program. The Compensation Committee continued to retain Radford through 2022 and 2023 in order to ensure that our compensation arrangements are competitive for 2023. After review and consultation with Radford, the Compensation Committee determined that Radford is independent and that there is no conflict of interest resulting from retaining Radford in 2022 or in 2023. In reaching these conclusions, our Compensation Committee considered the factors set forth in the SEC rules and the applicable Nasdaq rules.

Nominating and Corporate Governance Committee

Our Nominating and Corporate Governance Committee is comprised of Dr. Curnutte, Mr. Dunoyer, Mr. Geraghty and Ms. Secor, with Mr. Geraghty serving as chair of the committee. Our Board of Directors has determined that each member of the Nominating and Corporate Governance Committee is "independent" as defined under the applicable Nasdaq rules. The Nominating and Corporate Governance Committee held four meetings during 2022. The Nominating and Corporate Governance Committee's responsibilities include:

- drawing up selection criteria and appointment procedures for directors;
- recommending nominees for election to our Board of Directors and its corresponding committees;
- assessing the functioning of individual members of our Board of Directors and executive officers and reporting the results of such assessment to the Board of Directors; and
- developing corporate governance guidelines.

The Nominating and Corporate Governance Committee considers candidates for Board of Director membership suggested by its members and the Chief Executive Officer. Additionally, in selecting nominees for directors, the Nominating and Corporate Governance Committee will review candidates recommended by shareholders in the same manner and using the same general criteria as candidates recruited by the committee

and/or recommended by our Board of Directors. Any shareholder who wishes to recommend a candidate for consideration by the committee as a nominee for director should follow the procedures described later in this proxy statement under the heading "Additional Information—Shareholder Proposals for 2024 Annual General Meeting."

Our Board of Directors is responsible for filling vacancies on our Board of Directors and for nominating candidates for election by our shareholders each year in the class of directors whose term expires at the relevant annual general meeting. The Board of Directors delegates the selection and nomination process to the Nominating and Corporate Governance Committee, with the expectation that other members of the Board of Directors, and of management, will be requested to take part in the process as appropriate.

Director Nomination Process

The process followed by our Nominating and Corporate Governance Committee to identify and evaluate director candidates includes requests to board members and others for recommendations, including through the use of search firms or other advisors, meetings from time to time to evaluate biographical information and background material relating to potential candidates, and interviews of selected candidates by management, recruiters, members of the committee and our board.

Once candidates have been identified, the Nominating and Corporate Governance Committee confirms that the candidates meet all of the minimum qualifications for director nominees established by the Nominating and Corporate Governance Committee. The Nominating and Corporate Governance Committee may gather information about the candidates through interviews, detailed questionnaires, comprehensive background checks or any other means that the Nominating and Corporate Governance Committee then meets as a group to discuss and evaluate the qualities and skills of each candidate, both on an individual basis and taking into account the overall composition and needs of our Board of Directors. Based on the results of the evaluation process, the Nominating and Corporate Governance Committee recommends candidates for the Board of Directors' approval to fill a vacancy or as director nominees for election to the Board of Directors by our shareholders each year in the class of directors whose term expires at the relevant annual general meeting.

The qualifications, qualities and skills that our Nominating and Corporate Governance Committee believes must be met by a committeerecommended nominee for a position on our Board of Directors are as follows:

- The nominee shall have experience at a strategic or policymaking level in a business, government, non-profit or academic organization of high standing.
- The nominee shall be highly accomplished in his or her respective field, with superior credentials and recognition.
- The nominee shall be well regarded in the community and shall have a long-term reputation for the high ethical and moral standards.
- The nominee shall have sufficient time and availability to devote to the affairs of the Company, particularly in light of the number of boards of directors on which such nominee may serve.
- To the extent such nominee serves or has previously served on other boards, the nominee shall have a demonstrated history of actively contributing at board meetings.

We have no formal policy regarding board diversity. Our priority in selection of board members is identification of members who will further the interests of our shareholders through consideration of a number of facts and circumstances, including among other things, the skills of the prospective director candidate, his or her depth and breadth of business experience or other background characteristics, his or her independence and the needs of the Board of Directors.

BOARD DIVERSITY

Board Size	As of April 13, 2023			
Total Number of Directors:			8	
Part 1: Gender				Did Not
	Male	Female	Non-Binary	Disclose
Number of Directors Based on Gender Identity	6	2	0	0
Part 2: Demographic Information				
African American or Black	0	0	0	0
Alaskan Native or American Indian	0	0	0	0
Asian	1	0	0	0
Hispanic or Latinx	0	0	0	0
Native Hawaiian or Pacific Islander	0	0	0	0
White	5	2	0	0
Two or More Races or Ethnicities	0	0	0	0
LGBTQ+			0	
Did Not Disclose Demographic Information			0	
Did Not Disclose Demographic Information			0	

Shareholder Recommendations and Nominees

Our Nominating and Corporate Governance Committee considers both recommendations and nominations for candidates to the Board from shareholders so long as such recommendations and nominations comply with our Articles of Association and applicable laws, including the rules and regulations of the SEC. Shareholders may recommend director nominees for consideration by the Nominating and Corporate Governance Committee by writing to our Company Secretary at the address below, or the Company's registered office address from time to time, and providing evidence of the shareholder's ownership of our ordinary shares and/or ADSs, the nominee's name, home and business address, as well as the nominee's detailed biographical data and qualifications for board membership, and information regarding any arrangements or understandings between the shareholder and the recommended candidate.

Following verification of the shareholder status of the person submitting the recommendation, all properly submitted recommendations will be promptly brought to the attention of the Nominating and Corporate Governance Committee. Shareholders who desire to nominate persons directly for election to the Board at an annual general meeting of shareholders must meet the deadlines and other requirements set forth under "Additional Information—Shareholder Proposals for 2024 Annual General Meeting." Any vacancies on the Board of Directors occurring between our annual general meetings of shareholders may be filled by persons selected by a majority of the directors then in office, in which case any director so elected will serve until the next annual general meeting of shareholders when such director will offer himself or herself for re-election, or by persons elected by an ordinary resolution of the shareholders of the Company.

You may write to the Nominating and Corporate Governance Committee at:

c/o Christopher York Company Secretary Orchard Therapeutics plc 245 Hammersmith Road London W6 8PW United Kingdom

Science and Technology Committee

Our Science and Technology Committee is comprised of Dr. Altschuler, Dr. Beck, and Dr. Curnutte, with Dr. Curnutte serving as chair of the committee. Our Board of Directors has determined that each member of the



Science and Technology Committee is "independent" as defined under the applicable Nasdaq rules. The Science and Technology Committee held four meetings during 2022. The Science and Technology Committee's responsibilities include:

- reviewing, evaluating, and advising the Board of Directors and management regarding our long-term strategic goals and objectives;
- reviewing our research and development pipeline;
- reviewing, evaluating and advising the Board of Directors on the quality and direction of our research and development programs;
- monitoring and evaluating trends in research and development, and recommending to the Board of Directors and management emerging technologies for building our technological strength;
- recommending approaches to acquiring and maintaining technology positions and advising the Board of Directors and management on the scientific aspects of business development transactions;
- assisting the Board of Directors with its oversight responsibility for enterprise risk management in areas affecting our research and development; and
- reviewing such other topics as delegated to the Science and Technology Committee from time to time by the Board of Directors.

Director Attendance at Annual General Meeting of Shareholders

Directors are expected to try to attend our annual general meeting of shareholders to the extent practicable.

Code of Business Conduct and Ethics

We have adopted a Code of Business Conduct and Ethics applicable to all of our directors, officers, employees and certain designated agents. The Code of Business Conduct and Ethics is available on our website at *https://ir.orchard-tx.com/corporate-governance/governance-overview*. We expect that any amendments to this code or any waivers of its requirements will be disclosed on our website.

Shareholder Communication with the Board of Directors

Any interested party with concerns about our Company may report such concerns to the Board of Directors or the Chair of our Board of Directors and Nominating and Corporate Governance Committee. Communications may be addressed to the entire Board of Directors or to any individual director. All such communications will initially be received and processed by our Company Secretary. Spam, junk mail, advertisements and threatening, hostile, illegal and similar unsuitable communications will not be delivered to the Board. Shareholders can contact members of the Board Directors by writing care of our Company Secretary at the Company's registered office address.

A copy of any such written communication may also be forwarded to our legal counsel and a copy of such communication may be retained for a reasonable period of time. The director may discuss the matter with our legal counsel, with independent advisors, with non-management directors, or with our management, or may take other action or no action as the director determines in good faith, using reasonable judgment, and applying his or her own discretion.

Communications may be forwarded to other directors if they relate to important substantive matters and include suggestions or comments that may be important for other directors to know. In general, communications relating to corporate governance and long-term corporate strategy are more likely to be forwarded than communications relating to ordinary business affairs, personal grievances, and matters as to which we tend to receive repetitive or duplicative communications.

The Audit Committee oversees the procedures for the receipt, retention, and treatment of complaints received by us regarding accounting, internal accounting controls, or audit matters, and the confidential, anonymous submission by employees of concerns regarding questionable accounting, internal accounting controls or auditing matters. We have also established a toll-free telephone number for the reporting of such activity, which is +1 866-254-3199.

SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The following table and related footnotes set forth information with respect to the beneficial ownership of our ordinary shares, as of March 31, 2023, by:

- each beneficial owner of more than 5% of our ordinary shares;
- each of our named executive officers and directors; and
- all of our executive officers and directors as a group.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC. Under these rules, beneficial ownership includes any shares as to which a person has sole or shared voting power or investment power. In computing the number of ordinary shares beneficially owned by a person and the percentage ownership of that person, ordinary shares subject to options, or other rights held by such person that are currently exercisable or will become exercisable within 60 days of March 31, 2023 are considered outstanding. These ordinary shares, however, are not included in the computation of the percentage ownership of any other person. Applicable percentage ownership is based on 184,383,389 ordinary shares outstanding as of March 31, 2023 (which if all held in ADS form would be represented by 18,438,338 ADSs).

Unless otherwise indicated, the address for each of the shareholders listed in the table below is c/o Orchard Therapeutics plc, 245 Hammersmith Road, London W6 8PW, United Kingdom.

	Ordinary Shares Beneficially Owned	As-Converted to American Depositary Shares ⁽¹⁾	
Name of Beneficial Owner	Number	Number	Percent
Greater than 5% Shareholders			
Entities affiliated with RA Capital Management ⁽²⁾	18,608,550	1,860,855	9.99%
Entities affiliated with Zentree Investments Limited ⁽³⁾	17,210,561	1,721,056	9.33%
Entities affiliated with CHI Advisors LLC ⁽⁴⁾	14,654,096	1,465,409	7.95%
Glaxo Group Limited ⁽⁵⁾	12,455,252	1,245,525	6.76%
Entities affiliated with Deep Track Capital ⁽⁶⁾	11,666,700	1,166,670	6.33%
Named Executive Officers and Directors			
Bobby Gaspar, M.D., Ph.D. ⁽⁷⁾	2,398,798	239,879	1.29%
Frank Thomas ⁽⁸⁾	1,594,581	159,458	*
James A. Geraghty ⁽⁹⁾	474,501	47,450	*
Steven M. Altschuler, M.D. ⁽¹⁰⁾	125,000	12,500	*
Joanne T. Beck, Ph.D. ⁽¹¹⁾	199,324	19,932	*
John T. Curnutte, M.D., Ph.D. ⁽¹²⁾	125,000	12,500	*
Marc Dunoyer ⁽¹³⁾	227,209	22,720	*
Charles A. Rowland, Jr. ⁽¹⁴⁾	202,314	20,231	*
Alicia Secor ⁽¹⁵⁾	159,990	15,999	*
All Executive Officers and Directors as a Group (9 persons) (16)	5,506,715	550,671	2.91%

* Represents beneficial ownership of less than one percent.

(1) Our shareholders, executive officers and directors may hold ordinary shares, American Depositary Shares or a combination of both. This column shows each holder's beneficial ownership assuming all shares were held in American Depositary Share form, which may not be the case. Our American Depositary Shares are listed on The Nasdaq Capital Market under the trading symbol "ORTX." Ordinary shares are convertible to American Depositary Shares at a ten to one ratio. The Company does not issue fractional shares, so for purposes of these illustrative figures each figure has been rounded down to the nearest whole number.

- Based in part on a Schedule 13G filed with the SEC by RA Capital Management L.P. ("RA Capital"), by RA Capital Healthcare Fund, L.P. (the (2)"Fund"), Peter Kolchinsky and Rajeev Shah on March 20, 2023, consists of (i) 16,720,000 ordinary shares held by the Fund and (ii) 1,888,550 ordinary shares issuable upon the redesignation of non-voting ordinary shares held by the Fund. These amounts exclude 14,724,850 non-voting ordinary shares held by the Fund which may not be redesignated into ordinary shares if such redesignation would result in beneficial ownership of more than 9.99%. The Fund may increase or decrease such beneficial ownership limitation percentage not in excess of 19.99% by providing us with at least 61 days' prior notice. These amounts also exclude warrants held by the Fund through which it will have the right, once exercisable, to acquire 36,666,740 ordinary shares, subject to certain beneficial ownership limitations. RA Capital Healthcare Fund GP, LLC is the general partner of the Fund. The general partner of RA Capital is RA Capital Management GP, LLC, of which Dr. Kolchinsky and Mr. Shah are the controlling persons. RA Capital serves as investment adviser for the Fund and may be deemed a beneficial owner, for purposes of Section 13(d) of the Securities Exchange Act of 1934 ("Section 13(d)"), of any of the securities held by the Fund. The Fund has delegated to RA Capital the sole power to vote and the sole power to dispose of all securities held in the Fund's portfolio, including the securities described herein. Because the Fund has divested voting and investment power over the reported securities it holds and may not revoke that delegation on less than 61 days' notice, the Fund disclaims beneficial ownership of the securities it holds for purposes of Section 13(d) and therefore disclaims any obligation to report ownership of the reported securities under Section 13(d). As managers of RA Capital, Dr. Kolchinsky and Mr. Shah may be deemed beneficial owners, for purposes of Section 13(d), of any of our securities beneficially owned by RA Capital. RA Capital, Dr. Kolchinsky and Mr. Shah disclaim beneficial ownership of such securities other than for the purpose of determining their obligations under Section 13(d). The address of RA Fund is 200 Berkeley Street, 18th Floor, Boston MA 02116.
- (3) Based in part on a Schedule 13G/A filed with the SEC by Zentree Investments Limited ("Zentree") and Richard Magides on February 9, 2023, consists of (i) ordinary shares and ADSs held by Zentree, which if all held in ordinary share form would equal 7,398,947 shares and (ii) ordinary shares and ADSs held by Richard Magides, which if all held in ordinary share form would equal 9,811,314 shares. These amounts exclude (i) warrants held by Zentree through which it will have the right, once exercisable, to acquire 687,500 ordinary shares, subject to certain beneficial ownership limitations and (ii) warrants held by Mr. Magides through which he will have the right, once exercisable, to acquire 687,500 ordinary shares, subject to certain beneficial ownership limitations. Mr. Magides is the director of Zentree and may be deemed to have shared voting control and investment discretion over securities owned by Zentree. The address of Zentree and Mr. Magides is 18 Robinson Road, Level 15-01, Singapore 048547.
- (4) Based in part on a Schedule 13G/A filed with the SEC by CHI Advisors LLC ("CHI Advisors") on February 13, 2023, consists of (i) 7,987,396 ordinary shares beneficially owned by CHI Advisors LLC and (ii) 6,666,700 ordinary shares held by CHI IV Public Investments LP ("CHI IV Public Investments"). These amounts exclude warrants held by CHI IV Public Investments through which it will have the right, once exercisable, to acquire 7,333,370 ordinary shares, subject to certain beneficial ownership limitations. CHI Advisors is the investment manager of CHI IV Public Investments LP and may be deemed to have shared voting control and investment discretion over securities owned by CHI IV Public Investments LP. The address of CHI Advisors and CHI IV Public Investments LP is 599 Lexington Avenue, 19th Floor, New York, NY 10022.
- (5) Based on a Form 3 filed with the SEC by GlaxoSmithKline plc on January 2, 2020, consists of 12,445,252 of our ordinary shares. The board of directors of Glaxo Group Limited may be deemed to share voting and investment authority over the shares held by Glaxo Group Limited. The address of Glaxo Group Limited is 980 Great West Road, Brentford, Middlesex, London TW8 9GS, UK.
- (6) Based in part on a Schedule 13G filed with the SEC by Deep Track Capital, LP ("Deep Track Capital"), Deep Track Biotechnology Master Fund, Ltd. ("Deep Track Biotech") and David Kroin on March 20, 2023, consists of 11,666,700 ordinary shares held by Deep Track Biotech. This amount excludes warrants held by Deep Track Biotech through which it will have the right, once exercisable, to acquire 12,833,370 ordinary shares, subject to certain beneficial ownership limitations. Deep Track Capital and David Kroin have shared voting power and shared dispositive power over the shares held by the Deep Track Biotech. David Kroin

may be considered a control person for Deep Track Capital. The address of Deep Track Capital and David Kroin is 200 Greenwich Ave, 3rd Floor, Greenwich, CT 06830, and the address for Deep Track Biotech is 190 Elgin Avenue, George Town, KY1-9001, Cayman Islands.

- (7) Consists of (i) ordinary shares and ADSs, which if all held in ordinary share form would equal 366,158 ordinary shares, (ii) 2,000 of our ordinary shares held by Dr. Gaspar's child, (iii) 2,000 of our ordinary shares held by another of Dr. Gaspar's children, and (iv) 2,028,640 of our ordinary shares issuable upon exercise of options within 60 days of March 31, 2023.
- (8) Consists of (i) ordinary shares and ADSs, which if all held in ordinary share form would equal 92,081 ordinary shares and (ii) 1,502,500 of our ordinary shares issuable upon exercise of options within 60 days of March 31, 2023.
- (9) Consists of (i) ordinary shares and ADSs, which if all held in ordinary share form would equal 44,391 ordinary shares and (ii) 430,110 of our ordinary shares issuable upon exercise of options within 60 days of March 31, 2023.
- (10) Consists of 125,000 of our ordinary shares issuable upon exercise of options within 60 days of March 31, 2023.
- (11) Consists of (i) ordinary shares and ADSs, which if all held in ordinary share form would equal 9,294 ordinary shares and (ii) 190,030 of our ordinary shares issuable upon exercise of options within 60 days of March 31, 2023.
- (12) Consists of 125,000 of our ordinary shares issuable upon exercise of options within 60 days of March 31, 2023.
- (13) Consists of (i) ordinary shares and ADSs, which if all held in ordinary share form would equal 37,179 of our ordinary shares and (ii) 190,030 of our ordinary shares issuable upon exercise of options within 60 days of March 31, 2023.
- (14) Consists of (i) ordinary shares and ADSs, which if all held in ordinary share form would equal 12,294 of our ordinary shares (ii) 190,020 of our ordinary shares issuable upon exercise of options within 60 days of March 31, 2023.
- (15) Consists of 159,990 of our ordinary shares issuable upon exercise of options within 60 days of March 31, 2023.
- (16) Includes an aggregate of 4,941,320 of our ordinary shares issuable upon exercise of options within 60 days of March 31, 2023.

CERTAIN RELATIONSHIPS AND TRANSACTIONS WITH RELATED PERSONS

Other than the compensation arrangements described below under the sections "Director Compensation" and "Named Executive Officer Compensation" and the transactions described below, in the period from January 1, 2021 through the date of this proxy statement, we were not a party to any transactions between us and certain "related persons", which are generally considered to be our executive officers, directors, director nominees or 5% shareholders, or their immediate family members.

2023 Private Placement

In March 2023, we entered into the Securities Purchase Agreement with the purchasers named therein, pursuant to which we agreed to sell up to an aggregate of (i) 99,166,900 shares, consisting of a combination of ordinary shares, nominal value £0.10 per share, and non-voting ordinary shares, nominal value £0.10 per share, and (ii) warrants to purchase an aggregate of 109,083,590 ordinary shares or non-voting shares (the "2023 Private Placement").

The 2023 Private Placement consists of two closings. At the initial closing we sold (i) 56,666,900 ordinary shares and non-voting ordinary shares in the aggregate and (ii) warrants to purchase an aggregate of 62,333,590 ordinary shares and non-voting ordinary shares, at a purchase price of \$6.00 per ten shares and accompanying warrant. In addition, subject to satisfaction or waiver of certain conditions, we agreed to sell and issue in the second closing (i) 42,500,000 ordinary shares and non-voting ordinary shares in the aggregate and (ii) warrants to purchase an aggregate of \$8.00 per ten shares and non-voting ordinary shares, at a purchase price of \$8.00 per ten shares and accompanying warrant.

Each warrant has an exercise price equal to \$1.10 per ordinary share in the event OTL-200 receives approval by the Food and Drug Administration on or prior to December 31, 2024 and \$0.95 per ordinary share in the event OTL-200 is approved by the Food and Drug Administration after December 31, 2024. The warrants will expire on March 10, 2026.

The following table summarizes purchases of our ordinary shares, non-voting ordinary shares and warrants by related persons in connection with the initial closing of the 2023 Private Placement, each of which beneficially own five percent or more of our share capital:

	Number of Ordinary Shares Purchased at the Initial Closing*	Number of Non-Voting Ordinary Shares Purchased at the Initial Closing*	Number of Warrant Shares Underlying Warrants Issued at the Initial Closing*	I	Aggregate nitial Closing Purchase Price of Securities
RA Capital Healthcare Fund, L.P.	16,720,000	16,613,400	36,666,740	\$	20,000,040
Deep Track Biotechnology Master Fund, Ltd.	11,666,700	—	12,833,370	\$	7,000,020
CHI IV Public Investments LP	6,666,700	—	7,333,370	\$	4,000,020
Entities affiliated with Zentree Investments Limited	1,250,000	_	1,375,000	\$	750,000

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* Figures shown are ordinary shares. Each ADS represents ten ordinary shares.

The following table summarizes the agreement to purchase additional shares and warrants by related persons in connection with the second closing of the 2023 Private Placement, each of which beneficially own five percent or more of our share capital:

	Aggregate Number of Ordinary Shares and Non-Voting Ordinary Shares to be Purchased at the Second Closing*	Number of Warrant Shares Underlying Warrants to be Issued at the Second Closing*		Aggregate Second Closing Purchase Price of Securities
RA Capital Healthcare Fund, L.P.	25,000,000	27,500,000	5	5 20,000,000
Deep Track Biotechnology Master Fund, Ltd.	8,750,000	9,625,000	9	5 7,000,000
CHI IV Public Investments LP	5,000,000	5,500,000	9	4,000,000
Entities affiliated with Zentree Investments				
Limited	937,500	1,031,250	9	5 750,000

* Figures shown are ordinary shares. Each ADS represents ten ordinary shares.

In connection with the 2023 Private Placement, we also agreed to file a resale registration statement with the SEC within 60 days following the earliest of (i) the second closing, (ii) the date, if any, on which we determine not to proceed with our BLA submission for OTL-200 and (iii) March 6, 2026, to register (i) the ordinary shares issued and sold in the 2023 Private Placement, which may be represented by ADSs, including the ordinary shares into which the non-voting ordinary shares may be redesignated and (ii) the ordinary shares into which the non-voting ordinary shares may be redesignated and (ii) the ordinary shares into which the non-voting ordinary shares may be redesignated. We also agreed, among other things, to indemnify the purchasers from certain liabilities and to pay certain expenses in connection with the registration of such securities.

Investment and Shareholders' Agreement

We are party to an investment and shareholders' agreement with certain of our shareholders, pursuant to which certain of our shareholders, including certain holders with beneficial ownership of five percent or more of our ordinary shares, have the right to demand that we file a registration statement for their ordinary shares or request that their ordinary shares be covered by a registration statement that we are otherwise filing.

2021 Private Placement

In February 2021, we entered into a securities purchase agreement (the "2021 Purchase Agreement") with the purchasers named therein, pursuant to which we sold (i) 20,900,321 ordinary shares, nominal value £0.10 per share, at a purchase price of \$6.22 per share and (ii) 3,215,434 Non-Voting Ordinary Shares, nominal value £0.10 per share, at a purchase price of \$6.22 per share, for aggregate gross proceeds of approximately \$150 million. RA Capital Healthcare Fund, L.P. purchased 3,215,434 Non-Voting Ordinary Shares for an aggregate purchase price of approximately \$20 million. Pursuant to the 2021 Purchase Agreement, we filed a Registration Statement on Form S-3 (File No. 333-255127) with the SEC, which was automatically effective upon its filing on April 8, 2021.

Stable Cell Line Agreement with GSK

In July 2020, we entered into two worldwide royalty-bearing license agreements with GlaxoSmithKline plc ("GSK") for use of GSK's lentiviral stable cell line technology for our since-deprioritized programs OTL-103 for Wiskott Aldrich Syndrome and OTL-300 for beta-thalessemia. Under the terms of the agreements, we agreed to pay £1.0 million in upfront payments, £0.3 million upon approval of OTL-103 in the United States or Europe, and low-single digit percentage tiered royalties on net sales for each indication.

Indemnification Agreements

We have entered into a deed of indemnity with each of our directors and executive officers. These agreements and our Articles of Association require us to indemnify our directors and executive officers to the fullest extent permitted by law. We also maintain appropriate directors' and officers' liability insurance (including ensuring that premiums are properly paid) for their benefit for so long as any claims may lawfully be brought against them.

Related Person Transactions Policy

We have adopted a written related-person transactions policy, which requires that such transactions be approved by our Audit Committee. Pursuant to this policy, the Audit Committee has the primary responsibility for reviewing and approving or disapproving "related person transactions," which are transactions between us and related persons in which the related person has a direct or indirect material interest. For purposes of this policy, a related person will be defined as a director, executive officer, nominee for director, or greater than 5% beneficial owner of any class of our voting securities, and their immediate family members.

DIRECTOR COMPENSATION

Our Board of Directors adopted a non-employee director compensation policy that is designed to enable us to attract and retain, on a long-term basis, highly qualified non-employee directors. The following table describes the annual cash compensation applicable to each role performed by Non-Executive Directors for the fiscal year ended December 31, 2022.

Following a review of non-employee director compensation, for 2023, the Board resolved to reduce the base fee provided to the Chair and other Members of the Board by \$5,000. This replaces a supplement previously provided for time and commitment to international travel with a corresponding rebalancing in equity compensation.

As part of this review, the fee for the Chair of the Science and Technology Committee has been increased, recognizing the crucial role this committee holds in the long-term success of the Company.

In reinforcing the Board's stewardship of the Company, from 2023, all non-executive directors will be required to hold a shareholding equivalent to a value of three times the base annual retainer paid as a member of the Board. They will have five years to gain compliance with this new requirement. New appointments will have five years from election to the Board.

Collectively, the Board believes these are important changes and represent incremental improvements to the Company's Board compensation structure. The changes ensure that this structure matches long-term shareholder interest and remains market competitive.

	023 Cash npensation)22 Cash npensation
Board of Directors	\$ 40,000	\$ 45,000
Chairman (additional retainer)	\$ 40,000	\$ 40,000
Audit Committee Chair	\$ 18,000	\$ 18,000
Compensation Committee Chair (additional retainer)	\$ 15,000	\$ 15,000
Nominating and Corporate Governance Committee Chair (additional retainer)	\$ 10,000	\$ 10,000
Science and Technology Committee Chair (additional retainer)	\$ 15,000	\$ 10,000
Audit Committee member/non-Chair (additional retainer)	\$ 9,000	\$ 9,000
Compensation Committee member/non-Chair (additional retainer)	\$ 7,500	\$ 7,500
Nominating and Corporate Governance Committee member/non-Chair (additional retainer)	\$ 5,000	\$ 5,000
Science and Technology Committee member/non-Chair (additional retainer)	\$ 7,500	\$ 7,500

As approved in our 2022 Directors' Remuneration Policy, Non-Executive Directors may elect to receive fees as market value share options with an equivalent value calculated as the fair value on the date of grant.

In addition, each new non-employee director will be granted an initial, one-time equity award of 180,000 share options (equivalent to 18,000 ADSs) upon his or her election to the Board of Directors, which vests in equal monthly installments over a three-year period, subject to the director's continued service through such vesting date(s). On the date of each annual general meeting of shareholders of the Company, each continuing non-employee director, other than a director receiving an initial award, will receive an annual equity award of 105,000 share options (equivalent to 10,500 ADSs), which will vest in full upon the earlier to occur of the first anniversary of the date of grant or the date of our next annual general meeting of shareholders, subject to continued service as a director through such vesting date.

Non-Executive Director Appointment Letters

We have entered into letters of appointment with each of our Non-Executive Directors. These letters set forth the main terms on which each of our Non-Executive Directors serve on our Board of Directors. Continued appointment under the letter is contingent on continued satisfactory performance as a member of the Board of Directors and as a member of a committee, if applicable, as well as being re-elected at the annual general meetings in accordance with our Articles of Association. The appointment may be terminated by the Company or the Non-Executive Director with not less than three months' prior written notice. Upon termination, the Non-Executive Director is only entitled to a pro-rata amount of the annual fee (if applicable) that is outstanding and payable up to the date of termination, and reimbursement in the normal way of any expenses properly incurred before that date.

DIRECTOR COMPENSATION TABLE

Under our Directors' Remuneration Policy, the Board has the discretion to pay cash fees to our Non-Executive Directors for their Board and committee service. Our compensation arrangements for Non-Executive Directors during 2022, as set forth in our Non-Employee Director Compensation Policy, comprised an award of a fixed number of share options plus cash payment. The table below shows the compensation paid to our Non-Executive Directors during the year ended December 31, 2022. Other than as set forth in the table and described more fully below, we did not pay any compensation, make any equity awards or non-equity awards to, or pay any other compensation to any of our Non-Executive Directors in 2022. We also reimburse all reasonable out-of-pocket expenses incurred by directors for their attendance at meetings of our Board of Directors or any committee thereof.

Dr. Gaspar, our Chief Executive Officer, did not receive any compensation for his service as a member of our Board of Directors in 2022.

	Fees earned or paid in cash (\$)	Option Awards (\$) ⁽¹⁾	Total
Steven Altschuler ⁽²⁾	52,500	12,724	65,224
Joanne Beck ⁽³⁾	60,000	12,724	72,724
John Curnutte ⁽⁴⁾	60,000	12,724	72,724
Marc Dunoyer ⁽⁵⁾	59,000	12,724	71,724
James Geraghty ⁽⁶⁾	95,000	12,724	107,724
Charles Rowland ⁽⁷⁾	78,000	12,724	90,724
Alicia Secor ⁽⁸⁾	66,500	12,724	79,224

(1) The amounts reported represent the aggregate grant date fair value of the option awards granted during 2022 as computed in accordance with FASB ASC 718. The assumptions used in calculating the grant date fair value are set forth in the notes to our consolidated financial statements included in Note 12 of our audited consolidated financial statements for the year ended December 31, 2022 included in our Annual Report on Form 10-K, filed with the SEC on March 14, 2023. These amounts do not necessarily correspond to the actual value recognized or that may be recognized by the directors.

(2) As of December 31, 2022, Dr. Altschuler held unexercised options to purchase 122,222 ordinary shares.

⁽³⁾ As of December 31, 2022, Dr. Beck held unexercised options to purchase 190,030 ordinary shares.

(4) As of December 31, 2022, Dr. Curnutte held unexercised options to purchase 125,000 ordinary shares.

(5) As of December 31, 2022, Mr. Dunoyer held unexercised options to purchase 190,030 ordinary shares.

(6) As of December 31, 2022, Mr. Geraghty held unexercised options to purchase 430,120 ordinary shares.

(7) As of December 31, 2022, Mr. Rowland held unexercised options to purchase 190,030 ordinary shares.

(8) As of December 31, 2022, Ms. Secor held unexercised options to purchase 160,000 ordinary shares.

EXECUTIVE OFFICERS OF THE COMPANY

Below is a list of our executive officers and their positions and ages as of the date of this proxy statement. There are no family relationships between any of our executive officers, and there is no arrangement or understanding between any executive officer and any other person pursuant to which the executive officer was selected.

Name	Age	Position_
Bobby Gaspar, M.D., Ph.D.	59	Chief Executive Officer
Frank Thomas	53	President and Chief Operating Officer

Bobby Gaspar, M.D., Ph.D. has served as our Chief Executive Officer since March 2020 and as a member of our Board of Directors since February 2016. Prior to serving as our Chief Executive Officer, Dr. Gaspar served as our President of Research, Chief Scientific Officer from January 2020 to March 2020 and as our Chief Scientific Officer since February 2016. Since March 2020, he has been an honorary professor of pediatrics and immunology at the UCL Great Ormond Street Institute of Child Health after serving as a professor from October 2007 to March 2020. Dr. Gaspar holds an M.B.B.S. from Kings College London and a Ph.D. from UCL. We believe Dr. Gaspar is qualified to serve on our Board of Directors because of his scientific and industry experience in the field in which we operate.

Frank Thomas has served as our President and Chief Operating Officer since March 2020. He previously served as our Chief Operating Officer and Chief Financial Officer from January 2018 through December 2019. Prior to Orchard, Mr. Thomas served as President and Chief Operating Officer of AMAG Pharmaceuticals, Inc., a publicly traded specialty pharmaceutical company, from April 2015 to April 2017, as AMAG's Executive Vice President and Chief Operating Officer from May 2012 through April 2015 and as Executive Vice President, Chief Financial Officer and Treasurer from August 2011 through May 2012. Prior to AMAG, he served as Senior Vice President, Chief Operating Officer and Chief Financial Officer for Molecular Biometrics, Inc., a private commercial stage medical diagnostics company, from October 2008 to July 2011. Prior to Molecular Biometrics, Mr. Thomas spent four years at Critical Therapeutics, Inc., a public biopharmaceutical company, where he served as President and Chief Executive Officer and a member of the board of directors from 2006 to 2008 and Senior Vice President and Chief Financial Officer from 2004 to 2006. Prior to 2004, Mr. Thomas served as the Chief Financial Officer and Vice President of Finance and Investor Relations at Esperion Therapeutics, Inc., a public biopharmaceutical company. Since May 2020, Mr. Thomas has served on the board of directors of Larimar Therapeutics, a publicly traded, clinical-stage biotechnology company that completed a merger with Zafgen, Inc. where Mr. Thomas had previously served on the board of directors since June 2014. Since July 2017, Mr. Thomas has served of directors of the Massachusetts Biotechnology Council from 2007 to 2015. Mr. Thomas holds a B.B.A. from the University of Michigan, Ann Arbor.

NAMED EXECUTIVE OFFICER COMPENSATION

This section provides an overview of the compensation awarded to, earned by, or paid to our named executive officers in respect of their service to us for our fiscal year ended December 31, 2022. Our named executive officers are:

- Bobby Gaspar, Chief Executive Officer
- Frank Thomas, President & Chief Operating Officer

2022 Summary Compensation Table

The following table provides information regarding the total compensation for services rendered in all capacities that was earned during the fiscal year indicated by our named executive officers for fiscal years 2022 and 2021.

				Non-Equity Incentive						
Name	Year	Salary	Bonus	Stock Awards	Option Awards ⁽²⁾	Com	Plan pensation ⁽⁵⁾		ll Other pensation	Total
Bobby Gaspar ⁽¹⁾	2022	\$572,668			\$ 546,101(3)	\$	294,397	\$	34,360(7)	\$1,447,527
Chief Executive Officer	2021	\$605,114	_	_	\$3,504,354	\$	217,841	\$	27,230(7)	\$4,354,539
Frank Thomas	2022	\$506,833	_		\$ 441,855(4)	\$	245,520	\$	11,600(8)	\$1,205,637
President & COO	2021	\$470,000	—		\$1,257,233	\$	235,000(6)	\$	11,600(8)	\$1,973,833

(1) Dr. Gaspar's cash compensation was paid in Great British Pounds ("GBP"). Amounts paid in GBP have been converted to USD at an exchange rate of 1 GBP to 1.2495 USD in 2022 and 1 GBP to 1.3532 USD in 2021, based upon on a 12-month average rate during the financial year.

- (2) The amounts reported in the Option Awards column represent the aggregate grant date fair value for the fiscal years ended December 31, 2022, and 2021 of grants of time-based share options to each of the NEOs, calculated in accordance with the provisions of FASB ASC Topic 718. The assumptions we used in calculating these amounts are included in Note 12 of our audited consolidated financial statements for the year ended December 31, 2022 included in our Annual Report on Form 10-K, filed with the SEC on March 14, 2023. The amounts reported in the Summary Compensation Table for these time-based option awards may not represent the amounts that the NEOs will actually realize from the awards. The stated amounts for 2021 include the fair value of time-based share options awarded with an equivalent fair value to 50% of the 2020 annual bonus.
- (3) Dr. Gaspar received his 2022 annual equity award as a combination of market-price options and premium-price options. This figure represents the aggregate fair value of. share options granted to Dr. Gaspar during year with an exercise price set at the closing price of trading on the date of grant; and share options granted to Dr. Gaspar during year with an exercise price set at a 25% premium to the closing price of trading on the date of grant. This figure also includes the incremental fair value of Dr. Gaspar's outstanding awards as a result of the repricing of share options effective October 4, 2022.
- (4) Mr. Thomas was awarded 375,000 options pursuant to the terms of his Transitional Services Agreement. This figure also includes the incremental fair value of Mr. Thomas's outstanding awards as a result of the repricing of share options effective October 4, 2022. Simultaneous and calculated on an equivalent basis to awards included in the repricing, on October 4, 2022, Mr. Thomas was granted 532,811 options respectively in lieu of options where the terms of any outstanding awards prohibited a reprice.
- (5) The amounts reported in the Non-Equity Incentive Plan Compensation column reflect the annual cash incentive bonus earned by the NEOs for each respective year. The annual cash incentive bonuses were paid in the first quarter of the calendar year following the year to which the cash bonus relates.
- (6) Pursuant to the terms of his Transitional Services Agreement, Mr. Thomas received a bonus equivalent to 100% of target annual bonus from his 2019 employment agreement date in respect of 2021.

- (7) The amounts reported for Dr. Gaspar represent a cash allowance paid in lieu of employer pension contributions equivalent to 6% of salary paid since April 1, 2021.
- (8) The amounts reported represent a Company matching contribution under our 401(k) plan.

Narrative to Summary Compensation Table

2022 Base Salary and Bonus

Effective March 1, 2022, Dr. Gaspar and Mr. Thomas each received a salary increase of 5% to £462,000 and \$492,500, respectively. The increases were in-line with salary adjustments applied to all employees across the Company. There was no change to the target bonus opportunity for Dr. Gaspar, which remains at 60% salary. Mr. Thomas received a base salary of \$528,000 from July 1, 2022 and a target bonus of 50% based on a review of market data provided by our independent compensation consultant for his position and experience.

At their own request to the Compensation Committee, for 2023, Dr. Gaspar and Mr. Thomas did not receive a salary increase. The Committee approved and commended this proposal from both executives.

At the end of 2022, the Compensation Committee assessed 2022 performance against the Company's stated corporate objectives, which include objectives in the areas of:

i. extending the Company's cash runway through portfolio prioritization, expense management, new capital and business development;

ii. driving net revenue from Libmeldy sales;

iii. advancing our portfolio to key clinical and regulatory milestones;

iv. strategic decisions in pre-clinical research activities, notably relating to Crohn's disease.

The Compensation Committee's assessment of the performance against these objectives resulted in a performance score of 85%, which provided for a bonus of 51% of base salary for Dr. Gaspar. In recognition of his performance during the year and his commitment to the Company, the Committee awarded Mr. Thomas a bonus equivalent to 93% of target, which provided for a bonus of 47% of base salary for Mr. Thomas. The corporate performance score is used as a component of the calculation for all employee bonuses across the Company.

2022 Equity-Based Compensation

On June 1, 2022, Dr. Gaspar and Mr. Thomas were granted options to purchase 850,000 and 375,000 ordinary shares, respectively.

Dr. Gaspar's award was made as an award of share options, split into two tranches, with an equal split determined on a grant date fair value basis, each vesting in equal monthly installments over four years:

- Options with an exercise price set at the Company's closing share price on the date of grant ("market-priced options"); and
- Options with an exercise price set at a 25% premium to the Company's closing share price on the date of grant ("premium-priced options").

The Committee believes that granting share options to the Chief Executive Officer remains the most effective method to align executive compensation and long-term shareholder value. The addition of premium-priced options during 2022 reinforces this alignment and ensures that a substantial portion of Dr Gaspar's compensation package is performance-based and contingent on long-term and sustainable value growth of the Company.

Pursuant to the terms of his Transitional Services Agreement, Mr. Thomas's award was granted as market-priced options, vesting in equal monthly installments over two years.

Repricing of share options

In October 2022, under the terms of Orchard's 2018 Share Option and Incentive Plan, the Board of Directors approved a repricing of certain previously awarded share options to employees, which were underwater (*i.e.*, where the exercise prices were above the Company's recent trading price). This repricing took effect on October 4, 2022.

All employees at the Company hold share options, and a significant proportion of these awards were underwater prior to the repricing. In order to reengage staff with the future success of Orchard and provide additional retentive value to the investment previously made in our equity program, the Board approved the repricing of certain previously awarded share options. The Company has, and continues to, grant equity-based compensation to all employees, which the Compensation Committee believes aligns the entire workforce with the future value of the Company.

The Board of Directors considered several factors in determining which grants would be eligible for repricing and which grants would remain on the original terms. As a result of this consideration, the Board made the following decisions:

- No share options held by non-executive directors were repriced;
- Only options with an original exercise price above \$1.25 were repriced (representing an 150% premium to the ADS price on the date of repricing);
- No grants from 2022 were repriced; and
- The exercise price of the repriced options (\$0.58) was set at a 16% premium to the closing price of the Company's ADSs on the date of repricing, which was \$0.50.

Awards to Dr. Gaspar and Mr. Thomas were treated in the same manner as all other employees, except for grants where the equity incentive plan did not allow for repricing by the Board, in which case the original grant terms were retained. Where the terms of an outstanding award did not allow for an option to be repriced, supplemental grants were calculated on an equivalent value basis. Further details can be found in the section titled *"Outstanding Equity Awards at Fiscal Year-End."*

Employment Agreements

Bobby Gaspar

In May 2019, we entered into an amendment to Dr. Gaspar's January 2018 employment agreement, which was further amended on March 18, 2020, in connection with Dr. Gaspar's promotion to Chief Executive Officer. A summary of his employment agreement is provided below.

Dr. Gaspar's base salary is subject to annual review and redetermination. In addition, Dr. Gaspar is entitled to participate in our cash incentive compensation program. For 2022, the target amount for his annual bonus was 60% of his base salary, with the actual amount to be determined solely in the discretion of the Compensation Committee based on the Company's performance and the individual performance of Dr. Gaspar is also eligible to participate in all of our employee benefit plans and programs that are generally available to our U.K. employees.

Upon a termination of Dr. Gaspar's employment without cause or for good reason, which does not occur within a 12-month period following a change in control (a "Change in Control Period"), Dr. Gaspar will be entitled to severance pay and benefits as follows:

- in the case of a termination for good reason, salary continuation for a period of 12 months following his termination of employment; provided, that, in the case of a termination without cause, Dr. Gaspar shall be entitled to six months' written notice of his termination (or payment in lieu of such notice) and salary continuation for an additional six months;
- the amount of any annual cash incentive compensation for the year prior to any year in which Dr. Gaspar's employment terminates, to the extent that it has not already been paid and otherwise would have been earned had Dr. Gaspar remained employed through the payment date;
- a pro-rata portion of his target cash incentive compensation for the year in which Dr. Gaspar's employment terminates;
- · continued health, long-term disability and other insurance programs for up to twelve months; and
- up to £15,000 in outplacement benefits.

In the event Dr. Gaspar's employment is terminated without cause or if he resigns his position for good reason in the Change in Control Period, in lieu of the payments and benefits described above, he will be entitled to receive:

- in the case of a termination for good reason, a lump sum payment equal to 18 months of his base salary; provided, that, in the case of a termination without cause, Dr. Gaspar shall be entitled to receive 12 months' written notice of his termination (or payment in lieu of such notice), plus an amount equal to six months of his base salary;
- 1.5 times the amount of Dr. Gaspar's target annual incentive compensation for the year in which Dr. Gaspar's employment terminates;
- continued health, long-term disability and other insurance programs for up to 18 months;
- up to £15,000 in outplacement benefits; and
- accelerated vesting of all unvested equity awards.

All severance payments and benefits under Dr. Gaspar's employment agreement are subject to the execution of a separation and release agreement by Dr. Gaspar containing, among other provisions, a general release of claims in favor of us.

Frank Thomas

On October 4, 2022, the Company entered into an Amended and Restated Employment Agreement with Frank Thomas (the "Employment Agreement"), pursuant to which Mr. Thomas agreed to continue to serve as President and Chief Operating Officer of the Company. As previously disclosed, on November 3, 2021, Frank Thomas, President and Chief Operating Officer of the Company, submitted his resignation and entered into a Transitional Services Agreement with the Company, which was subsequently amended on March 30, 2022 (as amended, the "Transitional Services Agreement"). The Transitional Services Agreement was terminated concurrently with the parties' entrance into the Employment Agreement.

Mr. Thomas's Employment Agreement provides for an initial base salary of \$528,000, which is subject to annual review and redetermination. In addition, Mr. Thomas is entitled to participate in our cash incentive compensation program. For 2022, Mr. Thomas' annual target cash incentive compensation was 50% of his base salary. The actual amount received by Mr. Thomas is determined by the Compensation Committee in its sole discretion and is based on the Company's performance and the individual performance of Mr. Thomas. Mr. Thomas is also eligible to participate in each our generally-available employee benefit plans and programs in effect from time to time for our U.S. employees.

Upon a termination of Mr. Thomas's employment without cause or for good reason that does not occur within a Change in Control Period, Mr. Thomas will be entitled to severance pay and benefits as follows:

- salary continuation for a period of 12 months following his termination of employment;
- the amount of any annual cash incentive compensation for the year prior to any year in which Mr. Thomas's employment terminates, to the extent that it has not already been paid and otherwise would have been earned had Mr. Thomas remained employed through the payment date;
- continued health insurance coverage for up to 12 months; and
- up to \$20,000 in outplacement benefits.

In the event Mr. Thomas's employment is terminated without cause or if he resigns his position for good reason in the Change in Control Period, in lieu of the payments and benefits described above, he will be entitled to receive:

- a lump sum payment equal to the sum of (a) 12 months of his annual base salary and (b) one times his target annual cash compensation;
- continued health insurance coverage for up to 12 months;
- accelerated vesting of all unvested equity awards; and
- up to \$20,000 in outplacement benefits.

All severance payments and benefits under Mr. Thomas's employment agreement are subject to the execution of a separation and release agreement by Mr. Thomas containing, among other provisions, a general release of claims in favor of us.

In the event that any payments made to Mr. Thomas in connection with a change in control or termination would be subject to the excise tax imposed by Section 4999 of the Internal Revenue Code, the payments to Mr. Thomas would be reduced such that Mr. Thomas received the maximum amount payable without the imposition of an excise tax under Section 4999, but only if such reduction provided a higher benefit on an after-tax basis to Mr. Thomas. The Employment Agreement does not provide for any tax gross-up payments.

Outstanding Equity Awards at Fiscal Year-End

All share figures in the table below are shown as ordinary shares. Each ADS of the Company represents ten ordinary shares.

			Option Awards						wards
Name (a)	Vesting Commencement Date	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of nber of Securities urities Underlying erlying Unexercised sercised Options (#) Option Option ions (#) Unexercisable Exercise Expiration		Equity Incentive Plan Awards: Number of unearned shares, units or other rights that have not vested (#)	Incentive Plan Awards: Number of unearned Equity Ince shares, Plan Awar units or Market of other payout valu rights that unearned sh have units or other not vested that have not			
Bobby Gaspar	2/1/16	597,867	0	\$	0.00002	9/13/26	(1)		0)
Boool Subput	2/7/16	40,015	0	\$	0.00002	2/6/28			
	9/13/18	96,420	0	\$	0.00002	9/12/28			
	1/16/19(3)	48,958	1,042	Š	0.58	1/15/29			
	1/2/20(3)	145,833	54,167	Š	0.58	1/1/30			
	4/1/20(3)	200,000	100.000	\$	0.58	3/31/30			
	2/1/21(3)	389,583	460,417	\$	0.58	1/31/31			
	2/1/21(3)	55,006	0	\$	0.58	1/31/31			
	2/1/22	88,048	334,583	\$	0.46	5/31/32			
	2/1/22	89,035	338,334	\$	$0.57^{(4)}$	5/31/32			
	4/1/20						195,000(5)	\$	72,345
Frank Thomas	2/7/18	426,185	0	\$	2.44	2/6/28			
	9/13/18	184,229	0	\$	9.06	9/12/28			
	1/16/19(3)	73,650	2,080	\$	0.58	1/15/29			
	1/2/20(3)	145,820	54,170	\$	0.58	1/1/30			
	4/1/20(3)	99,990	50,000	\$	0.58	3/31/30			
	2/1/21(3)	142,080	167,910	\$	0.58	1/31/31			
	2/1/21(3)	27,730	0	\$	0.58	1/31/31			
	2/1/22(6)	156,250	218,750	\$	0.46	5/31/32			
	10/4/22	25,433	507,378	\$	0.58	10/3/32			

(1) All unvested share option awards were granted with a ten-year term and, unless otherwise noted, vest in 48 equal monthly installments following the vesting commencement date,

Air unvested share option awards were granted with a ten-year term and, unless otherwise noted, vest in 48 equal monthly installments following the vesting commencement date, subject to a continuous service relationship through each vesting date. Exercises prices are shown on an ordinary share basis. Each publicly-traded ADS is represented by ten ordinary shares. On October 4, 2022, these options were repriced at a 16% premium to the closing price of our ADSs on the Nasdaq Capital Market on October 4, 2022. Exercise price for half of Dr. Gaspar's 2022 annual equity award (on a value basis) set at a 25% premium to the closing price of our ADSs on the Nasdaq Capital Market on June 1, (2) (3) (4) 2022

(5) These PSU awards will vest upon achievement of specified clinical and regulatory milestones. The award vests on January 2, 2024 as to 1/3 of the award for each of the first three to occur of four milestones, if each such milestone is achieved by the Company on or before December 31, 2023 and Dr. Gaspar remains continuously employed with the Company through January 2, 2024. The market value of PSUs that have not vested is based on the number of unvested PSUs outstanding as of December 31, 2022, multiplied by \$0.37, which was the closing price of our ADSs on the Nasdaq Capital Market on December 30, 2022.

(6) These options vest in 24 equal monthly installments commencing on February 1, 2022.

Prohibition on Hedging and/or Pledging our Common Stock

We prohibit our executives and directors from engaging in short sales of Company securities; purchasing or selling puts, calls or other derivative securities based on our securities; and entering into hedging transactions, including through the use of financial instruments such as prepaid variable forwards, equity swaps, collars and exchange funds.

Securities Authorized for Issuance under Equity Compensation Plans

Equity Compensation Plans

The following table sets forth information as of December 31, 2022 regarding ordinary shares that may be issued under our equity compensation plans. Each ADS of the Company represents ten ordinary shares.

Plan Category	Number of Securities to be Issued upon Exercise of Outstanding Options, Warrants and Rights (#)(a)	E Price of Option	ted Average xercise Outstanding s, Warrants and hts (b) ⁽¹⁾	Number of Securities Remaining Available for Future Issuance under Equity Compensation Plans (Excluding Securities Reflected in Column (a)) (c)
Equity compensation plans approved by security				
holders ⁽²⁾	18,208,920(3)	\$	1.51(4)	5,970,860(5)
Equity compensation plans not approved by security				
holders ⁽⁶⁾	278,500	\$	3.09	721,500
Total	18,487,420	\$	1.53	6,063,390

(1) All exercise prices relate to ordinary shares and prices at December 31, 2022.

(2) Consists of our 2018 Share Option and Incentive Plan ("2018 Plan"), 2016 Share Option Plan ("2016 Plan") and 2018 Employee Share Purchase Plan (the "ESPP"). Following our initial public offering, we have not and will not grant any awards under our 2016 Plan, but all outstanding awards under the 2016 Plan will continue to be governed by their existing terms. The shares underlying any awards granted under the 2016 Plan or 2018 Plan that are forfeited, canceled, reacquired by us prior to vesting, satisfied without the issuance of shares, or otherwise terminated (other than by exercise) and the shares that are withheld upon exercise of an option or settlement of such award to cover the exercise price or tax withholding will be added to the shares available for issuance under the 2018 Plan.

(3) Includes 318,333 shares subject to restricted share units that will entitle the holder to one share for each unit that vests and is settled.

- (4) The calculation does not take into account the 2,063,840 shares subject to outstanding restricted share units. Such shares will be issued at the time the restricted share units vest and settle, without any cash consideration payable for those shares.
- (5) Consists of shares available for future issuance under the ESPP and the 2018 Plan. As of December 31, 2022, 628,970 shares were available for issuance under the ESPP and 6,063,390 shares were available for issuance under the 2018 Plan. Excludes 6,347,361 additional ordinary shares that were added to the number of shares that may be issued under the 2018 Plan and 1,269,472 additional ordinary shares that may be issued under the ESPP pursuant to automatic increases effective January 1, 2023.
- (6) Consists of shares under our 2020 Inducement Equity Plan. Our 2020 Inducement Equity Plan was adopted in June 2020 without shareholder approval pursuant to Nasdaq Stock Market Rule 5635(c)(4). Pursuant to the terms of the 2020 Inducement Equity Plan, the Company may grant nonqualified share options, share grants, and restricted share units to the individual who were not previously an employee or director of the Company or individuals returning to employment after a bona fide period of non-employment with the Company. Please see Note 12 to our Annual Report on Form 10-K for the year ended December 31, 2022 filed with the SEC on March 14, 2023 for additional information regarding the 2020 Inducement Equity Plan.

Pay for Performance

The Compensation Committee does not reference Total Shareholder Return or Net Income in determining executive compensation. The Company's performance is attributable to the successful execution of our commercial, regulatory, clinical and research goals.

The Compensation Committee evaluates the performance of the Company and sets objectives, which consequently influence executive compensation. These objectives include the Company's progress in commercializing OTL-200 (Libmeldy), as well as advancing our pre-clinical and clinical programs. The Compensation Committee believes that the compensation provided to our executives is appropriate when performance is measured against our strategic priorities and that decisions made in that respect are commensurate with our overall performance.

					Value of Initial	
			Average		Fixed \$100	
	Summary	Compensation	Summary Compensation	Average Compensation	Investment Based On	
	Compensation Table Total	Actually Paid ("CAP") to	Table Total for Non-PEO	Actually Paid to Non-PEO	Total Shareholder	Net Income
Year	for PEO	PEO ⁽¹⁾	NEOs ⁽²⁾	NEOs(1), (2)	Return ⁽³⁾	(000) (4)
(a)	(b)	(c)	(d)	(e)	(f)	(g)
2022	\$1,447,527	\$ 713,293	\$1,205,637	\$ 883,243	\$ 8.59	(\$150,660)
2021	\$4,354,539	\$ 455,135	\$1,973,833	\$ 541,023	\$ 30.56	(\$ 144,584)

(1) The table below reconciles the difference between the Summary Compensation Table and Compensation Actually Paid.

						Add		Awards		
						Change in	Awards	granted in		
					Change in	Value of	granted in	prior that		
		Summary	Subtract	Add	Value of	Vested	prior year	did not meet		
		Compensation	Equity	Year-end	Prior Equity	Equity	which vested	vesting	Com	pensation
Year 2022	Executive	Table Total	Awards	Equity Value	Awards	Awards	in year	conditions	Actu	ually Paid
2022	PEO	\$1,447,527	\$ 546,101	\$ 128,733	(\$131,581)	\$ 85,804	-\$ 85,838	(\$185,250)	\$ ´	713,293
	Average non-PEO	\$1,205,637	\$ 441,855	\$ 133,474	(\$ 50,523)	\$ 78,175	-\$ 41,663	\$ 0	\$	883,243
2021	PEO	\$4,354,539	\$3,504,354	\$ 289,246	(\$530,487)	\$446,565	-\$ 15,374	(\$585,000)	\$ 4	455,135
	Average non-PEO	\$1,973,833	\$1,257,233	\$ 106,019	(\$423,493)	\$175,665	-\$ 33,768	\$ 0	\$:	541,023

(2) Represents data for Frank Thomas, as the sole disclosed Non-PEO.

(3) Calculated as the Total Shareholder return in the periods between (a) December 31, 2020 and December 31, 2021 and (b) December 31, 2021 and December 31, 2022, respectively.

(4) Net Income figures corresponds to Net loss attributable to ordinary shareholders, which are included in our audited consolidated financial statements for the year ended December 31, 2022, which are included in our Annual Report on Form 10-K, filed with the SEC on March 14, 2023. Net loss from operations was \$127.0 million for 2022 and \$140.4 million for 2021, representing an approximately 10% decrease year-on-year.

Relationship between CAP, TSR and Net Income

Absent any dividends, Total Shareholder Return in the table above reflects the share price declines experienced in the last two years. This share price decline is impacted by both internal performance and external headwinds facing the global economy, the biotechnology sector, and in particular our subsector of cell and gene therapies. Net loss for the years analyzed remains fairly constant, while CAP increased year-on-year from 2021 to 2022. The Company undertook a reorganization of programs and cost structure in 2022, and the Company began realizing the financial benefits of such actions in the second quarter of 2022. The consistency of net loss factors in unrealized losses from foreign currencies; our underlying net losses from operations have declined year-on-year from 2021 to 2022. With substantial portions of our equity program based on share options, the Compensation Actually Paid is substantially lower than the annual amounts represented in the Summary Compensation Table. These amounts do not fully correspond to TSR due to a repricing of certain share options, effective October 4, 2022.

AUDIT COMMITTEE REPORT

The Audit Committee oversees the accounting and financial reporting processes of the Company and the audits of the Company's financial statements, evaluates auditor performance, manages relations with the Company's independent registered public accounting firm and evaluates policies and procedures relating to internal control systems. The Audit Committee operates under a written Audit Committee charter that has been adopted by the Board of Directors. All members of the Audit Committee currently meet the independence and qualification standards for Audit Committee membership set forth in the listing standards provided by Nasdaq and the U.S. Securities and Exchange Commission ("SEC"), and the Board has determined that Charles A. Rowland, Jr. is an "audit committee financial expert," as the SEC has defined that term in Item 407 of Regulation S-K.

The Audit Committee members are not professional accountants or auditors. The members' functions are not intended to duplicate or to certify the activities of management and the independent registered public accounting firm. The Audit Committee serves a board-level oversight role in which it provides advice, counsel and direction to management and the auditors on the basis of the information it receives, discussions with management and the auditors, and the experience of the Audit Committee's members in business, financial and accounting matters.

The Audit Committee oversees the Company's financial reporting process on behalf of the Board. The Company's management has the primary responsibility for the financial statements and reporting process, including the Company's system of internal controls. In fulfilling its oversight responsibilities, the Audit Committee reviewed with management the audited financial statements included in the Annual Report on Form 10-K for the fiscal year ended December 31, 2022. This review included a discussion of the quality and the acceptability of the Company's financial reporting, including the nature and extent of disclosures in the financial statements and the accompanying notes. The Audit Committee also reviewed the progress and results of the testing of the design and effectiveness of its internal controls over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act of 2002.

PricewaterhouseCoopers LLP ("PwC USA"), the Company's independent registered public accounting firm, which is responsible for expressing an opinion on the conformity of the audited financial statements with accounting principles generally accepted in the United States of America, also reviewed with the Audit Committee their judgments as to the quality and the acceptability of the Company's financial reporting and such other matters as are required to be discussed with the Committee by Public Company Accounting Oversight Board ("PCAOB") Auditing Standard No. 1301, *Communications with Audit Committees*, and SEC Regulation S-X Rule 207, *Communication with Audit Committees*.

The Audit Committee has received the written disclosures and the letter from PwC USA required by the applicable requirements of the PCAOB regarding communications with the audit committee concerning independence. The Audit Committee has discussed with PwC USA its independence from management and the Company.

In addition to the matters specified above, the Audit Committee discussed with PwC USA the overall scope, plans and estimated costs of their audit. The Committee met with PwC USA periodically, with and without management present, to discuss the results of PwC USA's examinations, the overall quality of the Company's financial reporting and PwC USA's reviews of the quarterly financial statements, and drafts of the quarterly and annual reports.

In reliance on the reviews and discussions referred to above, and subject to the limitations of the Audit Committee's role and responsibilities referred to above and in the Audit Committee charter, the Audit Committee

recommended to the Board that the Company's audited financial statements should be included in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2022.

The Audit Committee of the Board

Charles A. Rowland, Jr., Chairperson Marc Dunoyer Alicia Secor

The foregoing report of the Audit Committee shall not be deemed incorporated by reference by any general statement incorporating by reference this proxy statement into any filing under the Securities Act of 1933, as amended, or under the Securities Exchange Act of 1934, as amended, except to the extent that the Company specifically incorporates this information by reference, and shall not otherwise be deemed filed under such acts.

DELIVERY OF PROXY MATERIALS

Our Annual Report on Form 10-K for the fiscal year ended December 31, 2022 (the "Annual Report"), including audited financial statements, accompanies this proxy statement. Copies of our Annual Report and the exhibits thereto are available from the Company without charge upon written request of a shareholder. Copies of these materials are also available online through the SEC at *www.sec.gov*. The Company may satisfy SEC rules regarding delivery of proxy materials, including this proxy statement and our Annual Report, by delivering a single set of proxy materials to an address shared by two or more Company shareholders or ADS holders. This delivery method can result in meaningful cost savings for the Company. In order to take advantage of this opportunity, the Company may deliver only a single set of proxy materials to multiple shareholders or ADS holders who share an address, unless contrary instructions are received prior to the mailing date. Similarly, if you share an address with another shareholder or ADS holder and have received multiple copies of our proxy materials, you may write or call us at the address and phone number below to request delivery of a single copy of the proxy materials in the future. We undertake to deliver promptly upon written or oral request a separate copy of the proxy materials, as requested, to a shareholder or ADS holders at a shared address to which a single copy of the proxy materials was delivered. If you are an ordinary shareholder of record and prefer to receive separate copies of proxy materials either now or in the future, please contact Christopher York, Company Secretary, Orchard Therapeutics plc, 245 Hammersmith Road, London W6 8PW, United Kingdom or by telephone at +44 (0) 203 808 8286. If you hold ADSs and you prefer to receive separate copies of proxy materials either now or in the future, please contact the Depositary, your brokerage firm or bank, as applicable.

EACH ORDINARY SHAREHOLDER IS URGED TO COMPLETE, DATE, SIGN AND PROMPTLY RETURN THE ENCLOSED ORDINARY SHAREHOLDER PROXY FORM.

EACH ADS HOLDER IS URGED TO COMPLETE, DATE, SIGN AND PROMPTLY RETURN THE ADS PROXY CARD TO CITIBANK, N.A., THE DEPOSITARY FOR THE ADSs.

ADDITIONAL INFORMATION

U.K. Statutory Annual Accounts and Reports of the Board of Directors and Auditors of Orchard Therapeutics plc for the year ended December 31, 2022

Consistent with its obligations under the U.K. Companies Act 2006, our Board of Directors will present at the AGM our U.K. statutory annual accounts and reports for the year ended December 31, 2022, which have been approved by and, where appropriate, signed on behalf of our Board of Directors and will be delivered to the Registrar of Companies in the United Kingdom following the AGM. A copy of our U.K. statutory directors' remuneration report, including the annual report on remuneration, is included as Annex A to this proxy statement. A complete copy of our U.K. statutory annual accounts and reports, including the statutory Board of Directors report, strategic report, and auditor's report on our U.K. accounts will be sent separately to you no less than 21 days prior to the AGM. You will be provided an opportunity to raise questions in relation to such accounts and reports at the AGM. Full accounts and reports will be available for inspection prior to and during the AGM.

Shareholders' Rights to Call a General Meeting

Our shareholders have the right to call a meeting of our shareholders. The U.K. Companies Act 2006 generally requires the directors to call a general meeting once we have received requests to do so from shareholders representing at least 5% of our paid-up shares entitled to vote at a general meeting. The U.K. Companies Act 2006 prohibits shareholders of a U.K. public limited company from passing written resolutions. However, significant shareholders would, in any case, still have the power to call a general meeting and propose resolutions. These provisions are mandatory under the U.K. Companies Act 2006 and cannot be waived by our shareholders.

Shareholder Proposals for 2024 Annual General Meeting

Rule 14a-8 Proposals -- Pursuant to Rule 14a-8 under the Exchange Act, in order to be considered for inclusion in our proxy statement for our 2024 annual general meeting of shareholders, shareholder proposals must be received by the Company at the Office of the Company Secretary, 245 Hammersmith Road, London W6 8PW, United Kingdom no later than 120 days before the anniversary of the date on which we sent our proxy materials for the AGM (or []). However, if the date of the 2024 annual general meeting is more than 30 calendar days from the date of the anniversary of the AGM, then the notice must be received by our Company Secretary a reasonable time before we begin to print and send our proxy materials.

Other Proposals -- Shareholders intending to include a proposal on the agenda for the 2024 annual general meeting of shareholders, irrespective of whether they intend to have the proposal included in our proxy statement, must comply with the requirements under our Articles of Association and English law. Under section 338 of the U.K. Companies Act 2006, shareholders representing at least 5% of holders entitled to vote on a resolution at an annual general meeting may require the Company to include such resolution in its notice of an annual general meeting. Provided the applicable thresholds are met, notice of the resolution must be received by the Company at the Office of the Company Secretary, 245 Hammersmith Road, London W6 8PW, United Kingdom at least six weeks prior to the date of the annual general meeting, or, if later, at the time notice of the annual general meeting is delivered to shareholders.

To comply with the universal proxy rules, shareholders who intend to solicit proxies in support of director nominees other than the Company's nominees must provide notice at our principal executive offices that sets forth the information required by Rule 14a-19 under the Exchange Act no later than 60 days prior to the anniversary of the AGM (or []).

Proposals and nominations that are not received by the dates specified above, or otherwise do not meet all relevant requirements, will be considered untimely or improper, as applicable. We also encourage anyone sending in a shareholder proposal to additionally send such proposals via email to Christopher York, Company Secretary (Christopher.york@orchard-tx.com).

Questions?

If you have any questions or need more information about the Meeting, please write to us at:

Christopher York Company Secretary Orchard Therapeutics plc 245 Hammersmith Road London W6 8PW United Kingdom

Annual Statement from the Chair of the Compensation Committee

Dear Shareholder,

As the Chair of the Compensation Committee (the "Committee"), I am pleased to present, on behalf of the Board of Directors (the "Board") of Orchard Therapeutics plc (the "Company" or "Orchard"), the Directors' Remuneration Report for the year ended 31 December 2022 (the "Remuneration Report").

The Company's Remuneration Report will be subject to an advisory vote at the forthcoming Annual General Meeting on 25 May 2023 (the "AGM").

Introduction

Our executive compensation program seeks to incentivize and reward strong corporate performance. All compensation decisions at Orchard remain aligned to our key principle of paying for performance. Further, as a global biopharmaceutical company with major operations in the United States and Europe we operate within a global marketplace for talent. Given that the market for experienced directors and biopharmaceutical executive talent is very competitive, particularly in the United States, the Committee references the U.S. market as the leading indicator for remuneration levels and practices. This helps attract and retain directors and motivate the superior executive talent needed to successfully manage the Company's complex global operations. Being consistent in this market view of the United States as the primary benchmark for remuneration practices for our Executive and Non-Executive Directors is key for the Company as it builds its global operations in a manner designed to deliver sustainable, long-term growth and shareholder value.

As a Committee, we are also mindful of general UK compensation frameworks and investor guidance in that regard when making decisions on Orchard's executive compensation.

With these various factors in mind, we were pleased to receive shareholder support adopting our 2022 Remuneration Policy at the 2022 AGM. Gratefully supported by our shareholders, myself and the Compensation Committee believe that the overall structure of our Directors' Remuneration Policy remains appropriate to attract, retain and motivate directors to execute the Company's strategy.

Key remuneration decisions for 2022

The Committee and I were mindful of the prevailing economic environment, fiscal position and available cash resources of the Company at year-end 2022 and the Company's share price performance during the year. We acknowledge and celebrate the many achievements made by all our colleagues at Orchard while ensuring the broader context of the Company and the macro-economic environment are considered when making remuneration decisions.

In the first quarter of 2022, all employees' salaries at Orchard were increased by 5%. This decision was made in response to the competitive landscape of the biotechnology sector and a fast-paced compensation market for talent and skills we require as well as the inflationary environment in which we are operating. The CEO's salary was treated in the same manner as all other employees.

Two key decisions during 2022 related to equity-based compensation. Firstly, to reinforce the performance focus of our executive compensation program, the CEO's annual equity award, half of the award was granted as performance-based share options with an exercise price set at a 25% premium above the share price on the date of grant.

continued

Secondly, in October 2022 and under the terms of the Company's Share Option Incentive Plan 2018, the Board of Directors approved a repricing of previously awarded share options which were significantly 'underwater'. In the situation where substantial portions of employees' equity holding had little or no value, the Board took the decision to reprice these awards. This was done in order to reengage staff with the future success of Orchard and provide additional retentive value to the investment previously made in our equity program. The Company has, and continues to grant, equity-based compensation to all employees – aligning the entire workforce with the future value of the Company. The CEO's equity was treated in the same manner as all other employees, with details shown in the Annual Report on Remuneration. In making this decision, the Board of Directors considered several factors in determining which grants would be eligible for repricing and which grants would remain on the original terms, including (i) none of the non-executive director grants were repriced; (ii) only grants with an original exercise price above \$1.25¹ were repriced, representing a 150% premium to the share price on the date of repricing; (iii) none of the grants from 2022 were repriced; and (iv) the exercise price of the repriced options was set at a 16% premium to the closing market price on the date of repricing.

2022 Annual Bonus

Orchard's annual bonus is based on stated corporate objectives set by the Board and the Compensation Committee at the beginning of the year. For 2022 this was made up of a combination of objectives contributing to the foundation of a sustainable commercial business, advancing our portfolio towards key clinical and regulatory milestones, and maintaining a performance-driven culture both internally and with our partners.

For the CEO and consistent for all employees, the Committee determined a corporate score of 85% of target. This is reflective of the Company as a whole making considerable strides towards all of our stated objectives while also acknowledging that some key objectives were not achieved during the year due to either internal or external factors. The Committee does however recognize that the progress and achievements during 2022 puts the Company in a favorable position with considerable momentum going into 2023 and beyond.

The Committee's decision is taken in the context of the broader financial position of the Company, the share price performance during the year, and the competition for talent in the global biotechnology sector.

Remuneration for 2023

There are no substantial changes to our approach to executive compensation for 2023. At his own request and recommendation, the CEO will not receive a salary increase for 2023. The Committee commends Dr Gaspar for this proposal.

Consistent with our pay for performance philosophy, we continue to make an annual award of share options to Dr. Gaspar for 2023. Consistent with 2022, we have granted half of the 2023 award in performance-based, premium-priced options – options with an exercise price above the stock price on the date of grant. This instills a further hurdle before a portion of Dr. Gaspar's long-term incentive has any intrinsic value and further aligns our compensation approach with the shareholder experience. Similarly, a portion of the 2023 options granted to the entire executive team were also issued with an exercise price at a premium above the stock price on the date of grant.

As part of an on-going review of the Board's remuneration, an adjustment to the fees paid to Non-Executive Directors will be implemented for 2023. The principal adjustment is the reduction by \$5,000 in the base cash compensation provided for Board membership – this removes a supplement previously provided for time and

¹ Share price before 1:10 American Deposit Share (ADS) ratio change effective on 10 March 2023.

continued

commitment to international travel with a corresponding rebalancing in equity compensation. Additionally, from 2023 a shareholding guideline of threetimes this base fee is introduced for Non-Executive Directors with a five year period allowed for each Board member to gain compliance. We believe this is an important step in reinforcing the connection between the Board and the long-term value of the Company.

Conclusion

The Committee believes that the Directors' Remuneration Policy has been implemented fairly and consistently, as described in this report. We are confident that remuneration arrangements will continue to properly motivate our Directors and executive team to deliver sustainable growth and shareholder value over the long term and to do so in a responsible and cost-efficient manner.

I hope that you find the information in this report helpful, and I look forward to your support at the Company's AGM.

Yours sincerely,

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Charles Rowland, Jr. *Chair of the Compensation Committee*

13 April 2023

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Remuneration Policy

The following section sets out our Directors' Remuneration Policy (the "Policy") as approved by binding shareholder vote at the annual general meeting on 7 June 2022. The document, as approved, can be found in the Company's 2021 Annual Report.

The policy received strong shareholder support, as has the implementation of the policy in the annual voting.

Key considerations when determining the Remuneration Policy

The Policy is designed by the Committee with a number of specific principles in mind:

- attract, retain and motivate high calibre senior management and focus them on the delivery of the Company's strategic and business objectives;
- encourage a corporate culture that promotes the highest level of integrity, teamwork and ethical standards;
- be competitive against appropriate market benchmarks (being predominantly the US biotech sector) and have a strong link to performance, providing the ability to earn above-market rewards for strong performance;
- be simple and understandable, both internally and externally;
- encourage increased equity ownership to motivate executives in the overall interests of shareholders, the Company, employees and customers; and
- take due account of good governance and promote the long-term success of the Company.

In seeking to achieve the above objectives, the Committee is mindful of the views of a broad range of stakeholders in the business and accordingly takes account of a number of factors when setting remuneration including: market conditions; pay and benefits in relevant comparator organisations; terms and conditions of employment across the Company; the Company's risk appetite; the expectations of institutional shareholders; and any specific feedback received from shareholders and other stakeholders.

Key changes to the Remuneration Policy

The Committee maintains that the overall structure of remuneration is appropriate and no fundamental structural changes are proposed. The Committee does acknowledge that there are developments in market and best practices which include:

- Introduction of share ownership requirements for Executive Directors intends to ensure long- term alignment between our Executive Directors and shareholders.
- Introduction of recovery provisions (malus and clawback) provides mitigation against payment for failure and ensures that all future incentive-based compensation in subject to recovery.
- The retainer arrangements for Non-Executive Directors will include the flexibility for Directors to elect a portion, or all, of their fees as either cash or in equity equivalents. This is common practice in the US and is included to ensure our Director compensation arrangements are competitive within our sector landscape.

continued

Remuneration Policy table

The table in the following pages sets out, for each element of pay, a summary of how remuneration is structured and how it supports the Company's strategy.

Executive Directors Purpose and link to strategy Base salary	Operation	Maximum opportunity	Performance metrics		
To recruit and retain Executive Directors of the highest calibre who are capable of delivering the Company's strategic objectives, reflecting the individual's experience and role within the Company.	Salaries are normally reviewed annually. The annual salary review for Executive Directors takes a number of factors into consideration, including:	Whilst there is no prescribed formulaic maximum, any increases will take into account prevailing market and economic conditions and the approach to employee pay throughout the organisation.	Executive Directors' performance is a factor considered when determining any salary increases.		
Base salary is designed to provide an appropriate level of fixed income to avoid any over-reliance on variable pay elements that could encourage excessive risk taking.	 business performance; salary increases awarded to the overall employee population; skills and experience of the individual over time; scope of the individual's responsibilities; changes in the size and complexity of the Company; market competitiveness assessed by periodic benchmarking; and the underlying rate of inflation. 	Base salary increases are awarded at the discretion of the Committee; however, salary increases will normally be no greater than the general increase awarded to the wider workforce, in percentage of salary terms. However, a higher increase may be made where an individual had been appointed to a new role at below- market salary while gaining experience. Subsequent demonstration of strong performance may result in a salary increase that is higher than that awarded to the wider workforce.			

Annex A - Part I

	continued		
<u>Executive Directors</u> Purpose and link to strategy Benefits	Operation	Maximum opportunity	Performance metrics
Reasonable benefits-in- kind are provided to support Executive Directors in carrying out their duties and assist with retention and recruitment.	The Company aims to offer benefits that are in line with market practice. The main benefits currently provided include private health insurance, long-term disability, critical illness and death in service.	The value of each benefit is not predetermined and is typically based upon the cost to the Company of providing said benefit.	Not performance related.
	Under certain circumstances the Company may offer relocation allowances or assistance. Expatriate benefits may be offered where required.		
	Travel and any reasonable business- related expenses (including tax thereon) may be reimbursed.		
	Executive Directors may become eligible for other benefits in future where the Committee deems it appropriate. Where additional benefits are introduced for the wider workforce, Executive Directors may participate on broadly similar terms.		
	Benefits may also include payment by the Company of any stamp duty arising in respect of the settlement of equity incentives.		
Retirement benefits			
The Company aims to provide a	Executive Directors are eligible to receive	Up to 6% of salary per annum for	Not performance

The Company aims to provide a contribution towards life in retirement.

Executive Directors are eligible to receive employer contributions to the Company's Group Personal Pension Scheme or to a 401k plan or a salary supplement in lieu of pension benefits, or a mixture of both. Up to 6% of salary per annum for Executive Directors.

Not performance related.

6% is the contribution rate provided to all UK employees.

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DIRECTORS' REMUNERATION REPORT

Annex A - Part I

	continu	led	
Executive Directors Purpose and link to strategy Annual bonus	Operation	Maximum opportunity	Performance metrics
The annual bonus scheme rewards the achievement of stretching objectives that support the Company's corporate goals and delivery of the business strategy.	Bonuses are determined based on measures and targets that are agreed by the Committee at the start of each financial year. In exceptional circumstances, the Committee may add further performance measures and milestones during the year.	The target bonus opportunity for Executive Directors is up to 80% of salary, with a maximum bonus opportunity of up to two times the target opportunity. For threshold performance, no more than 50% of target bonus may be payable. For 2023, the target bonus opportunity for Executive Directors will be no more than 60% of salary, with a maximum bonus opportunity of up to 150% of the target opportunity. Any exceptional bonuses would operate within the overall annual maximum opportunity.	Performance measures are determined by the Committee each year and may vary to ensure that they promote the Company's business strategy and shareholder value. The annual bonus will be based on strategic goals, which may include financial, strategic and personal objectives. The Committee may alter the bonus outcome if it considers that the pay-out is inconsistent with the Company's overall performance, taking account of any factors it considers relevant. This will help ensure that pay-outs reflect overall Company performance during the year.

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DIRECTORS' REMUNERATION REPORT

	continu	ied	
Executive Directors Purpose and link to strategy Long-term incentives	Operation	Maximum opportunity	Performance metrics
At the date of this Policy, long-term incentives are normally granted under the 2018 Share Option and Incentive Plan ("SOIP"). The SOIP is designed to incentivise the successful execution of business strategy over the longer term and provide long-term retention. Facilitates share ownership to provide further alignment with shareholders.	The Committee will select the most appropriate form of SOIP award(s) each year. Awards will typically be granted annually, in the form of options and restricted share units ("RSUs") although may also be granted in the form of share appreciation rights, restricted shares, unrestricted shares, performance share units, cash or dividend equivalent rights.	There is no defined maximum opportunity under the SOIP. However, the Committee will generally work within the guidelines provided by our compensation consultants. We seek to establish equity-based remuneration competitive to that offered by a set of comparable companies with whom we may compete for talent.	Performance conditions may apply to awards. Such conditions may be strategic objectives which may include milestone events, financial, strategic and/or personal objectives. Share options are granted with an exercise price no less than the fair market value of the shares on the date of grant. Accordingly, share options will
	Currently, options normally vest over a period of four years on a monthly basis. Initial grants made in relation to appointment generally vest 25% after one year, and monthly thereafter for 36 months. Currently, time-based RSUs normally vest in equal installments annually over a total period of no less than three years. Performance Share Units ("PSUs") normally vest in three equal tranches on the meeting of agreed milestone events within a period of three years. The Committee may vary the vesting schedule of future grants of options and PSUs as it considers appropriate. At the discretion of the Committee, participants may also be entitled to receive the value of dividends paid between grant and vesting on vested shares. The payment may be in cash or shares and may assume dividend reinvestment.		 Any performance conditions will only have value to the extent the Company's share price appreciates following the date of grant. Any performance conditions set will be designed to incentivise performance in support of the Company's strategy and business objectives. The Committee has flexibility to vary the mix of measures or introduce new measures for each subsequent award taking into account business priorities at the time of grant. The Committee may alter the vesting outcome if it considers that the level of vesting is inconsistent with the underlying performance of the business, taking account of any factors it considers relevant. This will help ensure that vesting reflects overall Company performance during the year.
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Annex A - Part I

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DIRECTORS' REMUNERATION REPORT

Annex A - Part I

	continued		
Executive Directors Purpose and link to strategy All employee share schemes	Operation	Maximum opportunity	Performance metrics
Encourages employee share ownership and therefore increases alignment with shareholders. Executive Directors will be eligible to participate in any all-employee share scheme.	The Company currently operates an Employee Share Purchase Plan ("ESPP") that offers employees the opportunity to purchase shares in the Company through payroll deductions at a price equal to 85% of the lower of fair market value of the shares on the first business day or the last business day of the offering period. The ESPP is available to all employees whose customary employment is for more than 20 hours per week and have completed at least 30 days of employment. The Company may adopt equivalent	Employees may contribute up to 15% of their base compensation to purchase shares under the ESPP. However, the right to purchase shares under the ESPP may not accrue at a rate that exceeds \$25,000 worth of ordinary shares, valued at the start of the purchase period, under the ESPP, for each calendar year in the purchase period.	Not performance related.
	arrangements in any jurisdiction in order to comply with local requirements.		

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DIRECTORS' REMUNERATION REPORT

Annex A - Part I

	continued		
on-Executive Directors urpose and link to strategy	Operation	Maximum opportunity	Performance metrics
Fees To attract Non-Executive Directors who have a broad range of experience and skills to provide independent judgement on issues of strategy, performance, resources and standards of conduct.	Non-Executive Directors receive an annual retainer paid in cash, comprising a base fee plus additional fees for additional responsibilities, such as a Committee Chairpersonship or membership and the role of Chairperson.	When reviewing fee levels, account is taken of market movements in the fees of Non-Executive Directors, Board Committee responsibilities and ongoing time commitments, as well as the underlying rate of inflation.	Not performance related.
	At a Directors' election, cash retainers may be delivered as an equivalent number of share options – calculated at fair value on the date of grant - vesting quarterly over a one-year period.	Actual fee levels are disclosed in the annual Directors' Remuneration Report for the relevant financial year.	
	The Chair's fee is reviewed annually by the Committee (without the Chair present). Fee levels for the Non- Executive Directors are determined by the Company Chair and Executive Directors.		
	When reviewing fee levels, account is taken of market movements in fee levels, Board committee responsibilities, ongoing time commitments and the general economic environment.		
	In exceptional circumstances, if there is a temporary yet material increase in the time commitments for Non- Executive Directors, the Board may pay additional fees to recognise that additional workload.		
	Non-Executive Directors ordinarily do not participate in any pension, bonus or performance-based share incentive plans. Travel, accommodation and other business- related expenses incurred in carrying out the role will be paid by the Company including, if relevant, any gross-up for tax.		
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Annex A - Part I

DIRECTORS' REMUNERATION REPORT

continued

<u>Non-Executive Directors</u> Purpose and link to strategy Equity Awards	Operation	Maximum opportunity	Performance metrics
To facilitate share ownership and provide alignment with shareholders.	 Non-Executive Directors may receive an equity award in the form of options, share appreciation rights, restricted shares, restricted share units or such other form permitted under the SOIP. New Non-Executive Directors receive an initial equity award upon appointment or election. In addition, Non-Executive Directors receive annual equity awards at the time of the annual meeting. Currently any initial equity awards normally vest in equal monthly installments for 36 months, and any annual awards normally are awarded at the AGM and vest at the earlier of the next AGM or one year after the grant date. 	There is no maximum award level for equity awards to Non- Executive Directors. The size of the equity awards is determined by the full Board of Directors, upon recommendation of the Compensation Committee. When reviewing award levels, account is taken of market movements in equity awards, Board committee responsibilities, ongoing time commitments and the general economic conditions.	Not performance related.

An illustration of the application of the Remuneration Policy can be found in the Company's 2021 Annual Report.

Notes to the policy table

Legacy arrangements

For the duration of this Policy, the Company will honour any commitments made in respect of current or former Directors before the date on which either: (i) the Policy becomes effective; or (ii) an individual becomes a Director, even where not consistent with the Policy set out in this report or prevailing at the time such commitment is fulfilled. For the avoidance of doubt, all outstanding historic awards that were granted in connection with, or prior to, listing remain eligible to vest based on their original or modified terms.

Performance conditions

The choice of annual bonus performance metrics reflects the Committee's belief that any incentive remuneration should be appropriately challenging and tied to the delivery of key strategic objectives intended to ensure that Executive Directors are incentivised to deliver across a range of objectives for which they are accountable. The Committee has retained flexibility on the specific measures which will be used to ensure that any measures are fully aligned with the strategic imperatives prevailing at the time they are set.

continued

The targets for the bonus scheme for the forthcoming year will be set out in general terms, subject to limitations with regards to commercial sensitivity. The full details of the targets will be disclosed when they are in the public domain and are no longer considered commercially sensitive.

Where used, performance conditions applicable to SOIP awards will be aligned with the Company's objective of delivering superior levels of long-term value to shareholders. The full details of performance conditions will be disclosed when they are in the public domain and are no longer commercially sensitive. Prior to each award, the Committee has flexibility to select measures that are fully aligned with the strategy prevailing at the time awards are granted.

The Committee will review the calibration of targets applicable to the annual bonus, and the SOIP in years where performance measures apply, annually to ensure they remain appropriate and sufficiently challenging, taking into account the Company's strategic objectives and the interests of shareholders.

Shareholding guidelines

Executive Directors are expected to build up and maintain, a shareholding equivalent to a multiple of their respective base salary. For the Chief Executive Officer, this multiple is equal to two-times their base salary and for any other Executive Director, one-times base salary. Executive Directors will have five years from either the adoption of the policy or their appointment to the Board, whichever is later, to achieve the target level of share ownership.

Differences in remuneration policy between Executive Directors and other employees

The overall approach to reward for employees across the workforce is a key reference point when setting the remuneration of the Executive Directors. When reviewing the salaries of the Executive Directors, the Committee pays close attention to pay and employment conditions across the wider workforce and in normal circumstances the increase for Executive Directors will be no higher than the average increase for the general workforce.

The key difference between the remuneration of Executive Directors and that of our other employees is that, overall, at senior levels, remuneration is increasingly long-term, and 'at risk' with an emphasis on performance-related pay linked to business performance and share-based remuneration. This ensures that remuneration at senior levels will increase or decrease in line with business performance and provides alignment between the interests of Executive Directors and shareholders.

Committee discretion in operation of variable pay schemes

The Committee operates under the powers it has been delegated by the Board. In addition, it complies with rules that are either subject to shareholder approval or by approval from the Board. These rules provide the Committee with certain discretions which serve to ensure that the implementation of the remuneration policy is fair, both to the individual Director and to the shareholders. The Committee also has discretions to set components of remuneration within a range, from time to time. The extent of such discretions is set out in the relevant rules, the maximum opportunity or the performance metrics section of the policy table above. To ensure the efficient administration of the variable incentive plans outlined above, the Committee will apply certain operational discretions.

These include the following:

- selecting the participants in the plans on an annual basis;
- determining the timing of grants of awards and/or payments;

continued

- determining the quantum of awards and/or payments (within the limits set out in the policy table above);
- determining the choice (and adjustment) of performance measures and targets for each incentive plan in accordance with the policy set out above and the rules of each plan;
- determining the extent of vesting based on the assessment of performance and discretion relating to measurement of performance in certain events such as a change of control or reconstruction;
- making the appropriate adjustments required in certain circumstances, for instance for changes in capital structure;
- determining "good leaver" status, if applicable, for incentive plan purposes and applying the appropriate treatment; and
- undertaking the annual review of weighting of performance measures and setting targets for the annual bonus plan and other incentive schemes, where applicable, from year to year.

If an event occurs which results in the annual bonus plan or SOIP performance conditions and/or targets being deemed no longer appropriate (e.g. material acquisition or divestment), the Committee will have the ability to make appropriate adjustments to the measures and/or targets and alter weightings, provided that the revised conditions are not materially less challenging than the original conditions. Any use of the above discretion would, where relevant, be explained in the Annual Report on Remuneration and may, as appropriate, be the subject of consultation with the Company's major shareholders.

Recovery Provisions (malus and clawback)

Prior to vesting, the Compensation Committee may reduce or cancel any awards granted under the Company's 2018 SOIP, or impose additional conditions on awards in circumstances the Compensation Committees deems appropriate ('malus'). Such circumstances may include: a serious misstatement of the Group's audited financial results; a serious miscalculation of any relevant performance measure; a serious failure of risk management or regulatory compliance by a relevant entity; serious reputational damage to the Group; the participant's material misconduct, or a material corporate failure.

In addition, for cash bonus and SOIP awards the Compensation Committee may also apply malus and/or clawback in certain extreme circumstances (including those listed above) for up to two years following the determination of the relevant performance outcome of vesting of the award.

Prior to applying malus or clawback, the Compensation Committee will take into account all relevant factors (including, where a serious failure of risk management or regulatory compliance or serious reputational damage has occurred, the degree of involvement of the employee in that failure or damage in question and the employee's level of responsibility) in deciding whether, and to what extent, it is reasonable to operate malus and/or clawback. The Compensation Committee is satisfied that the above provisions provide robust safeguards against inappropriate payment of incentive awards.

Shareholder views

The Board is committed to dialogue with shareholders and intends to engage directly with them and their representative bodies when considering any significant changes to our remuneration arrangements. The Compensation Committee will consider shareholder feedback received following the AGM, as well as any

continued

additional feedback and guidance received from time to time. This feedback will be considered by the Committee as it develops the Company's remuneration framework and practices going forward. Assisted by its independent adviser, the Compensation Committee also actively monitors developments in the expectations of institutional investors and their representative bodies.

Employment conditions

The Committee is regularly updated throughout the year on pay and conditions applying to Company employees and has formal responsibility for human capital measures across the Company with a particular focus on diversity and inclusion activities. Where significant changes are proposed to employment conditions elsewhere in the Company these are highlighted for the attention of the Committee at an early stage.

Other remuneration policies

Remuneration for new appointments

Where it is necessary to appoint or replace an Executive Director or to promote an existing Executive Director, the Committee's approach when considering the overall remuneration arrangements in the recruitment of a new Executive Director is to take account of the calibre, expertise and responsibilities of the individual, his or her remuneration package in their prior role and market rates. Remuneration will be in line with our policy and the Committee will not pay more than is necessary to facilitate their recruitment.

The remuneration package for a new Executive Director will be set in accordance with the terms of the Company's approved remuneration policy in force at the time of appointment. Further details are provided below:

Salary	The Committee will set a base salary appropriate to the calibre, experience and responsibilities of the new appointee. In arriving at a salary, the Committee may take into account, amongst other things, the market rate for the role and internal relativities.
	The Committee has the flexibility to set the salary of a new Executive Director at a lower level initially, with a series of planned increases implemented over the following few years to bring the salary to the desired positioning, subject to individual performance.
	In exceptional circumstances, the Committee has the ability to set the salary of a new Executive Director at a rate higher than the market level to reflect the criticality of the role and the experience and performance of the individual.
Benefits	Benefits will be consistent with the principles of the policy. The Company may award certain additional benefits and other allowances including, but not limited to, those to assist with relocation support, temporary living and transportation expenses, educational costs for children and tax equalisation to allow flexibility in employing an overseas national.
Pension Benefits	A maximum pension contribution of 6% of salary may be payable for external appointments. For an internal appointment, his or her existing pension arrangements may continue to operate. Any new Executive Director based outside the UK will be eligible to participate in pension or pension allowance, insurance and other benefit programmes in line with local practice.

	continued
Annual bonus	The maximum bonus opportunity for new appointments is 150% of their target bonus.
Other cash or equity- based awards	Executive Directors may receive awards under the SOIP on appointment. The Committee will assess and determine the award level, award vehicle, performance conditions and vesting schedule for each individual on a case-by-case basis. In addition, Executive Directors are eligible to participate in any all employee share scheme (for example, ESPP) subject to the conditions set forth therein.
	In addition, the Committee may offer additional cash and/or equity-based elements in order to "buy-out" remuneration relinquished on leaving a former employer. Any awards made in this regard may have no performance conditions, or different performance conditions, or a different vesting schedule compared to the Company's existing plans, as the Committee considers appropriate. Depending on the timing and responsibilities of the appointment, it may be necessary to set different annual bonus or SOIP performance measures and targets as applicable to other Executive Directors.

The terms of appointment for a Non-Executive Director would be in accordance with the remuneration policy for Non-Executive Directors as set out in the policy table.

Service contracts and termination policy

Executive Directors have rolling service agreements which may be terminated in accordance with the terms of these agreements. The period of notice for Executive Directors will not normally exceed 12 months. Executive Directors' service agreements are available for inspection at the Company's registered office during normal business hours.

Name	Position	Date of service contract	Notice period
Bobby Gaspar ¹	Chief Executive Officer	2 January 2018	6 months either party

1 Hubert (Bobby) Gaspar.

The Company's policy on remuneration for Executive Directors who leave the Company is set out below. The Committee will exercise its discretion when determining amounts that should be paid to leavers, taking into account the facts and circumstances of each case. Generally, in the event of termination, the Directors' service contracts may provide for payment of basic salary over the notice period. Where applicable, the Company may elect to make a payment in lieu of notice (PILON) equivalent in value to basic salary for any unexpired portion of the notice period. PILON payments may be made in monthly instalments or as a lump sum, and the individual is expected to take reasonable steps to seek alternative income to mitigate the payments. The Company may also pay for outplacement services for Executive Directors on termination or the Company may elect to make a payment in lieu of outplacement services. The Company may continue to pay the employer health plan premium for the Executive Director on termination for a period of up to 12 months (up to 18 months in connection with a change in control).

continued

Any outstanding incentive awards will be treated in accordance with the plan rules, as follows:

	Termination without cause or for cause by participant	Termination for cause	Termination without cause or for cause by participant in connection with change of control
Salary	A payment equal to up to 12 months' salary payable as a lump sum or on a monthly basis, less any amounts payable pursuant to any restrictive covenant agreements (if applicable) ("Restrictive Covenants Agreement Setoff") paid or to be paid in the same calendar year.	No payment.	A payment of up to 18 months' salary payable as a lump sum or on a monthly basis for termination without cause, less any Restrictive Covenants Agreement Setoff (if applicable) paid or to be paid in the same calendar year.
Annual Bonus	Unpaid annual cash bonus in respect of prior year performance, which otherwise would have been earned if participant had remained employed through the payment date, should be paid in full. A pro-rata amount of the participant's target bonus for the current year should be paid, subject to the participant's actual performance.	Unpaid annual cash bonuses lapse in full.	Up to 1.5 times the participant's target bonus may be payable less any Restrictive Covenants Agreement Setoff (if applicable) paid or to be paid in the same calendar year.
Share Option Incentive Plan	Unvested awards lapse in full, except where the participant leaves in circumstances where they retain a statutory right to return to work (in which case, awards will continue to vest on normal terms).	Unvested awards lapse in full.	On a change of control, merger, reorganization or other corporate event, the Company may seek to replace awards with new awards in the successor company (to the extent agreed with the successor company). In the case of a termination without cause or for cause by the participant in connection with a change of control, such awards will accelerate and vest in full.
			Where there is no agreement to replac

Where there is no agreement to replace awards, on a corporate event awards with

continued

Termination without cause or for cause by participant	Termination for cause	Termination without cause or for cause by participant in connection with change of control
		time-based vesting conditions shall vest on the
		date of that event and awards with performance-
		based vesting conditions shall vest on the date of
		that event to the extent determined by the
		Company (regardless of the extent to which any performance conditions attached to awards have been satisfied).

The Company is unequivocally against rewards for failure; the circumstances of any departure, including the individual's performance, would be taken into account in every case. Statutory redundancy payments may be made, as appropriate. Service agreements may be terminated summarily without notice (or on shorter notice periods) and without payment in lieu of notice in certain circumstances, such as gross misconduct or any other material breach of the obligations under their employment contract. The Company may require the individual to work during their notice period or may place them on garden leave during which they would be entitled to salary, benefits and pension only.

Except in the case of gross misconduct or resignation, the Company may at its absolute discretion reimburse for reasonable professional fees relating to the termination of employment and, where an Executive Director has been required to re-locate, to pay reasonable repatriation costs, including possible tax exposure costs. This includes any statutory entitlements or sums to settle or compromise claims in connection with a termination (including, at the discretion of the Committee, reimbursement for legal advice and provision of outplacement services).

Policy on external appointments

The Board believes that it may be beneficial to the Company for executives to hold non-executive directorships outside the Company. Any such appointments are subject to approval by the Board, and the director may retain any fees received at the discretion of the Board. Dr Gaspar does not currently hold any outside directorships.

Non-Executive Directors' terms of engagement

Each of the Non-Executive Directors is engaged under a Non-Executive Director appointment letter. In any event, each appointment is terminable by either party on not less than three months' written notice. Our board of directors is classified, meaning that each of our directors is designated to one of three classes and is elected to serve a term of between one and three years. The Chair and Non-Executive Directors are only entitled to fees accrued to the date of termination.

continued

The dates of appointment of each of the Non-Executive Directors serving at 31 December 2022 are summarised in the table below. Dates prior to our incorporation in August 2018 as Orchard Rx Limited (now known as Orchard Therapeutics plc) are for Non-Executive Directors who served on the board of our predecessor company, Orchard Therapeutics Limited (now known as Orchard Therapeutics (Europe) Limited).

Non-Executive Directors	Date of contract or date of appointment	Service at 31.12.22
Joanne Beck	1 July 2018	4 years 6 months
Marc Dunoyer	6 June 2018	4 years 7 months
James Geraghty	4 June 2018	4 years 7 months
Charles Rowland	1 June 2018	4 years 7 months
Alicia Secor	7 December 2018	4 years 1 month
John Curnutte	30 August 2019	3 years 4 months
Steven Altschuler	3 February 2020	2 year 11 months

Directors' letters of appointment are available for inspection at the Company's registered office during normal business hours and will be available for inspection at the AGM.

continued

Annual Report on Remuneration

This part of the report has been prepared in accordance with Part 3 of The Large and Medium-sized Companies and Groups (Accounts and Reports) (Amendment) Regulations 2013 as amended, The Companies (Directors' Remuneration Policy and Directors' Remuneration Report) Regulations 2019 ("the 2019 regulations"). Since the Company is not FTSE-listed, it is under no obligation to comply with the UK Corporate Governance Code, but best practice and good governance have been considered when preparing this report. The Annual Report on Remuneration and the Annual Statement by the Chair of the Compensation Committee will be put to a single advisory shareholder vote at the AGM on 25 May 2023.

Compensation Committee (the "Committee")

The current members of the Committee, who are all independent, are Charles Rowland (Chair), Joanne Beck, Ph.D. and Alicia Secor.

The Chairman of the Board and members of management are invited to attend meetings where appropriate. The Company Secretary is the secretary to the Committee. Attendees are not involved in any decisions and are not present for any discussions regarding their own remuneration.

No conflicts of interest have arisen during the period and none of the members of the Committee has any personal financial interest in the matters discussed, other than as shareholders. The fees of the Non-Executive Directors are approved by the Board on the joint recommendation of the Committee in consultation with our independent compensation consultant.

Meetings attendance during 2022

	Attendance
Charles Rowland	5 of 5
Joanne Beck, Ph.D.	5 of 5
Alicia Secor	5 of 5

Independent advisors

Each year the Committee appoints a wholly independent advisor to provide advice on executive and board remuneration. For 2022, the Committee reappointed the Executive Compensation practice of Aon plc. Aon advises on remuneration arrangements and all aspects of senior executive and board remuneration. In 2022, Aon assisted the Committee and kept the Committee up to date on remuneration trends and regulations. During the 2022 financial year, fees charged by Aon for advice provided to the Committee amounted to \$115,943 (2021: \$131,226) (excluding VAT) on a time and materials basis. In addition, Aon provided advice to the Company's Human Resources function on implementation of HR initiatives. The Company's retained external legal counsel, Goodwin Procter LLP have also advised the Committee and the Company's Human Resources function on compensation. The Committee reviews the independence of all external advisors on an annual basis and considers that additional services by Aon and Goodwin in no way prejudices their position as independent advisors to the Committee.

Activity in the period

The Committee's principal function is to support Orchard's strategy by ensuring that those individuals responsible for delivering the strategy are appropriately incentivized and rewarded through the operation of

continued

Orchard's remuneration policy. In implementing the remuneration policy, and in constructing the remuneration arrangements for executive directors and senior employees, the Board, advised by the Committee, aims to provide remuneration packages that are competitive and designed to attract, retain and motivate Executive Directors and senior employees of the highest calibre.

The Committee is responsible for and considered, where applicable, during the period:

- evaluating the efficacy of the Company's remuneration policy and strategy;
- reviewing and determining remuneration to be paid to the Company's executive officers and directors;
- reviewing and making recommendations to the Board regarding remuneration for non-executive members of the Board;
- agreeing the design of all share incentive plans;
- preparing any report on executive remuneration required by the rules and regulations of the U.S. Securities and Exchange Commission, The Nasdaq Stock Market LLC and as required under UK law or other countries in which the Company operates;
- reviewing, evaluating, and approving employment agreements, severance agreements, change- of-control protections, equity grants, corporate performance goals and objectives, and other compensatory arrangements of the executive officers and other senior management and adjusting remuneration, as appropriate;
- evaluating and approving remuneration plans and programs and establishing equity remuneration policies;
- reviewing remuneration practices and trends to assess the adequacy and competitiveness of the executive remuneration programs as compared to industry peers, and determining the appropriate levels and types of remuneration to be paid;
- approving any loans by the Company to employees;
- reviewing and approving remuneration arrangements for any executive officer involving any subsidiary, special purpose or similar entity, with consideration of the potential for conflicts of interest; and
- reviewing the Company's practices and policies of employee remuneration as they relate to risk management and risk-taking incentives.

The Committee is formally constituted and operates on written terms of reference, which are available on Orchard's website, www.orchard-tx.com.

Statement of shareholder voting at 2022 AGM

At last year's AGM held on 7 June 2022, votes cast by proxy and at the meeting in respect of the Directors' remuneration were as follows:

	Votes For		Votes Against		Votes V	Withheld
	% of	Number	% of	Number	% of	Number
	votes cast	of votes	votes cast	of votes	votes cast	of votes
To approve the Directors' Remuneration Report	93.4%	48,023,460	6.3%	3,247,147	0.3%	150,066
To approve the Directors' Remuneration Policy	93.3%	47,965,263	6.5%	3,334,672	0.2%	120,738

continued

Single total figure of Directors' remuneration – year ended 31 December 2022 (audited)

The total remuneration of the individual Directors who served in the year ended 31 December 2022, is shown below. Total remuneration is the sum of emoluments plus Company pension contributions. The below table has been presented in US dollars (\$) which is the functional currency of the reporting entity:

		Base salary /fees \$000	Benefits ² \$000	Pension ³ \$000	Bonus \$000	SOIP ⁴ \$000	Total remun- eration \$000	Total fixed	Total variable
Executive Directors									
Bobby Gaspar ¹	2022	572.7	4.0	37.8	294.4	—	908.9	614.5	294.4
	2021	605.1	3.2	27.2	217.8		853.3	635.5	217.8
New Exception Disasters		Base salary /fees \$000	Benefits ² \$000	Pension \$000	Bonus \$000	SOIP ³ \$000	Total remun- eration \$000	Total fixed	Total variable
Non-Executive Directors	2022	52.7					50 7	50 7	
Steven Altschuler	2022	52.7					52.7	52.7	
	2021	51.9	_				51.9	51.9	
Joanne Beck	2022	60.2					60.2	60.2	—
	2021	59.4	—	—		_	59.4	59.4	—
John Curnutte	2022	60.2					60.2	60.2	—
	2021	63.7	—	—		—	63.7	63.7	—
Marc Dunoyer	2022	59.2					59.2	59.2	-
	2021	59.1		—		—	59.1	59.1	—
James Geraghty	2022	95.4					95.4	95.4	—
	2021	95.1		—			95.1	95.1	
Charles Rowland	2022	82.8					82.8	82.8	—
	2021	78.1		—	—	—	78.1	78.1	—
Alicia Secor ⁵	2022	66.8					66.8	66.8	
	2021	72.1					72.1	72.1	
Total	2022	1050.0	4.0	37.8	294.4	0.0	1386.2	1091.8	294.4
	2021	1084.6	3.2	27.2	217.8	0.0	1332.7	1114.9	217.8

 Dr Gaspar's salary is £462,000 per annum, which increased by 5% from £440,000 effective 1 March 2022. 2022 figures are converted at a 12-month average rate for 2022 of GBP 1 = USD 1.2495. 2021 figures are converted at a 12-month average rate for 2021 of GBP 1= USD 1.3753. Due to exchange rate fluctuation, the 2022 salary increase does not correspond to an increased reporting amount in USD.

2. For Executive Directors, benefits include private health insurance, long term disability, critical illness and death in service benefits.

3. Effective 1 April 2021, Dr. Gaspar began receiving a cash allowance in lieu of the Company's pension contribution equal to 6% of his salary. Dr. Gaspar received no pension benefits from the Company before this date.

4. The figures for the Share Option Incentive Plan (SOIP) represent the intrinsic value of the share options on the date of grant. All share options granted to Directors are awarded at the market value and therefore the intrinsic value at the time of grant is zero. Details of all options awarded to individual Directors during the year, including the number of options under award, the exercise price, vesting schedule and the grant date fair value can be found in the tables below. All awards in the column are subject to continued service only and are not subject to any further performance conditions.

5. Alicia Secor received a one-time retrospective payment of \$11,250 in April 2021 for prior services to the Nomination and Governance Committee which had previously not been paid.

continued

2022 Annual bonus

During a series of meetings between December 2022 and February 2023, the Compensation Committee evaluated the achievement of the 2022 corporate objectives and the Chief Executive's individual performance.

The Compensation Committee reviewed the corporate goals, below, and based on the results, approved an 85% achievement level of the 2022 corporate objectives.

Successes during 2022 spanned across all areas of the Company's activity, each individually and collectively critical for the long-term success of the Company. Overcoming a number of challenges in the year, the achievements assessed by the Committee have built considerable momentum for the Company across our portfolio and business operations.

Key achievements against agreed goals include those from commercial, regulatory, clinical- & pre-clinical research as well as financial. These are:

- i. extending the Company's cash runway through portfolio prioritization, expense management, new capital and business development;
- ii. driving net revenue from Libmeldy sales;
- iii. advancing our portfolio to key clinical and regulatory milestones;
- iv. strategic decisions in pre-clinical research activities, notably relating to Crohn's disease.

A series of scientific and business-related achievements during the year were also noted by the Committee in approving the achievement for the year.

Annual Bonus (audited)

As CEO, Dr Gaspar's annual bonus is directly linked to the performance of the Company. A Corporate Performance Score of 85% therefore corresponds to a bonus outcome equivalent to 85% of target for the CEO. This equates to a 2022 bonus payment equal to 51% of his base salary.

The Committee notes that the same corporate performance score has been applied to all employees across the Company.

		Target Annual			
	Base	Cash Bonus	Corporate	Cash payment	
Executive Director	salary (\$)	(% of salary)	performance	% salary	Cash outcome (\$)
Bobby Gaspar	\$577,250	60%	85%	51%	\$ 294,397

1 Dr. Gaspar's base salary and bonus are paid in GBP (£) and awards have been translated into USD at a rate of GBP 1 = USD 1.2495, which was the average rate during 2022. The salary basis for the bonus was Dr Gaspar's salary as CEO, £462,000.

Share Option Incentive Plan

Awards granted to Executive Directors in 2022 (audited)

During 2022, Dr Gaspar was granted an annual equity award. This award was made as an award of share options, split into two tranches:

• options with an exercise price set at the Company's closing share price on the date of grant ('market-priced' options); and

continued

options with an exercise price set at a 25% premium to the Company's closing share price on the date of grant ('premium-priced' options).

The Committee believes that granting share options to the CEO remains the most effective alignment between executive compensation and long-term shareholder interest. The addition of premium-priced options during 2022 reinforces this alignment and ensures that a substantial portion of Dr Gaspar's compensation package is contingent on long-term and sustainable value growth of the Company.

					Face	Fair				Value	
					Value	Value				realized at	
	Form of	Date of	Shares	Exercise	at Date	at Date		Vested in		exercise or	
Executive Director	Award	Grant	covered ¹	Price ^{1,2}	of Grant ²	of Grant ²	Expiry Date	20223	Exercised	vesting	Unvested
Bobby Gaspar	Market-priced Options	1 June 2022	422,631	\$ 0.4591	\$194,030	\$126,844	31 May 2032	88,048	nil	n/a	334,583
Bobby Gaspar	Premium-priced Options	1 June 2022	427,369	\$0.57388	\$196,205	\$120,094	31 May 2032	89,035	nil	n/a	338,334

The numbers of share and share prices are before the 1:10 American Deposit Share (ADS) ratio change which became effective on 10 March 2023.
 Market-priced options are granted at the market share price which is the exercise price. The face value at date of grant is calculated as the number of shares multiplied by the exercise price. The fair value at the date of grant is calculated as the Black Scholes value. The face value of the premium-priced options is the number of shares covered multiplied by the share

price on the date of grant.
The options vest, and become exercisable, over a four-year period on a monthly basis commencing upon the one-month anniversary of the vesting commencement date of 1 February 2022.

In October 2022 under the terms of Orchard's Share Option Incentive Plan 2018 the Board of Directors approved a repricing of previously awarded share options to employees which were significantly 'underwater' i.e., where the exercise prices were significantly above the Company's recent trading price. This repricing took effect on October 4, 2022.

All employees at the Company hold share options and in the situation where substantial portions of employees' equity holding had little or no value, the Board took the decision to reprice these awards. This was done in order to reengage staff with the future success of Orchard and provide additional retentive value to the investment previously made in our equity program. The Company has, and continues to grant, equity-based compensation to all employees – aligning the entire workforce with the future value of the Company.

The Board of Directors considered several factors in determining which grants would be eligible for repricing and which grants would remain on the original terms:

- None of the non-executive director grants were repriced;
- Only grants with an original exercise price above \$1.25 were repriced, representing a 150% premium to the price on the date of repricing;
- None of the grants from 2022 were repriced; and
- The exercise price of the repriced options (\$0.58) was set at a 16% premium to the closing market price on the date of repricing (\$0.50).

continued

As CEO, Dr Gaspar's awards were treated in the same manner as all other employees. Awards granted to Dr Gaspar during 2019, 2020 and 2021 were therefore impacted by this action, with a repriced exercise price for the awards listed below set at a premium of 16% above the Company's closing share price of \$0.50 on 4 October 2022.

Executive Director	Form of Award	Date of	Shares	Exercise Price on Date of Grant ¹	Exercise Price ¹	Face Value at Date of	Face Value on 4 October	Evniw Doto	Vested at 31.12.22	Evening	Unverted
	Awaru	Grant	covered ¹	Grant	Price	Grant	2022	Expiry Date		Exercised	Unvested
Bobby Gaspar	Market-price options	16 January 2019	50,000	\$ 12.54	\$ 0.58	\$ 627,000	\$ 29,000	15 January 2029	$48,958^{2}$	nil	1,042
	Market-price options	2 January 2020	200,000	\$ 13.58	\$ 0.58	\$2,716,000	\$116,000	1 January 2030	145,8332	nil	54,167
	Market-price options	1 April 2020	300,000	\$ 7.05	\$ 0.58	\$2,115,000	\$174,000	31 March 2030	200,0002	nil	100,000
	Market-price options	1 February 2021	850,000	\$ 5.98	\$ 0.58	\$5,083,000	\$493,000	31 January 2031	389,583 ²	nil	460,417
	Market-price options	1 February 2021	55,006	\$ 5.98	\$ 0.58	\$ 328,936	\$ 31,903	31 January 2031	55,006 ³	nil	n/a

The numbers of shares and share prices are before the ADS ratio change which became effective on 10 March 2023. The options vest, and become exercisable, over a four-year period on a monthly basis commencing upon the one-month anniversary of the date of grant.

23 These options vested in equal monthly tranches over 12 months.

Awards granted to Non-Executive directors between 1 January 2022 and 31 December 2022 (audited)

Non-executive directors received the following option awards during the year, each vesting based on continued service only.

					Face	Fair					
					Value	Value				Value	
	Form of	Date of	Shares	Exercise	at Date	at Date	Expiry			realized at	Unexe-
Non-Executive Directors	Award	Grant	Covered ¹	Price ¹	of Grant ¹	of Grant ¹	Date	Vested ¹	Exercised	exercise	rcised
Steven Altschuler	FMV Options*	7-Jun-22	46,000	\$ 0.47	\$ 21,836	\$ 13,880	6-Jun-32	nil	nil	nil	46,000
Joanne Beck	FMV Options*	7-Jun-22	46,000	\$ 0.47	\$ 21,836	\$ 13,880	6-Jun-32	nil	nil	nil	46,000
Marc Dunoyer	FMV Options*	7-Jun-22	46,000	\$ 0.47	\$ 21,836	\$ 13,880	6-Jun-32	nil	nil	nil	46,000
James Geraghty	FMV Options*	7-Jun-22	46,000	\$ 0.47	\$ 21,836	\$ 13,880	6-Jun-32	nil	nil	nil	46,000
Charles Rowland	FMV Options*	7-Jun-22	46,000	\$ 0.47	\$ 21,836	\$ 13,880	6-Jun-32	nil	nil	nil	46,000
Alicia Secor	FMV Options*	7-Jun-22	46,000	\$ 0.47	\$ 21,836	\$ 13,880	6-Jun-32	nil	nil	nil	46,000
John Curnutte	FMV Options*	7-Jun-22	46,000	\$ 0.47	\$ 21,836	\$ 13,880	6-Jun-32	nil	nil	nil	46,000

The numbers of shares and share prices are before the ADS ratio change which became effective on 10 March 2023.

The fair market value options are granted at the market price which is the exercise price. The face value at date of grant is calculated as the number of shares multiplied by the exercise price. The fair value at date of grant is calculated as the Black Scholes value. 2

3 The options vest and become exercisable at the earlier of one year from the date of grant or the next AGM.

Payments for loss of office (audited)

No payments were made for loss of office to Directors during the year.

Payments to former Directors (audited)

No payments were made to former Directors of the Company during the year.

External directorships

The Executive Directors do not currently hold any outside directorships.

continued

Statement of Directors' shareholding and share interests (audited)

The share interests of each Director as of 31 December 2022 (together with interests held by his or her connected persons) are set out in the table below.

During 2022 the Compensation Committee implemented formal shareholding requirements for Executive Directors. From 2022 onwards, Executive Directors will be expected to build up and maintain a shareholding with a value relative to their salaries. For the CEO, this guideline is 200% of salary and for other Executive Directors, 100% salary. Executive Directors will be expected to meet or exceed this guideline within 5 years of appointment or 5 years from the implementation of this requirement.

From 2023, a shareholding requirement will be extended to the full Board of Directors and the other Executive Officers of the Company.

			Restricted Shares			Share (Options
	Beneficially owned shares as at 31/12/22	% Salary held	Unvested without performance conditions	Unvested with performance conditions	Vested but unexercised	Unvested without performance conditions	Unvested with performance conditions
Executive Directors							
Bobby Gaspar	370,158	24% ¹	—	195,000 ²	1,750,765	950,209	338,3343
Non-Executive Directors							
Steven Altschuler	_	n/a	_	_	122,222	48,778	_
Joanne Beck	9,292	n/a	_		190,030	46,000	
John Curnutte	_	n/a		_	125,000	46,000	_
Marc Dunoyer	37,179	n/a	_	_	190,030	46,000	_
James Geraghty	44,391	n/a		_	430,120	46,000	_
Charles Rowland	12,294	n/a			190,030	46,000	
Alicia Secor	_	n/a		_	160,000	46,000	_

1 The value of Dr. Gaspar's beneficially owned shares is calculated using the closing price of Orchard's shares on 31 December 2022. As the CEO, Dr. Gaspar has a shareholding requirement of 5x base salary and has until 2027 to achieve this following the implementation of this requirement in 2022. The Committee notes Dr. Gaspar's vested and unvested holdings.

2 Refers to a one-time grant of Performance Share Units (PSUs) awarded to Dr. Gaspar on 1 April 2020. This PSU award vests as follows: 1/3 of the PSUs will vest on each of the first three of specific clinical and regulatory milestones achieved, subject to Bobby Gaspar remaining an employee of the Company on the date of achievement and provided that in each case the milestone is achieved on or before 2 January 2024. None of these awards have vested. The specific milestones are considered commercially sensitive. Details of the milestones and performance against them will be disclosed at the appropriate time.

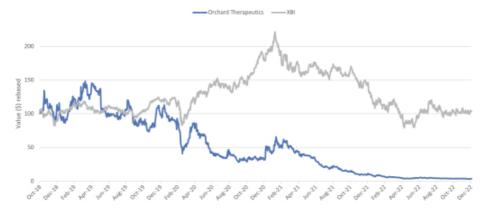
3 In 2022 Dr. Gaspar was awarded share options with an exercise price set at a 25% premium to the market price on the date of grant.

Performance graph and table

The chart below shows the Company's Total Shareholder Return (TSR) performance compared with that of the SPDR S&P Biotech Index (XBI) over the period from the date of the Company's admission to 31 December 2022. The XBI Index has been chosen as an appropriate comparator as a broad index comprising of small and mid-cap biotechnology companies. TSR is defined as the return on investment obtained from holding a company's shares over a period. It includes dividends paid, the change in the capital value of the shares and any other payments made to or by shareholders within the period.

continued

This graph shows the value, by 31 December 2022, of \$100 invested in Orchard Therapeutics on 31 October 2018 at the IPO price of \$14, compared with the value of \$100 invested in the XBI on the same date.



Aligning pay with performance

The total remuneration figure for the CEO is shown in the table below, along with the value of bonuses paid, and SOIP vesting, as a percentage of the maximum opportunity:

Chief Executive Officer	2018	2019	2020	2021	2022
Total remuneration (\$000) ¹	\$ 555	\$1,016	\$ 764	\$ 853	\$ 909
Actual bonus (% of the maximum) ²	N/A	44.0%	37.5%	22.5%	31.8%
SOIP vesting (% of the maximum) ³	N/A	N/A	N/A	N/A	N/A

- 1 For 2018 and 2019, these figures are for Orchard's previous CEO Mark Rothera and for 2020 and 2021 the full-year remuneration for Dr. Gaspar. These figures are also impacted by exchange rate fluctuations between the currency in which Dr. Gaspar is paid, GBP, and our reporting currency, USD.
- 2 Calculated as the bonus earned in the year by Dr. Gaspar expressed as a portion of the maximum available under the Company's Directors' Remuneration Policy 160% of salary.
- 3 There is no maximum grant policy under the SOIP; therefore, this information cannot be disclosed.

Relative importance of spend on pay

The table below illustrates the Company's expenditure on pay by the Group in comparison to total operating expenses. Total operating expenses is a combined total of R&D and selling, general & administrative expenses before any deduction for any research and development tax credits recognized in the year. This is chosen as an appropriate measure of the Company's major year-on- year expenditure. It is considered to be a more complete representation of our operations compared to R&D expenses which had been used in prior years.

	2021	2022	% change
Total operating expenses (\$'000)	\$194.4	\$170.8	-12.1%
Total employee pay expenditure (\$'000) ¹	\$ 71.1	\$ 61.5	-13.5%

1 Total employee pay expenditure in the table above is inclusive of cash payments for salaries and wages, as well as employer benefits and tax costs. It also includes \$11,418k and \$19,900k in non-cash share-based compensation expense for 2022 and 2021 respectively.

continued

Average percentage change in remuneration of Directors and Employees

The table below shows a comparison of the annual change of each individual director's pay to the annual change in average employee pay in the year ended 31 December 2022.

	31	Change in pay between 31/12/2021 and 31/12/2022		Change in pay between 31/12/2020 and 31/12/2021			Change in pay between 31/12/2019 and 31/12/2020		
	Base salary/ fee	Bonus	Benefit	Base salary/ fee	Bonus	Benefit	Base salary/ fee	Bonus	Benefit
Executive Directors									
Bobby Gaspar ¹	-5%	35%	38%2	12%	28% ³	361%2	58%	-54%	0%
Non-Executive Directors ⁴									
Steven Altschuler	1%	n/a	n/a	10%	n/a	n/a	n/a ⁵	n/a	n/a
Joanne Beck	1%	n/a	n/a	2%	n/a	n/a	41%	n/a	n/a
John Curnutte	-5%	n/a	n/a	5%	n/a	n/a	278%6	n/a	n/a
Marc Dunoyer	0%	n/a	n/a	-1%	n/a	n/a	27%	n/a	n/a
James Geraghty	0%	n/a	n/a	-1%	n/a	n/a	15%	n/a	n/a
Charles Rowland	6%	n/a	n/a	-1%	n/a	n/a	31%	n/a	n/a
Alicia Secor	-7%	n/a	n/a	36%7	n/a	n/a	23%	n/a	n/a
Average employee ⁸	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a

Please note that all figures are impacted by exchange rate fluctuation between the currency in which the Board is paid, GBP, and our reporting currency, USD.

- 1 Dr. Gaspar received a 5% salary increase, in GBP, effective1 March 2022. He did not receive a salary increase in 2021 for his services as CEO. The increases represented here correspond to a salary increase upon promotion to CEO during 2020. These figures are also impacted by exchange rate fluctuations.
- 2 Dr. Gaspar's company-provided benefits are unchanged year-on-year the reported figure combines the taxable value of private medical insurance and a cash allowance in lieu of pension. The 2021 increase relates to a cash allowance in lieu of pension contribution effective 1 April 2021 which he had not received prior to that date.
- 3 The 2020 bonus (paid in February 2021) figure represents the cash amount paid only. Dr. Gaspar received share options with a fair value equal to 50% of the 2020 annual bonus in lieu of cash.
- 4 None of the Non-Executive Directors are eligible for an annual bonus and none claimed any benefits during the year.
- 5 Steven Altschuler joined the Board during 2020 and therefore no comparative information is shown.
- 6 John Curnutte joined the Board in 2019 and the remuneration received in 2019 was not a full annual amount.
- 7 Alicia Secor received a one-off retrospective payment of \$11,250 in April 2021 for prior services to the Nomination and Governance Committee which has previously not been paid. Her fees for services to the Board were not increased during 2021.
- 8 As the parent company Orchard Therapeutics Plc has no direct employees. All employees are employed by the relevant legal entities.

continued

Statement of implementation of remuneration policy in 2023

Annual base salary

At his own request, the Committee reviewed and commended a proposal from Dr Gaspar that his salary not be adjusted for 2023. Dr Gaspar recognized the prevailing economic environment, fiscal position and available cash resources of the Company at year-end 2022. Based on the combination of these factors he, therefore, did not wish to receive a salary increase.

	Base salary 2023		salary 2022 March 2022)	% change
Bobby Gaspar, Chief Executive Officer	£462,000	£	462,000	nil

Benefits and pension

In 2022, Executive Directors are eligible for the same benefits (such as health insurance and pension) as provided to all employees in the jurisdiction in which they reside. Pension contributions for Executive Directors are up to 6% of base salary which may be taken as a cash allowance. 6% is the rate provided to all employees in the UK at the Company, and therefore representative of the rate for the rest of the workforce.

Annual Bonus

The CEO will be entitled to a target bonus of 60% of base salary, with the maximum payout up to 150% of target bonus (90% salary).

These 2023 targets and maximum have been set within the overall Directors' Remuneration Policy. Unless otherwise determined by the Compensation Committee, the bonus will be paid in cash and subject to the achievement of a number of strategic objectives determined by the Committee.

Specific targets are commercially sensitive and therefore are not disclosed in advance. However, full details of the targets and performance against them will be disclosed when they are no longer considered commercially sensitive.

Within the overall maximum annual bonus provision in the Directors' Remuneration Policy – currently 150% of salary per annum – the Committee reserves the right to provide an additional milestone- based bonus. This would only be applied in circumstances deemed appropriate to focus on and incentivize key fundamental objectives to the Company. The Executive Directors currently have no such arrangements in place.

Share Option Incentive Plan (SOIP)

Annual award of share options

In 2023, as part of the annual compensation package the CEO has been awarded an award of market-price and premium-price options in the Company at the same time as all eligible employees.

These premium priced options will have an exercise price set at 25% higher than the closing price of the Company's ADSs on the Nasdaq National Select Market on the date of grant. Consequently, approximately half of the CEO's 2023 share option award will have no intrinsic value until the share price increases by at least 25%.

The Committee believes that granting share options to the CEO remains the most effective alignment between executive compensation and long-term shareholder interest. The addition of premium-priced options since 2022

continued

reinforces this alignment and ensures that a substantial portion of Dr Gaspar's compensation package is performance-based and contingent on long-term and sustainable value growth of the Company.

Examples Disaster			Maximum Shares	Exercise	Vest
Executive Director	Form of Award	Date of Grant	Covered	Price	Terms
Bobby Gaspar	Market-priced share options	1 March 2023	563,410	\$0.4636	(1)
	Premium-priced share options	1 March 2023	581,590	\$0.5795	(1)

(1) The share options will expire 10 years from the date of grant. The share options vest monthly over a 4-year period and are not subject to any further performance conditions.

At the date of this report, there is no intention to make any further awards under the SOIP to any Directors. Any awards made during the year, including the full details of the award described for Dr. Gaspar, will be disclosed in the relevant Directors' Remuneration Report.

Non-Executive Directors' fees for 2023

Non-Executive Directors are eligible to receive the following cash compensation annually. Following a review of the fees paid to the Board, the Company resolved to reduce by \$5,000 the base fee provided to the Chair and Members of the Board. This removes a supplement previously provided for time and commitment to international travel with a corresponding rebalancing in equity compensation.

Additionally, the fee for the Chair of the Science and Technology Committee has been increased, recognizing the crucial role this position holds in the long-term success of the Company.

In reinforcing the Board's stewardship of the Company, from 2023, all Non-Executive Directors will be required to build up a shareholding equivalent to three times the base fee and they will have five years to gain compliance with this new requirement.

Collectively, the Compensation Committee believes these are important changes and represent incremental improvements to the Company's Board remuneration structure. The changes ensure that this structure matches long-term shareholder interest and remains market competitive.

	 2023 Fee in \$'000		2022 Fee in \$'000	
Base fee:				
Board Chair	\$ 80	\$	85	
Board Member	\$ 40	\$	45	
Additional fees:				
Audit Committee Chair	\$ 18	\$	18	
Audit Committee Member	\$ 9	\$	9	
Compensation Committee Chair	\$ 15	\$	15	
Compensation Committee Member	\$ 7.5	\$	7.5	
Nominating and Corporate Governance Committee Chair	\$ 10	\$	10	
Nominating and Corporate Governance Committee Member	\$ 5	\$	5	
Science and Technology Committee Chair	\$ 15	\$	10	
Science and Technology Committee Member	\$ 7.5	\$	7.5	

continued

The Company intends to provide an initial, one-time equity award of 180,000 stock options (equivalent to 18,000 ADS following the 1:10 ratio change implemented on 10 March 2023) to each new Non-Executive Director upon his or her election to our board of directors. Under normal circumstances, initial share awards vest monthly over three years. The Company intends to provide an annual equity incentive award of 105,000 stock options (equivalent to 10,500 ADS from 10 March 2023) to each Non-Executive Director at the 2023 AGM. Options awarded annually will usually vest upon the earlier to occur of the first anniversary of the date of grant or the date of the next annual general meeting.

As approved in our 2022 Directors' Remuneration Policy Non-Executive Directors may elect to receive fees as market value share options with an equivalent value calculated as the fair value on the date of grant.

Non-Executive Directors will not be eligible to participate in any performance-based incentive plans.

Each Non-Executive Director will also be entitled to reimbursement of reasonable expenses and reimbursement of up to \$5,000 for tax preparation assistance if Board services requires a Non-Executive Director to file a tax return in a jurisdiction that the director otherwise would not have been required to file on his own.

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On behalf of the Board **Charles Rowland, Jr.** *Chair of the Compensation Committee*

13 April 2023

ORCHARD THERAPEUTICS PLC

Form of Proxy for Ordinary Shareholders 2023 Annual General Meeting

This proxy is solicited by the Board of Directors

I/We

(name in full in block capitals)

of

being a member/members of Orchard Therapeutics plc (the "**Company**") hereby appoint the Chair of the meeting (*see note 1 below*)

as my/our proxy to attend, speak and vote for me/us and on my/our behalf in relation to all ordinary shares of the Company that I/we am/are entitled to vote (unless otherwise specified in accordance with note 6 below) at the Annual General Meeting of the Company to be held at [] on [] and at any adjournment or postponement thereof, on the following resolutions as indicated by an 'X' in the appropriate box:

Ordinary Resolutions		For	Against	Withheld (See note 9)	Discretion (See note 9)
1.	To re-elect James Geraghty as a director, who retires by rotation in accordance with the Company's Articles of Association				
2.	To re-elect Steven M. Altschuler as a director, who retires by rotation in accordance with the Company's Articles of Association				
3.	To re-elect Marc Dunoyer as a director, who retires by rotation in accordance with the Company's Articles of Association				
4.	To re-appoint PricewaterhouseCoopers LLP, a United Kingdom entity, as U.K. statutory auditors of the Company, to hold office until the conclusion of the next annual general meeting of shareholders				
5.	To ratify the appointment of PricewaterhouseCoopers LLP, a Delaware limited liability partnership, as the Company's independent registered public accounting firm, for the fiscal year ending December 31, 2023				
6.	To authorize the Audit Committee to determine the Company's auditors' remuneration for the fiscal year ending December 31, 2023				
7.	To receive the U.K. statutory annual accounts and reports for the fiscal year ended December 31, 2022 and to note that the Company's directors do not recommend the payment of any dividend for the year ended December 31, 2022				
8.	To approve the compensation of the Company's named executive officers for the year ended December 31, 2022 on an advisory basis				
9.	To receive and approve the Company's U.K. statutory directors' remuneration report for the year ended December 31, 2022 on an advisory basis				
10.	To authorize the Board of Directors, generally and unconditionally for the purpose of s551 of the U.K. Companies Act 2006 (the "Act"), to allot shares in the Company or to grant rights to subscribe for or to convert any security into shares in the Company up to a maximum aggregate nominal amount of £18,398,450				
11.	To authorize the Board of Directors, generally and unconditionally for the purpose of s551 of the Act, to allot non-voting ordinary shares of the Company, nominal value £0.10 each, and voting ordinary shares of the Company, nominal value £0.10 each (together, "Ordinary Shares"), and/or to grant rights to subscribe for or to convert any security into Ordinary Shares ("Warrant Rights") up to a maximum nominal amount of £15,158,359, pursuant to the Securities Purchase Agreement, dated March 6, 2023 (including, upon exercise of any Warrant Rights granted and/or				

to be granted in accordance with the Securities Purchase Agreement, the allotment and issue of

any resulting Ordinary Shares)

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Special Resolutions		For	Against	Withheld (See note 9)	Discretion (See note 9)	
12.	Subject to the passing of Resolution 10, to empower the securities, under s570 of the Act as if $s561(1)$ of the Act maximum aggregate nominal amount of £18,398,450	1 5				
13.	Subject to the passing of Resolution 11, to empower the securities, under s570 of the Act as if $s561(1)$ of the Act maximum aggregate nominal amount of £15,158,359					
Sig	ature	Dated	202	23		

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Notes:

- 1. You may strike out the words "Chair of the meeting" and insert the name of some other person to act as your proxy in the space provided. All amendments to this form must be initialed. If you sign and return this form with no name inserted in the space, the Chair of the meeting will be deemed to be your proxy. A proxy need not be a member of the Company but must attend the Meeting. Where someone other than the Chair is appointed as a proxy, the member appointing him or her is responsible for ensuring that he or she attends the Meeting and should be aware of his or her voting intentions. If a member wishes his or her proxy to speak on his or her behalf at the Meeting, he or she will need to appoint someone other than the Chair and give his or her instructions directly to them.
- 2. A member entitled to attend, speak and vote at the Meeting is entitled to appoint a proxy or proxies to exercise all or any of his or her rights to attend, speak and to vote at the Meeting instead of him or her. A proxy can only be appointed by following the procedure set out in these notes and the notes to the Notice of Annual General Meeting. A validly appointed proxy shall be authorized (at his or her discretion) to consent to any adjournment or postponement of the Meeting and, unless otherwise terminated or amended in accordance with these notes, the form of proxy shall remain effective at any such adjourned or postponed Meeting.
- 3. Completion and return of a form of proxy will not preclude a member from attending, speaking and voting at the Meeting or any adjournment or postponement thereof in person. If a proxy is appointed and the member attends the Meeting in person, the proxy appointment will automatically be terminated.
- 4. To be valid this form of proxy must be completed and lodged with the Registrars of the Company, Equiniti, Aspect House, Spencer Road, Lancing, West Sussex, BN99 6DA not less than 48 hours (excluding non-business days) before the time fixed for the Meeting and, in the event of adjournment or postponement, not less than 48 hours (excluding non-working days) before the time fixed for the Meeting together with, if appropriate, the power of attorney or other authority (if any) under which it is signed or a notarially certified or office copy of such power or authority. In the case of a member that is a company, the proxy form must be executed under its common seal or signed on its behalf by an officer of the company or an attorney for the company.
- 5. In the case of joint holders, signature of any one holder will be sufficient, but the names of all the joint holders should be stated. The vote of the senior holder who tenders the vote whether in person or by proxy will be accepted to the exclusion of the votes of any other joint holders. For these purposes, seniority shall be determined by the order in which the names stand in the Company's relevant register or members for the certificated or uncertificated shares of the Company (as the case may be) in respect of the joint holding.
- 6. A member may appoint more than one proxy provided each proxy is appointed to exercise rights attached to different shares. A member may not appoint more than one proxy to exercise rights attached to any one share. To appoint more than one proxy, please sign and date the form of proxy and attach a schedule listing the names and addresses (in block letters) of all of your proxies, the number of shares in respect of which each proxy is appointed (which, in aggregate, should not exceed the number of shares held by you) and indicating how you wish each proxy to vote or abstain from voting. If you wish to appoint the Chair as one of your multiple proxies, simply write "the Chair of the Meeting".
- 7. If a member submits more than one valid proxy appointment, the appointment received last before the latest time for the receipt of proxies will take precedence.
- 8. The appointment under this form of proxy may be terminated by the member prior to the commencement of the meeting (or any adjournment or postponement of the meeting). To be valid, the notice of termination of the authority of the person appointed to act as proxy must be deposited at the offices of the Company's registrar, Equiniti, Aspect House, Spencer Road, Lancing, West Sussex, BN99 6DA not less than 48 hours (not including non-business days) before the time fixed for the holding of the Annual General Meeting or any adjournment or postponement thereof (as the case may be).
- 9. Please indicate with an "X" in the appropriate boxes how you wish your votes on the resolutions to be cast. Unless otherwise instructed, your proxy may vote or abstain from voting as he or she thinks fit. If you select "Discretion" or fail to select any of the given options your proxy can vote as he or she chooses or can decide not to vote at all. The proxy can also do this on any other resolution that is put to the meeting. The vote "Withheld" option is to enable you to abstain on any particular resolution. A vote withheld is not a vote in law, which means that the vote will not be counted in the calculation of votes for or against the resolution. If no voting indication is given, your proxy will vote or abstain from voting at his/her discretion.
- 10. CREST members should use the CREST electronic proxy appointment service in accordance with the procedures set out in the CREST manual (ID:RA19) and refer to the notes of the Notice of Annual General Meeting in relation to the submission of a proxy via CREST.
- 11. You may not use any electronic address provided in this proxy form to communicate with the Company for any purposes other than those expressly stated.
- 12. Only those members registered in the register of members of the Company at [] on [] or, in the event that the meeting is adjourned or postponed, in such register not later than 48 hours before the time of the adjourned or postponed meeting, will be entitled to attend and vote (whether in person or by proxy) at the Annual General Meeting in respect of the number of ordinary shares registered in their name at the time.

The shares represented by this proxy, when properly executed, will be voted in accordance with the specifications indicated herein. If no such direction is made and the Chair of the Meeting is appointed as the proxy, this proxy will be voted in accordance with the Board of Directors' recommendations.