

**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

Filed by a Party other than the Registrant

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
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April 27, 2022

Re: 2022 Annual General Meeting of Orchard Therapeutics plc (the “AGM”)

Dear Fellow Shareholders,

This letter, the notice of the AGM set out in this document (the “**Notice**”) and associated materials for the AGM are being sent to you because, as of April 21, 2022 (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 Orchard Therapeutics plc (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 **1 pm London time (8 am Eastern time) on Tuesday, June 7, 2022 at Goodwin Procter LLP, 100 Northern Avenue, Boston, Massachusetts, 02210**. 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 quorate meeting will be formed by one or more qualifying persons present at a meeting and between them holding at least 33 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 IN THE COMPANY

If you are a holder of ADSs, please ignore this section and refer instead to the section below—“*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 for use at the AGM is enclosed. **You are encouraged to appoint the Chairman of the AGM as your proxy. If you appoint any person other than the Chairman of the AGM as your proxy, that person may not be entitled to attend the AGM.**

You are advised to complete and return the form of proxy in accordance with the instructions printed on it. Your proxy 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 pm London time (8 am Eastern time) on Friday, June 3, 2022**.

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 **6:30 pm London time (1:30 pm Eastern time) on Friday, June 3, 2022**.

Therefore, if you sell or transfer your ordinary shares in the Company on or prior to Friday, June 3, 2022, your form of proxy 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 form of proxy for its use.

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

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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 form of proxy. 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—“*Holders of American Depositary Shares*”.

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 depository, Citibank, N.A., at **10 pm London time (5 pm Eastern time) on Wednesday, April 27, 2022 (the record date for ADS holders)**.

If you hold ADSs through a bank, broker or nominee on April 27, 2022, the AGM documentation, including the ADS proxy card, will be sent to your broker who should forward the materials to you. Please reach out to your broker 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 3 pm London time (10 am Eastern time) on Wednesday, June 1, 2022**.

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.

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

RECOMMENDATION

Your Directors unanimously recommend 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. The Directors consider 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. 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,

/s/ JAMES GERAGHTY

James Geraghty
Chairman



Orchard Therapeutics plc
108 Cannon Street
London EC4N 6EU
United Kingdom
Registered Company No. 11494381

NOTICE OF 2022 ANNUAL GENERAL MEETING OF SHAREHOLDERS
TO BE HELD ON TUESDAY, JUNE 7, 2022

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 Tuesday, June 7, 2022 at 1 pm London time (8 am Eastern time) at Goodwin Procter LLP, 100 Northern Avenue, Boston, Massachusetts, 02210, for transaction of the following business:

1. To re-elect as a director John T. Curnutte, who retires by rotation in accordance with the Company's Articles of Association.
2. To re-elect as a director Bobby Gaspar, who retires by rotation in accordance with the Company's Articles of Association.
3. To re-elect as a director Alicia Secor, 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, 2022.
6. To authorize the Audit Committee to determine the Company's auditors' remuneration for the fiscal year ending December 31, 2022.
7. To receive the U.K. statutory annual accounts and reports for the fiscal year ended December 31, 2021 and to note that the Company's directors do not recommend the payment of any dividend for the year ended December 31, 2021.
8. To approve the compensation of the Company's named executive officers for the year ended December 31, 2021 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, 2021 on a non-binding, advisory basis, which is set forth as *Part II of Annex A* to the attached proxy statement.
10. To approve the Company's U.K. directors' remuneration policy, which is set forth as *Part I of Annex A* to the attached proxy statement and which, if approved, will take effect upon the conclusion of the Annual General Meeting.

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Each of the proposals 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. If a poll is demanded, an ordinary resolution is passed if it is approved by holders representing a simple majority of the total voting rights of shareholders present (in person or by proxy) who (being entitled to vote) vote on the resolution.

The result of the shareholder votes on the ordinary resolutions in proposals 4, 5, 7, 8 and 9 regarding re-appointment of PricewaterhouseCoopers LLP, a United Kingdom entity, as our U.K. statutory auditors, ratification of the appointment of PricewaterhouseCoopers LLP, a Delaware limited liability partnership, as our independent registered public accounting firm for the fiscal year ending December 31, 2022, receipt of our U.K. statutory annual accounts and reports for the year ended December 31, 2021, approval of the compensation of our named executive officers for the year ended December 31, 2021, and approval of our U.K. statutory directors' annual report on remuneration for the year ended December 31, 2021 will not require our Board of Directors or any committee thereof to take any action. Our Board of Directors values the opinions of our shareholders as expressed through such votes and will carefully consider the outcome of the votes on proposals 4, 5, 7, 8 and 9.

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

Christopher York
Company Secretary
April 27, 2022

Registered Office

108 Cannon Street
London
EC4N 6EU, United Kingdom
Registered in England and Wales
No. 11494381

Notes

(a) Only those members registered in the register of members of the Company at 6:30 pm London time (1:30 pm Eastern time) on June 3, 2022 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 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 cast) at the adjourned AGM. Should the AGM be adjourned for a longer period, then to be so entitled, members must be entered on the Register at the time which is 48 hours before the time fixed for the adjourned AGM or, if the Company gives notice of the adjourned 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. Proxy forms should be lodged with the Company's Registrar (Equiniti Limited) not later than 1 pm London time (8 am Eastern time) on June 3, 2022. Completion and return of the appropriate proxy form does not prevent a member from attending and voting in person if he or she is entitled to do so and so wishes. 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 they do not do so in relation to the same shares.

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(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 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 1 pm London time (8 am Eastern time) on June 3, 2022. 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 1 pm London time (8 am Eastern time) on June 3, 2022 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 21, 2022 (being the last practicable date before circulation of this Notice), the Company's issued ordinary share capital consisted of 125,904,945 ordinary shares, carrying one vote each. Therefore, the total voting rights in the Company as of that date are 125,904,945.

(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

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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 member 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
108 Cannon Street
London EC4N 6EU
United Kingdom
Registered Company No. 11494381

**PROXY STATEMENT FOR THE 2022 ANNUAL GENERAL MEETING OF
SHAREHOLDERS TO BE HELD ON JUNE 7, 2022**

INFORMATION CONCERNING PROXY SOLICITATION AND VOTING

We have sent you this proxy statement and the enclosed form of proxy 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 Tuesday, June 7, 2022, at 1 pm London time (8 am Eastern time), at Goodwin Procter LLP, 100 Northern Avenue, Boston, Massachusetts, 02210.

- 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 form of proxy is the means by which you actually authorize another person to vote your shares in accordance with your 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 2022 AGM, this proxy statement and the form of proxy to our ordinary shareholders of record as of April 21, 2022 (being the latest practicable date before the circulation of this document) for the first time on or about April 27, 2022. In this mailing, we are also including our U.K. statutory annual accounts and reports for the year ended December 31, 2021 (“2021 U.K. Annual Report”) and our annual report on Form 10-K for the year ended December 31, 2021 (“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 2021 U.K. Annual Report and the 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 June 7, 2022:

Our Notice of the 2022 AGM, this proxy statement, the Annual Report on Form 10-K, the 2021 U.K. Annual Report and our form of proxy are available in the Investors & Media section of our website at www.orchard-tx.com.

QUESTIONS AND ANSWERS ABOUT VOTING

1) *Why am I receiving these materials?*

We have sent you this proxy statement and the enclosed form of proxy 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 form of proxy. All proxies, however submitted, must be lodged with our registrar, Equiniti, by no later than **1 pm London time (8 am Eastern time) on Friday, June 3, 2022**. CREST members may appoint a proxy by using the CREST electronic proxy appointment service.

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

We intend to mail this proxy statement and the accompanying form of proxy on or about April 27, 2022 to all ordinary shareholders of record entitled to vote at the Meeting.

Materials for ADS holders of record, including this proxy statement, the Annual Report on Form 10-K and an ADS proxy card, will be mailed on or about April 27, 2022 to all ADS holders, including banks, brokers and nominees, who are registered as holders of ADSs in the ADS register at 10 pm London time (5 pm Eastern time) on April 27, 2022 (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 6:30 pm London time (1:30 pm Eastern time) on Friday, June 3, 2022 will be entitled to vote at the Meeting.

As of April 21, 2022 (being the last practicable date before the circulation of this proxy statement) there were 125,904,945 ordinary shares issued and outstanding and entitled to vote.

As a result of the ongoing Covid-19 pandemic, we encourage you to fill out and return the enclosed form of proxy to ensure your vote is counted. You are encouraged to appoint the Chairman of the Meeting as your proxy. If you appoint any person other than the Chairman of the Meeting as your proxy, that person may not be entitled to attend the Meeting.

If you sell or transfer your ordinary shares in the Company on or prior to June 3, 2022, your form of proxy 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 form of proxy for its use.

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

If, on April 21, 2022, 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 or other agent so that they may submit a proxy.

Holders of American Depositary Shares

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 10 pm London time (5 pm Eastern time) on Wednesday, April 27, 2022 (the record date for ADS holders).**

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If you hold ADSs through a brokerage firm, bank or nominee on April 27, 2022, the materials for ADS holders, including the ADS voting instructions 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 voting instructions cards submitted by ADS holders must be received by Citibank, N.A. **no later than 3 pm London time (10 am Eastern time) on Wednesday, June 1, 2022.**

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

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.

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

3) *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.

Each proposal will be proposed as an ordinary resolution. 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. If a poll is demanded, an ordinary resolution is passed if it is approved by holders representing a simple majority of the total voting rights of shareholders present (in person or by proxy) who (being entitled to vote) vote on the resolution.

The result of the shareholder votes on the ordinary resolutions in proposals 4, 5, 7, 8, and 9 regarding re-appointment of PricewaterhouseCoopers LLP, a United Kingdom entity, as our U.K. statutory auditors, ratification of the appointment of PricewaterhouseCoopers LLP, a Delaware limited liability partnership, as our independent registered public accounting firm for the fiscal year ending December 31, 2022, receipt of our U.K. statutory annual accounts and reports for the year ended December 31, 2021, approval of the compensation of our named executive officers for the year ended December 31, 2021, and approval of our U.K. statutory directors' annual report on remuneration for the year ended December 31, 2021 will not require our Board of Directors or any committee thereof to take any action. Nonetheless, our Board of Directors values the opinions of our shareholders as expressed through such votes and will carefully consider the outcome of the votes on proposals 4, 5, 7, 8, and 9.

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4) *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 John T. Curnutte to the Board of Directors	FOR
2	Re-election of Bobby Gaspar to the Board of Directors	FOR
3	Re-election of Alicia Secor 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, 2022	FOR
6	Authorization for the Audit Committee to determine the Company's auditors' remuneration for the fiscal year ending December 31, 2021	FOR
7	To receive the U.K. statutory annual accounts and reports for the fiscal year ended December 31, 2021	FOR
8	Approval of the compensation of the Company's named executive officers for the year ended December 31, 2021, on a non-binding, advisory basis, which is set forth in this proxy statement	FOR
9	Approval of our U.K. statutory directors' annual report on remuneration for the year ended December 31, 2021, on a non-binding, advisory basis, which is set forth as Part II of Annex A	FOR
10	Approval of our U.K. directors' remuneration policy, which, if approved, will take effect upon the conclusion of the Meeting, which is set forth as Part I of Annex A	FOR

5) *What constitutes a quorum?*

Consistent with the Nasdaq Stock Market LLC ("Nasdaq") rules applicable to us as a U.S. domestic registrant and in accordance with our Articles of Association, we require qualified persons present at a meeting and between them holding (or being the proxy or corporate representative of the holders of) at least 33¹/₃ 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. A member represented by a proxy at the Meeting will be counted towards the quorum requirement even where the proxy abstains from voting. If a form of proxy 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 chairperson of the Meeting (being not less than 10 clear days after the date of the original meeting). We require a

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quorum of at least 33¹/₃ percent in number of the issued shares (excluding any shares held as treasury shares) entitled to vote on the business to be transacted if the Meeting is reconvened, consistent with the Nasdaq rules applicable to us as a U.S. domestic registrant and our Articles of Association. If such quorum is not present at the adjourned meeting within 15 minutes (or such longer interval as the chairman in their 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).

6) How do I vote my shares?

If you are an ordinary “shareholder of record,” you may appoint a proxy to vote on your behalf by completing and signing the form of proxy and returning it in the envelope provided. All proxies must be lodged with our registrar (Equiniti) by no later than **1 pm London time (8 am Eastern time) on Friday, June 3, 2022.**

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

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.

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

If you sign and send your form of proxy 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 sees fit or such person may abstain in relation to any business of the Meeting.

If you are a beneficial owner of ordinary shares 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 either vote these shares on behalf of the beneficial owners if permitted by applicable rules or return a proxy leaving these shares un-voted (a “broker non-vote”). We encourage you to submit your proxy with instructions and exercise your right to vote as a shareholder.

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”), holders of ADSs as of 10 pm London time (5 pm Eastern time) on April 27, 2022 (the record date for ADS holders) who do not provide the depositary with voting instructions on or before 3 pm London time (10 am Eastern time) on Wednesday, June 1, 2022 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. Accordingly, we do not expect any broker non-votes on any of the proposals.

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

A registered shareholder can revoke his or her proxy before the time of voting at the Meeting in several ways by:

- (1) mailing a revised form of proxy dated later than the prior form of proxy;
- (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) 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?*”

9) 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 form of proxy to Equiniti for tabulation (see instructions on the form of proxy). If you hold your ordinary shares through a broker, your broker will return the form of proxy to Equiniti.

If you are a holder of record 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.

10) 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 are not treated as entitled to cast a vote and, therefore, will have no effect on any proposal.

11) 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, but a proxy has 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 share held by the shareholder.

12) 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 6:30 pm London time (1:30 pm Eastern time) on Friday, June 3, 2022. In order to obtain admittance to the Meeting each 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 Chairman.

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In addition, due to COVID-19 safety precautions, only shareholder attendees who have been fully vaccinated (i.e., two weeks have passed since receiving a one-dose or two-dose vaccine regimen) will be allowed admission, unless a medical professional has advised such shareholder against the vaccine due to disability or they have a sincerely held religious belief that prevents them from receiving the vaccine. Masks will be required for everyone, regardless of vaccination status, when federal, state or local mask mandates are in place and for those who are not vaccinated because of a medical or religious exemption. The situation with respect to COVID-19 continues to evolve and we are actively monitoring the situation as part of our effort to maintain a healthy and safe environment at the Meeting. If the arrangements for our AGM need to change materially, we will issue a further communication via a Form 8-K filing with the U.S. Securities and Exchange Commission and on the Investors & Media section of our website at www.orchard-tx.com.

13) *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 \$25,000 and those costs will be borne by us (in addition to our paying the cost of mailing proxy materials). We have also agreed to indemnify and hold MacKenzie Partners and its employees harmless against losses that arise or relate to the services they are providing to us, except for losses that result from willful misconduct or bad faith. 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.

14) *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 a form of proxy 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.

15) *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 10 may be presented at this 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.

16) *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.

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.

17) *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.

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:

- the Class I directors are John T. Curnutte, Bobby Gaspar and Alicia Secor and their terms will expire at the Meeting;
- the Class II directors are Steven M. Altschuler, Marc Dunoyer and James Geraghty and their terms will expire at the annual general meeting to be held in 2023; and
- the Class III directors are Joanne T. Beck and Charles A. Rowland Jr., and their terms will expire at the annual general meeting to be held in 2024.

Upon the expiration of the term of a class of directors, directors 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 their term expires.

Our Board of Directors has nominated John T. Curnutte, Bobby Gaspar and Alicia Secor for election as the Class I 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 proposals 1, 2 and 3, we set forth the biographical information for the nominees to our Board of Directors. For biographical information for the other directors see “*Board of Directors and Corporate Governance.*”

**Proposal 1:
RE-ELECTION OF JOHN T. CURNUTTE TO THE BOARD OF DIRECTORS**

John T. Curnutte 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 2025 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. Curnutte has agreed to serve if elected, and we have no reason to believe that he will be unable to serve.

John T. Curnutte, M.D., Ph.D. has been a member of our Board of Directors since August 2019. Dr. Curnutte previously served as Executive Vice President of Research and Development at Portola Pharmaceuticals, Inc., 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 served as an independent consultant, from April 2010 to January 2011, and as the Chief Executive Officer of 3-V Biosciences, Inc., a biotechnology company, from May 2008 to March 2010. 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. We believe Dr. Curnutte's extensive experience as a clinician, researcher and drug development executive in the biotechnology and pharmaceutical industries qualifies him to serve as a member of our Board of Directors.

***The Board of Directors recommends a vote
FOR the re-election of John T. Curnutte to the Board of Directors.***

**Proposal 2:
RE-ELECTION OF BOBBY GASPAR TO THE BOARD OF DIRECTORS**

Bobby Gaspar 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 2025 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. Gaspar has agreed to serve if elected, and we have no reason to believe that he will be unable to serve.

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.

***The Board of Directors recommends a vote
FOR the re-election of Bobby Gaspar to the Board of Directors.***

**Proposal 3:
RE-ELECTION OF ALICIA SECOR TO THE BOARD OF DIRECTORS**

Alicia Secor is currently a member of our Board of Directors and has been nominated for re-election as a director. If elected, she will hold office from the date of her election until the 2025 annual general meeting of shareholders where she must retire by rotation and offer herself for re-election, or until her earlier death, resignation or removal. Ms. Secor has agreed to serve if elected, and we have no reason to believe that she will be unable to serve.

Alicia Secor has been a member of our Board of Directors since November 2018. Ms. Secor currently serves as President, Chief Executive Officer and a member of the board of directors of Atalanta Therapeutics, Inc. 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. and the Foundation for Prader-Willi Research. Ms. Secor was previously a member of the board of GW Pharmaceuticals, plc, prior to its acquisition by Jazz Pharmaceuticals. 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.

***The Board of Directors recommends a vote
FOR the re-election of Alicia Secor to the 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
**FOR 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, 2022

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, 2022.

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, 2022. Our Audit Committee has selected PwC USA as our independent registered public accounting firm for the fiscal year ending December 31, 2022, 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 with the fiscal year 2019. 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, 2021 and December 31, 2020, 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, 2021 <u>(\$) (in thousands)</u>	December 31, 2020 <u>(\$) (in thousands)</u>
Audit Fees(1)	1,350	1,421
Audit-related fees	—	—
Tax fees(2)	3	—
All Other Fees(3)	5	3
Total	1,358	1,424

- (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.

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- (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

FOR 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, 2022**

Proposal 6 authorizes the Audit Committee to determine our auditors' remuneration for the fiscal year ending December 31, 2022. Fees for PwC USA, our independent registered public accounting firm, and PwC UK, our statutory auditor, in respect of the years ended December 31, 2021 and December 31, 2020, are set forth in Proposal 5 above.

*The Board of Directors recommends a vote
FOR 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, 2021 through December 31, 2021, 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

FOR 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 2021 Summary Compensation Table and the related compensation tables, notes, and narrative 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 voted on June 17, 2020, to have advisory votes every 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" 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 2021 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" are effective in achieving our goals.

The vote under this Proposal 8 is advisory, and therefore not binding on the Company, the Board of Directors or our Compensation Committee. However, our Board of Directors and 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 as Part II of 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 as Part II of Annex A.*

Proposal 10:
APPROVAL OF OUR U.K. DIRECTORS' REMUNERATION POLICY

Our U.K. statutory directors' remuneration policy is set forth as Part I of Annex A to this proxy statement. Our directors' remuneration policy is used to determine the remuneration for our directors, including our Chief Executive Officer (our sole executive director), and our senior executive officers. The key objective of the policy is to engage and retain high-quality directors and senior executive officers. The last approved remuneration policy was approved by the shareholders at our 2019 annual general meeting and the new remuneration policy is proposed for approval at the Meeting, as required by the U.K. Companies Act 2006.

Our Board of Directors has determined that the proposed remuneration policy is competitive and consistent with current market practices. The proposed policy is largely similar to our previously approved policy, but includes the following material changes.

- The proposed policy includes share ownership requirements for executive directors. Our Chief Executive Officer will be expected to build up and maintain a shareholding equivalent to two-times his base salary. Executive directors will have five years from the earlier of the adoption of the policy or their appointment to the Board to achieve the target level of share ownership.
- The proposed policy includes recovery provisions, which intends to provide mitigation against payment for failure and to ensure that future incentive-based compensation is subject to recovery.
- The retainer arrangement for non-executive directors will allow directors to elect to receive a portion, or all, of their fees as either cash or in equity.

Our Board of Directors has approved the proposed directors' remuneration policy and believes it will be effective. The directors' remuneration policy, if approved, will take effect immediately upon conclusion of the Meeting. The policy is set forth as Part I of Annex A to this proxy statement.

*The Board of Directors recommends you vote
FOR approval of our U.K. Directors' Remuneration Policy set forth as Part I of Annex A.*

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	67	Chairman of the Board of Directors
Steven M. Altschuler, M.D.	68	Non-Executive Director
Joanne T. Beck, Ph.D.	61	Non-Executive Director
John T. Curnutte, M.D., Ph.D.	70	Non-Executive Director
Marc Dunoyer	69	Non-Executive Director
Bobby Gaspar, M.D., Ph.D.	58	Chief Executive Officer and Director
Charles A. Rowland, Jr.	63	Non-Executive Director
Alicia Secor	59	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 2021.

Director Nominees

The biographical information for each of John T. Curnutte, Bobby Gaspar and Alicia Secor, 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.

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 Mead 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 Medical 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 industry, his service on the boards of directors of other life sciences companies and his extensive leadership experience.

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Joanne T. Beck, Ph.D. has been a member of our Board of Directors since July 2018. Since December 2019, Dr. Beck has served as the Chief Operating Officer at Boston Pharmaceuticals, Inc. Previously, Dr. Beck 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 of Alliance for Regenerative Medicine, an international multi-stakeholder advocacy organization. Additionally, since February 2019, Dr. Beck has 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 is qualified to serve on our Board because of her executive experience in our industry.

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. At AstraZeneca, Mr. Dunoyer also held the role of Executive Vice President, Global Portfolio & Product Strategy from June 2013 to October 2013. Additionally, Mr. Dunoyer serves on the board of directors of AstraZeneca. 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 GSK, 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.

James A. Geraghty has been chairman of our Board of Directors since May 2018. He also serves as the chairman of the board of directors of publicly-traded biopharmaceutical company Pieris Pharmaceuticals, and as a member of the boards of directors of publicly traded Voyager Therapeutics, Fulcrum Therapeutics, and Idera Pharmaceuticals. He served as an Entrepreneur in Residence at Third Rock Ventures, a biotech venture capital firm, from May 2013 to October 2016. 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.

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., and as a member of the board of directors of Aurinia from July 2014 to 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. Mr. Rowland previously held positions of increasing responsibility at the following companies: Biovail Pharmaceuticals, Inc., Breakaway Technologies, Inc., Endo Pharmaceuticals Inc., Pharmacia Corporation, Novartis AG, and Bristol-Myers Squibb Co. Mr. Rowland has served as a member of the board of directors and chairman of the audit committee of Generation Bio since July 2018. Since July 2017, he has served as a member of the board of directors and chairman of the compensation committee and member of the audit committee of

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Viking Therapeutics, Inc. Since January 2015, he has served as a member of the board of directors and chairman of the compensation committee of Nabriva Therapeutics, AG, based in Dublin, Ireland. Since March 2015, Mr. Rowland has served as a member of the board of directors and compensation committee and as chairman of the audit committee of Blueprint Medicines Corporation, a publicly traded biopharmaceutical company. Mr. Rowland served as a member of the board of directors and audit committee of Idenix Pharmaceuticals, Inc., a biopharmaceutical company, from June 2013, until it was acquired by Merck & Co., Inc. in August 2014. Mr. Rowland served as a member of the board of directors and chairman of the audit committee of Vitae Pharmaceuticals, Inc., from September 2014 until it was acquired by Allergan Inc., in September 2016. Mr. Rowland served as a member of the board of directors and chairman of the audit committee of BIND Therapeutics, Inc., from May 2014 to July 2016. 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.

CORPORATE GOVERNANCE

Structure of our Board of Directors

The leadership structure of our Board of Directors separates the positions of Chief Executive Officer and Chairman 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 Company while the Chairman can focus on leading the Board in overseeing management, and for a sharing of ideas between individuals having different perspectives.

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

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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 such committee reviews its respective charter at least annually.

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

Audit Committee

Our Audit Committee is currently composed of Mr. Dunoyer, Mr. Rowland and Ms. Secor, with Mr. Rowland serving as chairman 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 five meetings during 2021. 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 composed of Dr. Beck, Mr. Rowland and Ms. Secor, with Mr. Rowland serving as chairman of the committee. Our Board of Directors has determined that each member of

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the Compensation Committee is “independent” as defined under the applicable Nasdaq rules. The Compensation Committee held seven meetings during 2021. 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; and
- overseeing and administering our employee share option scheme or equity incentive plans in operation from time to time.

During 2021, the Committee’s charter was extended to oversee 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 2021, 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 2021 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 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 Committee in determining competitive levels of executive and non-executive compensation and specific design elements of our executive compensation program and non-executive directors’ compensation program. The Compensation Committee continued to retain Radford through 2021 and 2022 in order to ensure that our compensation arrangements are competitive for 2022. 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 2021 or in 2022. 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 composed of Dr. Curnutte, Mr. Dunoyer, Mr. Geraghty and Ms. Secor, with Mr. Geraghty serving as chairman 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 2021. The Nominating and Corporate Governance Committee’s responsibilities include:

- drawing up selection criteria and appointment procedures for directors;

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- 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 2023 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 deems to be appropriate in the evaluation process. 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 committee-recommended 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.

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- 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

Total Number of Directors	<i>As of April 27, 2022</i>			
	8			

Part 1: Gender

	Male	Female	Non-Binary	Did Not Disclose Gender
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	

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 2023 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/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

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

Science and Technology Committee

Our Science and Technology Committee is composed of Dr. Altschuler, Dr. Beck, and Dr. Curnutte, with Dr. Curnutte serving as chairman 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 2021. 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 chairman 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

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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 April 21, 2022, 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 April 21, 2022 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 125,904,945 ordinary shares outstanding as of April 21, 2022.

Unless otherwise indicated, the address for each of the shareholders listed in the table below is c/o Orchard Therapeutics plc, 108 Cannon Street, London EC4N 6EU United Kingdom.

Name of Beneficial Owner	Ordinary Shares Beneficially Owned	
	Number	Percent
Greater than 5% Shareholders		
Glaxo Group Limited ⁽¹⁾	12,445,252	9.88%
Entities affiliated with Artisan Partners ⁽²⁾	9,816,108	7.80%
Entities affiliated with RA Capital Management ⁽³⁾	9,694,789	7.70%
Entities affiliated with F-Prime ⁽⁴⁾	8,611,375	6.84%
Entities affiliated with Federated Hermes, Inc. ⁽⁵⁾	8,309,859	6.60%
Entities affiliated with Deerfield Management Company ⁽⁶⁾	6,949,416	5.52%
CHI Advisors LLC ⁽⁷⁾	6,449,856	5.12%
Named Executive Officers and Directors		
Bobby Gaspar, M.D., Ph.D. ⁽⁸⁾	1,762,813	1.38%
Frank Thomas ⁽⁹⁾	1,069,543	*
James A. Geraghty ⁽¹⁰⁾	474,511	*
Steven M. Altschuler, M.D. ⁽¹¹⁾	113,888	*
Joanne T. Beck, Ph.D. ⁽¹²⁾	199,324	*
John T. Curnutte, M.D., Ph.D. ⁽¹³⁾	120,812	*
Marc Dunoyer ⁽¹⁴⁾	227,209	*
Charles A. Rowland, Jr. ⁽¹⁵⁾	202,324	*
Alicia Secor ⁽¹⁶⁾	160,000	*
<i>All Executive Officers and Directors as a Group (9 persons)</i> ⁽¹⁷⁾	4,330,424	3.34%

* Represents beneficial ownership of less than one percent.

(1) Based solely 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.

(2) Based on a Schedule 13G filed with the SEC on February 4, 2022. Consists of 9,816,108 ADSs beneficially owned by Artisan Partners Limited Partnership (“APLP”), of which 6,460,147 ADSs are held on behalf of

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Artisan Partners Funds, Inc. (“Artisan Funds”). Artisan Partners Holdings LP (“Artisan Holdings”) is the sole partner of APLP and the sole member of Artisan Investments GP LLC (“Artisan Investments”). Artisan Investments is the general partner of APLP. Artisan Partners Asset Management Inc. is the general partner of Artisan Holdings. The address of the entities is 875 East Wisconsin Avenue, Suite 800, Milwaukee, WI 53202.

- (3) Based on a Schedule 13G/A filed with the SEC on February 14, 2022. Consists of 9,694,789 ADSs held by RA Capital Healthcare Fund, L.P. (“RA Fund”). The general partner of RA Capital Management, L.P. (“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 RA Fund and may be deemed a beneficial owner of the ADSs held by RA Fund for purposes of Section 13(d) of the Securities Exchange Act of 1934 (“Section 13(d)"). RA Fund has delegated to RA Capital the sole power to vote and the sole power to dispose of all securities held in RA Fund’s portfolio, including the ADSs reported herein. Because RA 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, RA 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 of the ADSs, for purposes of Section 13(d). RA Capital, Dr. Kolchinsky and Mr. Shah disclaim beneficial ownership of the ADSs other than for the purpose of determining their obligations under Section 13(d). RA Fund’s address is 200 Berkeley Street, 18th Floor, Boston, MA 02116.
- (4) Based on a Schedule 13G/A filed with the SEC on February 9, 2022. Consists of 8,611,375 of our ordinary shares and ADSs beneficially owned by FMR LLC. Abigail P. Johnson is a Director, the Chairman and the Chief Executive Officer of FMR LLC. Members of the Johnson family, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders’ voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders’ voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. The address of these entities is 245 Summer Street, Boston, MA 02210.
- (5) Based on a Schedule 13G filed with the SEC on February 14, 2022. Consists of 8,309,859 ADSs beneficially owned by Voting Shares Irrevocable Trust. Federated Hermes, Inc. is the parent holding company of Federated Equity Management Company of Pennsylvania and Federated Global Investment Management Corp. (the “Investment Advisers”), which act as investment advisers to registered investment companies and separate accounts that own ADSs in the Company. The Investment Advisers are wholly owned subsidiaries of FII Holdings, Inc., which is wholly owned subsidiary of Federated Hermes, Inc., the parent. All of the parent’s outstanding voting stock is held in the Voting Shares Irrevocable Trust for which Thomas R. Donahue, Rhodora J. Donahue and J. Christopher Donahue act as trustees. The address of Federated Hermes, Inc. is 1001 Liberty Avenue, Pittsburgh, PA 15222.
- (6) Based on a Schedule 13G/A filed with the SEC on February 11, 2022. Consists of (i) 3,474,708 ADSs held by Deerfield Private Design Fund III, L.P. and (ii) 3,474,708 ADSs held by Deerfield Private Design Fund IV, L.P. Deerfield Mgmt III, L.P. is the general partner of Deerfield Private Design Fund III, L.P. Deerfield Mgmt IV, L.P. is the general partner of Deerfield Private Design Fund IV, L.P. Deerfield Management Company, L.P. is the investment advisor to Deerfield Private Design Fund III, L.P. and Deerfield Private Design Fund IV, L.P. James E. Flynn is the sole member of the general partner of each of Deerfield Mgmt III, L.P., Deerfield Mgmt. IV, L.P. and Deerfield Management Company, L.P. Deerfield Mgmt III, L.P. may be deemed to beneficially own the ADSs held by Deerfield Private Design III, L.P. Deerfield Mgmt IV, L.P. may be deemed to beneficially own the ADSs held by Deerfield Private Design Fund IV, L.P. Each of Deerfield Management Company, L.P. and Mr. James E. Flynn may be deemed to beneficially own the ADSs held by Deerfield Private Design Fund III, L.P. and Deerfield Private Design Fund IV, L.P. The address of the filing persons is 345 Park Avenue South, 12th Floor, New York, NY 10010.

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- (7) Based on a Schedule 13G filed with the SEC on February 11, 2022. The address of CHI Advisors LLC is 599 Lexington Avenue, 19th Floor, New York, NY 10022.
- (8) Consists of (i) 370,158 of our ordinary shares and ADS, (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) 1,392,655 of our ordinary shares issuable upon exercise of options within 60 days of April 21, 2022.
- (9) Consists of (i) 52,082 of our ordinary shares and ADS and (ii) 1,017,462 of our ordinary shares issuable upon exercise of options within 60 days of April 21, 2022.
- (10) Consists of (i) 44,391 of our ordinary shares and ADSs and (ii) 430,120 of our ordinary shares issuable upon exercise of options within 60 days of April 21, 2022.
- (11) Consists of 113,888 of our ordinary shares issuable upon exercise of options within 60 days of April 21, 2022.
- (12) Consists of (i) 9,292 of our ordinary shares and ADSs and (ii) 190,030 of our ordinary shares issuable upon exercise of options within 60 days of April 21, 2022.
- (13) Consists of 120,812 of our ordinary shares issuable upon exercise of options within 60 days of April 21, 2022.
- (14) Consists of (i) 37,179 of our ordinary shares and ADSs and (ii) 190,030 of our ordinary shares issuable upon exercise of options within 60 days of April 21, 2022.
- (15) Consists of (i) 12,294 of our ordinary shares and ADSs and (ii) 190,030 of our ordinary shares issuable upon exercise of options within 60 days of April 21, 2022.
- (16) Consists of 160,000 of our ordinary shares issuable upon exercise of options within 60 days of April 21, 2022.
- (17) Includes an aggregate of 3,805,027 of our ordinary shares issuable upon exercise of options within 60 days of April 21, 2022.

DELINQUENT SECTION 16(a) REPORTS

Section 16(a) of the Exchange Act requires our executive officers, directors, and persons who own more than 10% of a registered class of our equity securities to file reports of ownership on Form 3 and changes in ownership on Form 4 or Form 5 with the SEC. Such executive officers, directors and 10% shareholders are also required by securities laws to furnish us with copies of all Section 16(a) forms they file. Based solely on our review of copies of these reports, or written representations from reporting persons, we believe that during the year ended December 31, 2021, our executive officers, directors and persons who own more than 10% of a registered class of our equity securities filed under Section 16(a) on a timely basis, with the exception of one late Form 4 filed for FMR LLC on February 10, 2021 to report a transaction that occurred on February 5, 2021.

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, 2020 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.

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.

Private Placement

In February 2021, we entered into a securities purchase agreement (the “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 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-thalassemia. 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, 2021.

	2021 Cash Compensation (through March 31)	2021 Cash Compensation (from April 1)
Board of Directors	\$ 45,000	\$ 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)	\$ 10,000	\$ 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)	\$ 5,000	\$ 7,500

In addition, each non-employee director will be granted an initial, one-time equity award of 92,000 share options 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 46,000 share options, 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 U.K. statutory 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 2021, 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, 2021. 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 2021.

	<u>Fees earned or paid in cash (\$)</u>	<u>Option Awards (\$)(1)</u>	<u>Total</u>
Steven Altschuler(2)	51,875	121,592	173,467
Joanne Beck(3)	59,375	121,592	180,967
Marc Dunoyer(4)	59,000	121,592	180,592
Jon Ellis(5)	—	—	0
James Geraghty(6)	95,000	121,592	216,592
Charles Rowland(7)	78,000	121,592	199,592
Alicia Secor(8)	72,000	121,592	193,592
John Curnutte(9)	60,000	121,592	181,592

- (1) The amounts reported represent the aggregate grant date fair value of the option awards granted during 2021 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 14 of our audited consolidated financial statements for the year ended December 31, 2021 included in our Annual Report on Form 10-K, filed with the SEC on March 30, 2022. These amounts do not necessarily correspond to the actual value recognized or that may be recognized by the directors.
- (2) As of December 31, 2021, Dr. Altschuler held unexercised options to purchase 125,000 ordinary shares.
- (3) As of December 31, 2021, Dr. Beck held unexercised options to purchase 190,030 ordinary shares.
- (4) As of December 31, 2021, Mr. Dunoyer held unexercised options to purchase 190,030 ordinary shares.
- (5) In October 2018, we entered into a director nomination agreement with Glaxo Group Limited, or GSK, pursuant to which we agreed to nominate and appoint to our Board of Directors a designee of GSK, Dr. Ellis, during the period commencing upon our IPO until such time as we obtained marketing approval and commercially launched OTL-200 for metachromatic leukodystrophy. The director nomination agreement has since been terminated. Dr. Ellis did not receive cash or equity compensation from the Company for his service on our Board. Dr. Ellis did not stand for re-election at the 2021 annual general meeting of shareholders, and he retired from his position as Director upon the conclusion of that meeting on June 16, 2021.
- (6) As of December 31, 2021, Mr. Geraghty held unexercised options to purchase 430,120 ordinary shares.
- (7) As of December 31, 2021, Mr. Rowland held unexercised options to purchase 190,030 ordinary shares.
- (8) As of December 31, 2021, Ms. Secor held unexercised options to purchase 160,000 ordinary shares. The fees shown for Ms. Secor includes a one-time retrospective payment of \$11,250 in April 2021 for prior services to the Nominating and Corporate Governance Committee that had not been previously paid.
- (9) As of December 31, 2021, Dr. Curnutte held unexercised options to purchase 125,000 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.

<u>Name</u>	<u>Age</u>	<u>Position</u>
Bobby Gaspar, M.D., Ph.D.	58	Chief Executive Officer
Frank Thomas	52	President and Chief Operating Officer

Bobby Gaspar, M.D., Ph.D. For biographical information regarding Dr. Gaspar, please refer to “*Proposal 2—Re-election of Bobby Gaspar to the Board of Directors*”.

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 2020 to March 2020 and as our Chief Financial Officer and Chief Business 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 on the board of directors of Spero Therapeutics, Inc., a publicly traded biopharmaceutical company. Mr. Thomas was a member of the board 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, 2021. Our named executive officers are:

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

2021 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 2021 and 2020.

<u>Name</u>	<u>Year</u>	<u>Salary(1)</u>	<u>Bonus</u>	<u>Stock Awards(2)</u>	<u>Option Awards(3)</u>	<u>Non-Equity Incentive Plan Compensation(4)</u>	<u>All Other Compensation</u>	<u>Total</u>
Bobby Gaspar(5)	2021	\$605,114	—	—	\$3,504,354	\$ 217,841	\$ 27,230(6)	\$4,354,539
Chief Executive Officer	2020	\$542,513	—	\$ 0	\$3,070,610	\$ 169,897	—	\$3,783,020
Frank Thomas	2021	\$470,000	—	—	\$1,257,233	\$ 235,000	\$ 11,600(7)	\$1,973,833
President & COO	2020	\$469,693	—	—	\$2,399,615	\$ 105,750	\$ 10,738(7)	\$2,985,796

- (1) Neither Dr. Gaspar nor Mr. Thomas received a salary increase during 2021. The increase in Dr. Gaspar’s salary reflects the different exchange rates used to convert his salary from Great British Pounds (“GBP”) to USD for purposes of this table. See note 5 below for additional details.
- (2) In accordance with SEC rules, the grant date fair value to be reported for restricted share units subject to performance-based vesting (“PSUs”) in the Stock Awards column is calculated in accordance with the provisions of FASB ASC Topic 718 based on the probable outcome of the performance condition as of the grant date. We determined that as of the date of the grant of the PSU award granted to Dr. Gaspar in 2020, it was not probable, as defined under applicable accounting guidance, that the performance conditions would be achieved and assigned a grant date fair value of \$0 in the Stock Awards column for 2020. However, if we had determined that as of the date of grant it was probable that the performance conditions would be achieved at maximum levels, we would have assigned a grant date fair value of \$1,366,950. Details of this valuation are included in Note 14 of our audited consolidated financial statements for the year ended December 31, 2021 included in our Annual Report on Form 10-K, filed with the SEC on March 30, 2022.
- (3) The amounts reported in the Option Awards column represent the aggregate grant date fair value for the fiscal years ended December 31, 2021, and 2020 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 14 of our audited consolidated financial statements for the year ended December 31, 2021 included in our Annual Report on Form 10-K, filed with the SEC on March 30, 2022. 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 include the fair value of time-based share options awarded with an equivalent fair value to 50% of the 2020 annual bonus.
- (4) 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.
- (5) Dr. Gaspar’s cash compensation was paid in GBP. Amounts paid in GBP have been converted to USD at an exchange rate of 1 GBP to 1.3575 USD in 2021 and 1 GBP to 1.2781 USD in 2020, based upon the exchange rate as of December 31, 2021 and December 31, 2020, respectively.

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

Narrative to Summary Compensation Table

2021 Base Salary and Bonus

During 2021, neither Dr. Gaspar nor Mr. Thomas received a salary increase and their salaries remained at £440,000 and \$470,000, respectively. There was no change to Dr. Gaspar's target bonus opportunity, which remained at 60% of his base salary. Mr. Thomas's target bonus opportunity was increased from 45% of his base salary to 50%.

At the end of the year, the Committee assessed 2021 performance against our stated corporate objectives, which include objectives in the areas of:

- i. building a foundation for a sustainable commercial business;
- ii. advancing our portfolio to key clinical and regulatory milestones;
- iii. maintaining a performance-driven culture internally and with our partners.

The Committee's assessment of the performance against these objectives resulted in a performance score of 60%, which provided for a bonus of 36% of base salary for Mr. Gaspar. Please refer to the section below titled "*Frank Thomas Transitional Services Agreement*" for details of Frank Thomas's 2021 bonus. The corporate performance score is used as a part of the calculation for all employee bonuses across the Company.

2021 Equity-Based Compensation

On February 1, 2021, Dr. Gaspar and Mr. Thomas were granted options to purchase 850,000 and 310,000 ordinary shares, respectively.

On January 16, 2019, Dr Gaspar was granted 18,750 Performance Share Units subject to defined milestones in relation to clinical programs and share-price performance. On December 17, 2020, the Company received full (standard) market authorization of Libmeldy for the treatment of MLD in all 27 member states of the European Union. As a result of this authorization, and following subsequent ratification by the Board, 6,250 shares under the award (or 1/3 of the total shares) vested on January 8, 2021.

Employment Agreements

Bobby Gaspar

In May 2019, we entered into an amendment to Dr. Gaspar's January 2018 employment agreement in connection with his continued employment as our Chief Scientific Officer. Dr. Gaspar was promoted to Chief Executive Officer on March 18, 2020.

On appointment to CEO, Dr. Gaspar's base salary was increased to £440,000. In addition, Dr. Gaspar is entitled to participate in our executive variable cash compensation program at an initial annual target variable cash compensation payment. For 2021 this target amount was 60% of his base salary, with the actual amount to be determined in the discretion of the Compensation Committee based on the Company's performance and the individual performance of Dr. Gaspar. 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.

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Upon a termination of Dr. Gaspar's employment without cause or for good reason that does not occur within the 12-month period following a change in control (the "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 nine 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 three months;
- the amount of any annual cash incentive compensation for the year prior to the 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;
- continued health, long-term disability and other insurance programs for up to nine 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 12 months of his base salary; provided that, in the case of a termination without cause, Dr. Gaspar shall be entitled to receive six months' written notice of his termination (or payment in lieu of such notice), plus an amount equal to six months of his base salary;
- 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 12 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

In September 2019, we entered into an employment agreement with Mr. Thomas in connection with his continued employment as our Chief Financial Officer and Chief Business Officer, which supersedes his prior employment agreement with our U.K. subsidiary entered into in 2018. Mr. Thomas was promoted to President and Chief Operating Officer on March 18, 2020.

Mr. Thomas's employment agreement provides for an initial base salary of \$430,090, which is subject to annual review and redetermination. This salary was increased to \$470,000, effective January 1, 2020. Mr. Thomas did not receive a salary increase in 2021. In addition, Mr. Thomas is entitled to participate in our executive variable cash compensation program. For 2020, Mr. Thomas' annual target variable cash compensation payment was 45% of his base salary. This increased to 50% for 2021. The actual amount received by Mr. Thomas is determined by the Compensation Committee in its discretion and is based on the Company's performance and the individual performance of Mr. Thomas. Mr. Thomas is also eligible to participate in all of our generally-available employee benefit plans and programs in effect from time to time.

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

- salary continuation for a period of nine months following his termination of employment;
- the amount of any annual cash incentive compensation for the year prior to the 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 nine 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, the payments to Mr. Thomas would be reduced to the maximum amount that can be paid without the imposition of an excise tax under Section 4999, but only if such reduction provides a higher benefit on an after-tax basis to Mr. Thomas. The employment agreement does not provide for any tax gross-up payments.

Frank Thomas Transitional Services Agreement

On November 3, 2021, we entered into a Transitional Services Agreement with Frank Thomas, which was amended on March 30, 2022 (as amended, the "Agreement"). Pursuant to the Agreement, Mr. Thomas will continue to serve as President and Chief Operating Officer of the Company and provide services for the Company on a full-time basis until December 31, 2022, unless his employment ends earlier or the Company and Mr. Thomas agree to an extension (such period, the "Transition Period"). During the Transition Period, the Agreement provides, among other things, that in exchange for entering into and complying with the Agreement, which includes a customary release of claims, Mr. Thomas will (i) continue to receive his base salary, subject to an increase in the base salary rate in an amount determined by the Board of Directors of the Company (or the Compensation Committee thereof) to be effective at the time that other executive team members of the Company receive base salary rate increases, (ii) remain eligible to participate in the Company's group employee benefit plans, (iii) continue to vest in his stock options, and (iv) subject to the approval of the Company's Board of Directors (or the Compensation Committee thereof), receive an award of stock options to purchase shares of the Company and/or other form of equity. Further, if Mr. Thomas remains employed by the Company on October 1, 2022, or in the event that he is terminated without "Cause" (as defined in the Agreement) prior to October 1, 2022 but has, among other things, executed an updated release of claims, then Mr. Thomas will be eligible to receive a cash payment equal to 25% of Mr. Thomas' then current base salary, to be paid no later than October 31, 2022. In addition, at the conclusion of his employment with the Company, provided that, among

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other things, Mr. Thomas' employment is not terminated by the Company for "Cause" and subject to the execution and effectiveness of an updated release, Mr. Thomas will be entitled to the following benefits (a) for up to six months, the Company shall pay the monthly employer COBRA premium for the same level of group health coverage as in effect at the conclusion of Mr. Thomas' employment, (b) be eligible to receive a cash payment equal to 25% of Mr. Thomas' then current base salary, to be paid at the time that the Company pays it executives their annual incentive compensation for 2022, which will be no later than March 15, 2023, and (c) subject to approval by the Company's Board of Directors (or the Compensation Committee thereof) (x) continued vesting of all equity awards until April 1, 2023 and (y) an extension of the exercise period with respect to the vested shares of his stock options as of the date that the Company receives Mr. Thomas' executed updated release of claims, until the earlier of (A) April 1, 2024 or (B) the expiration date of the applicable share option.

Outstanding Equity Awards at Fiscal Year-End

Name	Vesting Commencement Date	Option Awards				Stock Awards	
		Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price (\$)	Option Expiration Date	Equity Incentive Plan Awards: Number of unearned shares, units or other rights that have not vested (#)	Equity Incentive Plan Awards: Market or payout value of unearned shares, units or other rights that have not vested (\$)
(a)		(b)	(c)	(e)	(f)	(i)	(j)
Bobby Gaspar	2/1/2016	597,867	0	\$ 0.00002	9/13/2026		
	2/7/2016 ⁽²⁾	38,347	1,668	\$ 0.00002	2/6/2028		
	9/13/2018	78,341	18,079	\$ 0.00002	9/12/2028		
	1/16/2019	36,458	13,542	\$ 12.54	1/15/2029		
	1/2/2020	95,833	104,167	\$ 13.58	1/1/2030		
	4/1/2020	125,000	175,000	\$ 7.05	3/31/2030		
	2/1/2021	177,083	672,917	\$ 5.98	1/31/2031		
	2/1/2021 ⁽³⁾	45,838	9,168	\$ 5.98	1/31/2031		
Frank Thomas	2/7/2018 ⁽⁵⁾	415,847	10,338	\$ 2.44	2/6/2028	195,000 ⁽⁴⁾	\$ 257,400
	9/13/2018	149,686	80,599	\$ 9.06	9/12/2028		
	1/16/2019	72,916	27,084	\$ 12.54	1/15/2029		
	1/2/2020	95,833	104,167	\$ 13.58	1/1/2030		
	4/1/2020	62,500	237,121	\$ 7.05	3/31/2030		
	1/2/2021	64,583	245,417	\$ 5.98	1/31/2031		
	1/2/2021 ⁽³⁾	23,109	4,622	\$ 5.98	1/31/2031		

- (1) All 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.
- (2) 10,004 shares subject to this option vested on February 7, 2019 and the remaining shares vest in equal monthly installments over the three years thereafter, subject to a continuous service relationship through each vesting date.
- (3) These options vest in 12 equal monthly installments.
- (4) 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, 2021, multiplied by \$1.32, which was the closing price of our ADSs on The Nasdaq Global Select Market on December 31, 2021.
- (5) 124,407 shares subject to this option vested on January 15, 2019 and the remaining shares vest in equal monthly installments over the three years thereafter, subject to a continuous service relationship through each vesting date. 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 individuals who were not previously an employee or director of the Company or individuals returning to employment after a bona fide period of

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non-employment with the Company. Please see Note 14 to our Annual Report on Form 10-K for the year ended December 31, 2021 filed with the SEC on March 30, 2022 for additional information regarding the 2020 Inducement Equity Plan.

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, 2021 regarding ordinary shares that may be issued under our equity compensation plans:

Plan Category	Number of Securities to be Issued upon Exercise of Outstanding Options, Warrants and Rights (#)(a)	Weighted Average Exercise Price of Outstanding Options, Warrants and Rights (b)	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 ⁽¹⁾	17,340,573 ⁽²⁾	\$ 6.50 ⁽³⁾	7,785,422 ⁽⁴⁾
Equity compensation plans not approved by security holders ⁽⁵⁾	278,500	\$ 3.09	721,500
Total	17,619,073	\$ 6.45	8,506,922

- (1) 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.
- (2) 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.
- (3) The calculation does not take into account the 318,333 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.
- (4) Consists of shares available for future issuance under the ESPP and the 2018 Plan. As of December 31, 2021, 850,948 shares were available for issuance under the ESPP and 6,934,474 shares were available for issuance under the 2018 Plan. Excludes 6,283,704 additional ordinary shares that were added to the number of shares that may be issued under the 2018 Plan pursuant to an automatic increase effective January 1, 2022.
- (5) Consists of shares under our 2020 Inducement Equity Plan.

AUDIT COMMITTEE REPORT

The Audit Committee oversees the accounting and financial reporting processes of Orchard Therapeutics plc (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 of the Company (the “Board”). 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, 2021. 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.

The Audit Committee also reviewed with PricewaterhouseCoopers LLP (“PwC USA”) , our 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, 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

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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, 2021.

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, 2021 (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, 108 Cannon Street, London EC4N 6EU 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 SHAREHOLDER IS URGED TO COMPLETE, DATE, SIGN
AND PROMPTLY RETURN THE ENCLOSED FORM OF PROXY.**

**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, 2021

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, 2021, 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 generally 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 2023 Annual General Meeting

Pursuant to Rule 14a-8 under the Exchange Act, in order to be considered for inclusion in our proxy statement for our 2023 annual general meeting of shareholders, shareholder proposals must be received by the Company at the Office of the Company Secretary, 108 Cannon Street, London EC4N 6EU, United Kingdom no later than 120 days before the anniversary of the date on which we sent our proxy materials for the AGM, or December 28, 2022. However, if the date of such 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.

If a shareholder wishes to present a proposal at an annual general meeting but does not wish to have the proposal considered for inclusion in our proxy statement and proxy card, such shareholder proposal must be received by the Company at the Office of the Company Secretary, 108 Cannon Street, London EC4N 6EU, United Kingdom no later than 45 days before the anniversary of the date on which the Company first mailed its proxy materials for the prior year's annual general meeting. However, if the date of the annual general meeting is changed by more than 30 calendar days from the date of the anniversary of the prior year's annual general meeting, the notice must be received by our Company Secretary within a reasonable time before we begin to print and send our proxy materials with respect to such annual general meeting. If a shareholder does not timely provide notice as described above, proxies solicited on behalf of our management for such annual general meeting will confer discretionary authority to vote with respect to any such matter, as permitted by the proxy rules of the SEC.

To comply with the universal proxy rules (once effective), shareholders who intend to solicit proxies in support of director nominees other than the Company's nominees must provide notice 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 April 8, 2023.

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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, 108 Cannon Street, London EC4N 6EU, 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.

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
108 Cannon Street
London EC4N 6EU
United Kingdom

DIRECTORS' REMUNERATION REPORT

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 proposed 2022 Directors' Remuneration Policy and the Directors' Remuneration Report for the year ended 31 December 2021 (the "Remuneration Report").

The Company's Remuneration Report, will be subject to an advisory vote at the forthcoming Annual General Meeting on 7 June 2022 (the "AGM") and our 2022 Directors' Remuneration Policy subject to a binding vote and, if approved, valid for a maximum of three years from that date.

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 US 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, 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. We recognize the evolving best practices in remuneration governance, and we have incorporated the following into our proposed Policy beginning this year: (i) shareholding requirements for Executive Directors and, (ii) recovery provisions (malus and clawback) on to all incentive compensation. We believe these are important updates to a Policy which serves our shareholders well in our competitive landscape in the global biotechnology sector.

Key remuneration decisions for 2021

The Committee and I were mindful of the Company's overall financial position and the Company's share price performance during the year. We acknowledge and celebrate the many achievements made by all of our colleagues at Orchard while ensuring the broader context of the Company is considered when making remuneration decisions.

In January 2021, the Committee welcomed, and endorsed a proposal from the CEO, that he would not receive any increase in base salary during 2021. This was consistent with the remainder of the leadership team at that time. His target bonus also remained at 60% salary. As CEO, we granted Dr. Gaspar the option to purchase 850,000 shares, effective February 1, 2021 – the level of this award benchmarked against our industry peers.

DIRECTORS' REMUNERATION REPORT

continued

2021 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 2021 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, executive team and consistent for all employees, the Committee determined a corporate score of 60% of target. This is reflective of the Company as a whole making considerable strides towards all of our stated objectives while also acknowledging that a number of key objectives fell short of expectations due to either internal or external factors. 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 2022

There are no substantial changes to our approach to executive compensation for 2022.

Consistent with our pay for performance philosophy, we intend to grant Dr. Gaspar an annual award of share options in 2022. In prior years all options have been awarded at market value. For 2022, and reflecting the Company's share price performance, we propose to grant half of the 2022 award in premium-priced options – options with an exercise price above the stock price on the date of grant. This installs a further hurdle before any of Dr. Gaspar's long-term incentive has any intrinsic value and further aligns our compensation approach with the shareholder experience.

Changes to the Board

Jon Ellis did not seek re-election to the Board at the 2021 AGM and ceased to be a Director on 16 June 2021. Dr. Ellis received no remuneration from Orchard and we thank him for his services to the Company.

Conclusion

The Committee believes that the Directors' Remuneration Policy has been implemented fairly and consistently, as described in this report. With the governance updates we are proposing, we are confident that it will continue to properly motivate our Executive Directors 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,



Charles Rowland, Jr.
Chair of the Compensation Committee

25 April 2022

DIRECTORS' REMUNERATION REPORT

continued

Remuneration Policy

The following section sets out our Directors' Remuneration Policy (the "Policy") which will be put to a binding shareholder vote at the annual general meeting on 7 June 2022. If approved, it will be effective from that date.

The current Directors' Remuneration Policy was approved by shareholders in June 2019, therefore a new policy is being presented under the standard three-year renewal cycle. The current policy received strong shareholder support, as has the implementation of the policy in the annual voting. The Compensation Committee is of the view that the overall structure continues to be appropriate for a company in Orchard's position reflecting the competitive environment for talent while including developments in market and governance best practices.

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 is 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.

DIRECTORS' REMUNERATION REPORT

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.

<u>Executive Directors</u> <u>Purpose and link to strategy</u>	<u>Operation</u>	<u>Maximum opportunity</u>	<u>Performance metrics</u>
<p>Base salary</p> <p>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.</p> <p>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.</p>	<p>Salaries are normally reviewed annually.</p> <p>The annual salary review for Executive Directors takes a number of factors into consideration, including:</p> <ul style="list-style-type: none"> • 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. 	<p>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.</p> <p>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.</p>	<p>Executive Directors' performance is a factor considered when determining any salary increases.</p>

DIRECTORS' REMUNERATION REPORT

continued

<u>Executive Directors</u>	<u>Operation</u>	<u>Maximum opportunity</u>	<u>Performance metrics</u>
<p>Purpose and link to strategy Benefits</p>	<p>The Company aims to offer benefits that are in line with market practice.</p> <p>The main benefits currently provided include private health insurance, long-term disability, critical illness and death in service.</p> <p>Under certain circumstances the Company may offer relocation allowances or assistance. Expatriate benefits may be offered where required.</p> <p>Travel and any reasonable business- related expenses (including tax thereon) may be reimbursed.</p> <p>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.</p> <p>Benefits may also include payment by the Company of any stamp duty arising in respect of the settlement of equity incentives.</p>	<p>The value of each benefit is not predetermined and is typically based upon the cost to the Company of providing said benefit.</p>	<p>Not performance related.</p>
<p>Retirement benefits</p> <p>The Company aims to provide a contribution towards life in retirement.</p>	<p>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.</p>	<p>Up to 6% of salary per annum for Executive Directors.</p> <p>6% is the contribution rate provided to all UK employees.</p>	<p>Not performance related.</p>

DIRECTORS' REMUNERATION REPORT

continued

<u>Executive Directors</u>	<u>Operation</u>	<u>Maximum opportunity</u>	<u>Performance metrics</u>
<p>Purpose and link to strategy Annual bonus</p>	<p>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.</p>	<p>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 2022, 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.</p>	<p>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.</p>
<p>The annual bonus scheme rewards the achievement of stretching objectives that support the Company's corporate goals and delivery of the business strategy.</p>			

DIRECTORS' REMUNERATION REPORT

continued

Executive Directors

Purpose and link to strategy

Long-term incentives

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.

Operation

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.

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.

Maximum opportunity

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 metrics

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 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.

DIRECTORS' REMUNERATION REPORT

continued

Executive Directors

Purpose and link to strategy

All employee share schemes

Encourages employee share ownership and therefore increases alignment with shareholders. Executive Directors will be eligible to participate in any all- employee share scheme.

Operation

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 arrangements in any jurisdiction in order to comply with local requirements.

Maximum opportunity

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.

Performance metrics

Not performance related.

DIRECTORS' REMUNERATION REPORT

continued

<u>Executive Directors</u>			
<u>Purpose and link to strategy</u>	<u>Operation</u>	<u>Maximum opportunity</u>	<u>Performance metrics</u>
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.	<p>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.</p> <p>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.</p> <p>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.</p> <p>When reviewing fee levels, account is taken of market movements in fee levels, Board committee responsibilities, ongoing time commitments and the general economic environment.</p> <p>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.</p> <p>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.</p>	<p>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.</p> <p>Actual fee levels are disclosed in the annual Directors' Remuneration Report for the relevant financial year.</p>	Not performance related.

DIRECTORS' REMUNERATION REPORT

continued

<u>Executive Directors</u>			
<u>Purpose and link to strategy</u>	<u>Operation</u>	<u>Maximum opportunity</u>	<u>Performance metrics</u>
Equity Awards			
To facilitate share ownership and provide alignment with shareholders.	<p>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.</p> <p>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.</p> <p>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.</p>	<p>There is no maximum award level for equity awards to Non- Executive Directors.</p> <p>The size of the equity awards is determined by the full Board of Directors, upon recommendation of the Compensation Committee.</p> <p>When reviewing award levels, account is taken of market movements in equity awards, Board committee responsibilities, ongoing time commitments and the general economic conditions.</p>	Not performance related.

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.

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

DIRECTORS' REMUNERATION REPORT

continued

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 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;
- 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;

DIRECTORS' REMUNERATION REPORT

continued

- 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 Committee 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 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.

DIRECTORS' REMUNERATION REPORT

continued

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	<p>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.</p> <p>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.</p> <p>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.</p>
Benefits	<p>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.</p>
Pension benefits	<p>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.</p>
Annual bonus	<p>The maximum bonus opportunity for new appointments is 150% of their target bonus.</p>

DIRECTORS' REMUNERATION REPORT

continued

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.

<u>Name</u>	<u>Position</u>	<u>Date of service contract</u>	<u>Notice period</u>
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).

DIRECTORS' REMUNERATION REPORT

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 replace awards, on a corporate event awards with time-based vesting conditions shall vest on the

DIRECTORS' REMUNERATION REPORT

continued

<u>Termination without cause or for cause by participant</u>	<u>Termination for cause</u>	<u>Termination without cause or for cause by participant in connection with change of control</u>
		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.

DIRECTORS' REMUNERATION REPORT

continued

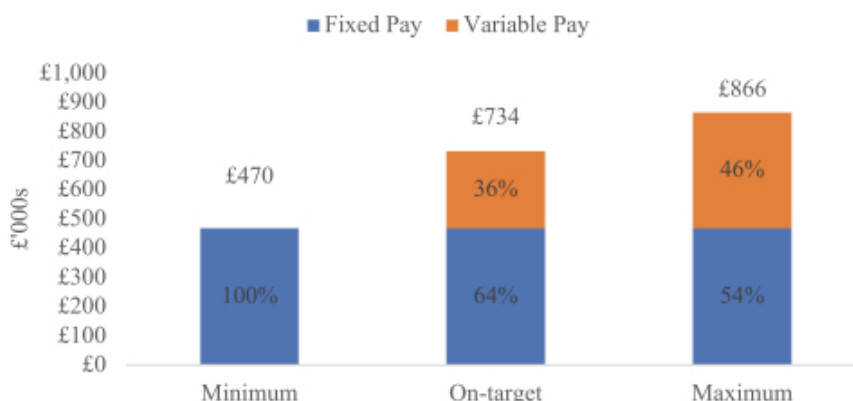
The dates of appointment of each of the Non-Executive Directors serving at 31 December 2021 are summarised in the table below. Dates prior to our incorporation in August 2018 as Orchard Rx Limited (now known as Orchard Therapeutics plc) are for Non-Executive Directors who served on the board of our predecessor company, Orchard Therapeutics Limited (now known as Orchard Therapeutics (Europe) Limited).

<u>Non-Executive Directors</u>	<u>Date of contract or date of appointment</u>	<u>Service at 31.12.21</u>
Joanne Beck	1 July 2018	3 years 6 months
Marc Dunoyer	6 June 2018	3 years 7 months
James Geraghty	4 June 2018	3 years 7 months
Charles Rowland	1 June 2018	3 years 7 months
Alicia Secor	7 December 2018	3 years 1 month
John Curnutte	30 August 2019	2 years 4 months
Steven Altschuler	3 February 2020	1 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.

Illustration of remuneration policy

The remuneration arrangements are designed to ensure that a significant proportion of pay is dependent on the Company's performance. The Compensation Committee considers the level of remuneration that may be received under different performance outcomes to ensure that this is appropriate in the context of the success of the Company. The chart below provides illustrative values of the annual compensation package for the Chief Executive Officer in 2022 under three assumed performance scenarios. This chart below is for illustrative purposes only and actual outcomes may differ from those shown. The variable remuneration in the charts below only include annual bonus opportunity. Executive Directors typically receive an annual award of market value options, the intrinsic value of which is zero at grant, and is therefore only included in the share price appreciation element.



DIRECTORS' REMUNERATION REPORT

continued

	<u>Assumed performance</u>	<u>Assumptions</u>
Fixed pay	All performance scenarios	Consists of fixed pay including base salary, benefits and retirement benefits. <ul style="list-style-type: none">– Base salary – as effective 1 January 2022– Benefits – using 2021 values– Retirement benefits – 6% salary
Variable pay	Minimum On-target Maximum performance	<ul style="list-style-type: none">– No pay-out on annual bonus– CEO target bonus for 2022 = 60% salary– Maximum bonus pay-out of annual bonus, at 1.5x target i.e. 90% salary
Share price appreciation	Impact of 50% Share-price appreciation	<ul style="list-style-type: none">– Orchard typically awards long-term incentives to Executive Directors in the form of share options.– The number of share options granted to the CEO in 2021 and 2022 is 850,000 share options.– For illustrative purposes, were 850,000 share options granted at market value using closing price on 31 December 2021- \$1.32, a 50% appreciation in the share price would result in a gain of \$561,000.

DIRECTORS' REMUNERATION REPORT

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") and Rule 9.8.6 of the Listing Rules. 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 7 June 2022.

Compensation Committee (the "Committee")

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

The Company Chair 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 and the Executive Directors.

Meetings attendance during 2021

	<u>Attendance</u>
Charles Rowland	7 of 7
Joanne Beck	7 of 7
Alicia Secor	7 of 7

Independent advisors

Wholly independent advice on executive remuneration is received from the Executive Compensation practice of Aon plc. Aon advises on remuneration arrangements and all aspects of senior executive remuneration. In 2021, Aon assisted the Committee and kept the Committee up to date on remuneration trends and regulations. During the 2021 financial year, fees charged by Aon for advice provided to the Committee amounted to \$131,226 (2020: \$171,329) (excluding VAT). In addition, Aon provided advice to the Company's Human Resources function on implementation, which the Committee considers in no way prejudices Aon's position as the Committee's independent advisor. Goodwin Procter LLP have also advised the Company's Human Resources function on compensation.

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 incentivised and rewarded through the operation of 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.

DIRECTORS' REMUNERATION REPORT

continued

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;
- reviewing, evaluating, and approving employment agreements, severance agreements, change-of-control protections, 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. During 2021, the Committee's remit was extended to oversee the Company's policies and strategies relating to culture and human capital management, including diversity and inclusion.

Statement of shareholder voting at 2021 AGM

At last year's AGM held on 16 June 2021, votes cast by proxy and at the meeting in respect of the Directors' remuneration were as follows:

	Votes For		Votes Against		Votes Withheld	
	% of votes cast	Number of votes	% of votes cast	Number of votes	% of votes cast	Number of votes
To approve the Directors' Remuneration Report	94.9%	62,998,348	5.0%	3,299,947	0.1%	61,446

DIRECTORS' REMUNERATION REPORT

continued

The Directors' Remuneration Policy was approved the Company's AGM held on 26 June 2019 as follows:

	Votes For		Votes Against		Votes Withheld	
	% of votes cast	Number of votes	% of votes cast	Number of votes	% of votes cast	Number of votes
To approve the Directors' Remuneration Policy	91.6%	33,863,941	8.4%	3,110,196	0%	750

Single total figure of Directors' remuneration – year ended 31 December 2021 (audited)

The total remuneration of the individual Directors who served in the year ended 31 December 2021, 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	PSUs ⁵ \$000	Total remuneration \$000	Total fixed	Total variable
Executive Directors										
Bobby Gaspar	2021	605.1	3.2	27.2	217.8	—	—	853.4	635.5	217.8
	2020	542.5	6.6	—	169.9	—	44.8	763.8	549.1	214.7

		Base salary /fees \$000	Benefits ² \$000	Pension \$000	Bonus \$000	SOIP ³ \$000	PSUs ⁴ \$000	Total remuneration \$000	Total fixed	Total variable
Non-Executive Directors										
Steven Altschuler ⁶	2021	51.9	—	—	—	—	—	51.9	51.9	—
	2020	47.2	—	—	—	—	—	47.2	47.2	—
Joanne Beck	2021	59.4	—	—	—	—	—	59.4	59.4	—
	2020	58.0	—	—	—	—	—	58.0	58.0	—
John Curnutte	2021	63.7	—	—	—	—	—	63.7	63.7	—
	2020	60.5	—	—	—	—	—	60.5	60.5	—
Marc Dunoyer	2021	59.1	—	—	—	—	—	59.1	59.1	—
	2020	59.5	—	—	—	—	—	59.5	59.5	—
Jon Ellis ⁷	2021	—	—	—	—	—	—	—	0.0	—
	2020	—	—	—	—	—	—	—	0.0	—
James Geraghty	2021	95.1	—	—	—	—	—	95.1	95.1	—
	2020	95.8	—	—	—	—	—	95.8	95.8	—
Charles Rowland	2021	78.1	—	—	—	—	—	78.1	78.1	—
	2020	78.7	—	—	—	—	—	78.7	78.7	—
Alicia Secor ⁸	2021	72.1	—	—	—	—	—	72.1	72.1	—
	2020	53.0	—	—	—	—	—	53.0	53.0	—
Total	2021	1084.6	3.2	27.2	217.8	—	—	1332.8	1115.0	217.8
	2020	995.2	6.6	0.0	169.9	—	44.8	1216.5	1001.8	214.7

1. Dr Gaspar's salary is £440,000 per annum. 2021 figures are converted at a 12-month average rate for 2021 of GBP 1 = USD 1.3753. 2020 figures are converted at a 12-month average rate of GBP 1 = USD 1.2871.
2. For Executive Directors, included private health insurance, long term disability, critical illness and death in service benefits.

DIRECTORS' REMUNERATION REPORT

continued

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 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. 6,250 PSUs vested for Dr. Gaspar as a result of Libmeldy's approval by the European Commission on the 17 December 2020. These shares vested on 8 January 2021 and are valued using the closing price of \$7.17. None of this value was attributable to share price appreciation from the time of grant.
6. Steven Altschuler joined the Board of Directors on 3 February 2020.
7. Jon Ellis did not stand for re-election at the 2021 AGM and left the Board on 16 June 2021. He received no remuneration for his services to the Board of Directors.
8. 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.

2021 Annual bonus

During a series of meetings between December 2021 and February 2022, the Compensation Committee evaluated achievement of the 2021 corporate objectives and each Executive Director's individual performance.

The Compensation Committee reviewed the corporate goals, below, and based on the results approved a 60% achievement level of the 2021 corporate objectives.

Key achievements against agreed goals were as follows:

Build a foundation for a sustainable commercial business – A key element of Orchard's commercial model is expanding newborn screening programs for patient identification. During 2021, studies were established in US and Europe.

Important technology transfers to a U.S. CDMO were initiated and we advanced certain lentiviral vector manufacturing technology by establishing a stable cell line research bank which could eventually lead to a reduction in costs of product manufacturing. The manufacturing platform strategy was reviewed by our board of directors during 2021 and designed to achieve robust, reproducible and at-scale processes, another foundational element of our future commercial business.

We have also established internal process development labs in London to continue to enhance our viral vector and drug product manufacturing processes.

Advance our portfolio to key milestones – Interim clinical data was presented at medical conferences for OTL-203 (MPS-I) and OTL-201 (MPS-IIIa) that supports further advancement of our clinical programs in those indications. The data was presented for both programs at the WORLD medical meeting in February 2021. In addition, pre-clinical data in two research programs (e.g. FTD and Crohn's disease) that supported further development activities was also presented during 2021.

DIRECTORS' REMUNERATION REPORT

continued

Maintain a performance-driven culture internally and with partners – Importantly, we completed a financing during 2021 with gross proceeds totaling \$150 million, which extended our cash runway and executed a partnership with Pharming Group, which provided additional validation to the HSC gene therapy platform. Strimvelis was also returned to the European market following a favorable risk/benefit determination by regulatory bodies.

Internally, we completed the initial phase of our global diversity & inclusion initiative. This resulted in significant employee participation and engagement to support a strong culture and employee retention.

Additional achievements and considerations

Further to the corporate goals, a number of additional achievements are considered noteworthy for the company's performance during 2021. In terms of our pipeline

- we completed the enrollment in the OTL-201 (MPS-IIIa) proof-of-concept clinical trial;
- initiated new discovery projects and work on vectorizing antibodies, including the presentation of the scientific basis for these programs at a September R&D Day with investors and analysts;
- re-initiated patient recruitment for OTL-102 (X-CGD); and
- received EU Orphan Drug Designation for two new pre-clinical programs in our pipeline.

Our scientific activities were recognised with the publication of OTL-203 (MPS-I) clinical data and OTL-101 (ADA-SCID) clinical data in the New England Journal of Medicine and an integrated manuscript of OTL-200 (MLD) was accepted to Lancet. We also presented OTL-203 (MPS-I) clinical data during the Presidential Symposia at EHA 2021. In total, 46 posters or presentations covering our portfolio were made at medical meetings and congresses in 2021.

From a commercial perspective, launch activities are ongoing for Libmeldy with the first commercial price established in Germany and market access progress in France, UK and Italy.

Financially, we were able to refinance our credit facility allowing for increased borrowing capacity and a lower overall cost of capital.

The Committee also notes the successful changes to the Company's executive team including the additional capabilities of Nicoletta Loggia as Chief Technical Officer and Fulvio Mavilio as Chief Scientific Officer.

The achievements above contribute to the performance score of 60%.

Annual Bonus (audited)

A Corporate Performance Score of 60% corresponds to a bonus outcome equivalent to 60% of target for the CEO. This equates to a 2021 bonus payment equal to 36% of base salary.

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

<u>Executive Director</u>	<u>Base salary (\$)</u>	<u>Target Annual Cash Bonus (% of salary)</u>	<u>Corporate performance</u>	<u>Cash payment % salary</u>	<u>Cash outcome (\$)</u>
Bobby Gaspar	\$605,114	60%	60%	36%	\$ 217,841

DIRECTORS' REMUNERATION REPORT

continued

- 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 1.3753, which was the average rate during 2021. The salary basis for the bonus was Dr Gaspar's salary as CEO, £440,000.

Share Option Incentive Plan**Awards granted to Executive Directors in 2021 (audited)**

During 2021, Dr Gaspar received two equity awards:

- an annual equity award of share options; and
- an award of share options delivered in lieu of 50% of the 2020 annual bonus. The number of shares covered under this award was calculated using the grant date fair value. The delivery of a portion of the 2020 annual bonus was consistent with all members of the company's leadership team and the cash saving made by the Company as a result of this decision was used as additional funding to the available employee bonus pool.

<u>Executive Director</u>	<u>Form of Award</u>	<u>Date of Grant</u>	<u>Shares Covered</u>	<u>Exercise Price</u>	<u>Face Value at Date of Grant (000)</u>	<u>Fair Value at Date of Grant (000)</u>	<u>Expiry Date</u>	<u>Vest Terms</u>	<u>Vested (as at 31.12.21)</u>	<u>Exercised</u>	<u>Value realized at exercise or vesting</u>	<u>Un-vested</u>
Bobby Gaspar	FMV Options	1 Feb 2021	850,000	\$ 5.98	\$5,083.0	\$3,295.0	31/1/2031	(1)	177,083	nil	n/a	672,917
	FMV Options	1 Feb 2021	55,006	\$ 5.98	\$ 328.9	\$ 209.7	31/1/2031	(2)	45,838	nil	n/a	9,168

* 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.

- (1) 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 2021.
- (2) The options vest, and become exercisable, over a one-year period on a monthly basis commencing upon the one-month anniversary of the vesting commencement date of 1 February 2021.

PSUs Vesting in the period

On 16 January 2019, Dr Gaspar had been granted 18,750 Performance Share Units subject to performance conditions.

On 17 December 2020, the Company received full marketing authorization of Libmeldy for the treatment of MLD in all 27 member states of the European Union. As a result of this authorization, and following subsequent ratification by the Board, one-third of the shares under award, 6,250, vested on 8 January 2021 and were released to Dr. Gaspar.

<u>Executive Director</u>	<u>Form of Award</u>	<u>Date of Grant</u>	<u>Shares Covered</u>	<u>Vested due to milestone achievement</u>	<u>Number of shares vesting</u>	<u>Share price on vesting date</u>	<u>Vested Value 8 January 2021</u>
Bobby Gaspar	PSUs	16 January 2019	18,750	1/3rd	6,250	\$ 7.17	\$ 44,812

The remaining 12,500 PSUs were subject to additional performance conditions.

These additional performance conditions related to share price performance and clinical and regulatory milestones in relation to OTL-101 and OTL-103. Of the four performance conditions attributed to the PSU award, each had a 1/3rd weighting, with three of the four required for full vesting. Across these four, only the milestone relating to MLD was achieved. As none of the further conditions were met before 31 December 2021 the remainder of Dr. Gaspar's award – 12,500 shares – lapsed in full.

DIRECTORS' REMUNERATION REPORT

continued

Awards granted to Non-Executive directors between 1 January 2021 and 31 December 2021 (audited)

Non-executive directors received the following option awards during the year, each vesting based on continued service only (in thousands, except for share and per share amounts):

Non-Executive Directors	Form of Award	Date of Grant	Shares Covered	Exercise Price	Face Value at Date of Grant	Fair Value at Date of Grant	Expiry Date	Vest Terms	Vested	Exercised	Value realized at exercise	Unexercised
Steven Altschuler	FMV Options*	16-Jun-21	40,000	\$ 4.79	\$ 191,600	\$ 121,592	15-Jun-31	(1)	nil	nil	nil	40,000
Joanne Beck	FMV Options*	16-Jun-21	40,000	\$ 4.79	\$ 191,600	\$ 121,592	15-Jun-31	(1)	nil	nil	nil	40,000
Marc Dunoyer	FMV Options*	16-Jun-21	40,000	\$ 4.79	\$ 191,600	\$ 121,592	15-Jun-31	(1)	nil	nil	nil	40,000
James Geraghty	FMV Options*	16-Jun-21	40,000	\$ 4.79	\$ 191,600	\$ 121,592	15-Jun-31	(1)	nil	nil	nil	40,000
Charles Rowland	FMV Options*	16-Jun-21	40,000	\$ 4.79	\$ 191,600	\$ 121,592	15-Jun-31	(1)	nil	nil	nil	40,000
Alicia Secor	FMV Options*	16-Jun-21	40,000	\$ 4.79	\$ 191,600	\$ 121,592	15-Jun-31	(1)	nil	nil	nil	40,000
John Curmutte	FMV Options*	16-Jun-21	40,000	\$ 4.79	\$ 191,600	\$ 121,592	15-Jun-31	(1)	nil	nil	nil	40,000

* 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.

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

Jon Ellis received no option grants 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.

Statement of Directors' shareholding and share interests (audited)

The share interests of each Director as at 31 December 2021 (together with interests held by his or her connected persons) are set out in the table below.

DIRECTORS' REMUNERATION REPORT

continued

For 2021, Orchard Therapeutics did not operate any formal shareholding guidelines for Directors' shareholding requirements. 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 exceed this guideline within 5 years of appointment or the implementation of this requirement.

	Beneficially owned shares as at 31/12/21	Shares		Vested but unexercised	Share Options	
		Unvested without performance conditions	Unvested with performance conditions		Unvested without performance conditions	Unvested with performance conditions
Executive Directors						
Bobby Gaspar	355,158	—	—	1,194,767	1,189,541	—
Non-Executive Directors						
Joanne Beck	9,294	—	—	150,030	40,000	—
John Curnutte	—	—	—	73,833	51,167	—
Marc Dunoyer	37,179	—	—	150,030	40,000	—
Jon Ellis ¹	—	—	—	—	—	—
James Geraghty	44,391	—	—	390,120	40,000	—
Charles Rowland	12,294	—	—	150,030	40,000	—
Alicia Secor	—	—	—	120,000	40,000	—
Steven Altschuler	—	—	—	65,555	59,445	—

1. Jon Ellis left the Board on 16 June 2021.

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 2021. 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.



DIRECTORS' REMUNERATION REPORT

continued

This graph shows the value, by 31 December 2021, 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:

<u>Chief Executive Officer</u>	<u>2018</u>	<u>2019</u>	<u>2020</u>	<u>2021</u>
Total remuneration (\$000) ¹	\$ 555	\$1,016	\$ 764	\$ 853
Actual bonus (% of the maximum)	N/A	44%*	37.5%*	22.5%*
SOIP vesting (% of the maximum) **	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.

* 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.

** 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 recognised 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.

	<u>2020</u>	<u>2021</u>	<u>% change</u>
Total operating expenses	\$181,866	\$157,850	-13.2%
Total employee pay expenditure (\$'000) ¹	\$ 87,091	\$ 73,704	-15.4%

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 \$22,536 and \$27,962k in non-cash share-based compensation expense for 2021 and 2020 respectively.

DIRECTORS' REMUNERATION REPORT

continued

Average percentage change in remuneration of Directors and Employees

As required by the 2019 regulations, 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 2021.

	Change in pay between 31 December 2020 and 31 December 2021			Change in pay between 31 December 2019 and 31 December 2020		
	Base salary/ fee change	Bonus change	Benefit change	Base salary/ fee change	Bonus change	Benefit change
Executive Directors						
Bobby Gaspar ¹	12%	28% ²	361% ³	57.7%	-54%	0%
Non-Executive Directors⁴						
Joanne Beck	2%	n/a	n/a	41.4%	n/a	n/a
John Curnutte ⁵	5%	n/a	n/a	278.0%	n/a	n/a
Marc Dunoyer	-1%	n/a	n/a	26.5%	n/a	n/a
Jon Ellis ⁶	n/a	n/a	n/a	n/a	n/a	n/a
James Geraghty	-1%	n/a	n/a	15.0%	n/a	n/a
Charles Rowland	-1%	n/a	n/a	31.1%	n/a	n/a
Alicia Secor ⁷	36%	n/a	n/a	23.0%	n/a	n/a
Steven Altschuler ⁸	10%	n/a	n/a	n/a	n/a	n/a
Average employee⁹	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 did not receive a salary increase in 2021 for his services as CEO. The increases represented here corresponds to a salary increase upon promotion to CEO during 2020. This figure is also impacted by exchange rate fluctuations
- 2 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.
- 3 Dr. Gaspar's increase relates to a cash allowance in lieu of pension contribution effective 1 April 2021 which he had not received prior to that date.
- 4 None of the Non-Executive Directors are eligible for an annual bonus and none claimed any benefits during the year.
- 5 John Curnutte joined the Board in 2019 and the remuneration received in 2019 was not a full annual amount.
- 6 Jon Ellis did not receive any remuneration for his services to the Board and left the Board on 16 June 2021.
- 7 Alicia Secor receive 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 Steven Altschuler joined the Board during 2020 and therefore no comparative information is shown.
- 9 As the parent company Orchard Therapeutics Plc has no direct employees. All employees are employed by the relevant local entities.

DIRECTORS' REMUNERATION REPORT

continued

Statement of implementation of remuneration policy in 2022

Annual base salary

On March 1 2022 Dr. Gaspar's salary was increased by 5%. This increase is in line with salary increases awarded to all employees at the Company who are eligible for a 2022 salary review.

	<u>Base salary 2021</u>	<u>Base salary 2022</u>	<u>% change</u>
Bobby Gaspar, Chief Executive Officer,	£ 440,000	£ 462,000	5%

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 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 2022 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 160% 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. Such an award would only be made to Executive Directors if equivalent incentives are provided to a significant proportion of, if not all, employees of the Company. In such circumstances, full details including performance conditions would be provided in the Directors' Remuneration Report for the relevant financial year.

Share Option Incentive Plan (SOIP)

Annual award of share options

In 2022, as part of the annual compensation package, the CEO will be granted no more than 850,000 share options in the Company at the same time as all eligible employees. At the date of this report, the Committee notes that these options have not been granted.

The Committee recognizes that the Company's share price has declined significantly and for that reason – half of the award – on a grant date fair value basis – will be granted as premium-priced share options. These premium priced options will have an exercise price set at 25% higher than the closing price of the Company's ADSs on the

DIRECTORS' REMUNERATION REPORT

continued

Nasdaq Global Select Market on the date of grant. Consequently, approximately half of the CEO's 2022 share option award will have no intrinsic value until the share price increases by at least 25%. The Committee believes that this further aligns the CEO with the shareholders of the Company considering recent share price performance and implementing an additional performance hurdle reinforces our pay for performance principle.

The overall maximum number of options that will be awarded is equal to the number of share options granted as an annual award made in 2021.

Executive Director	Form of Award	Anticipated Date of Grant	Maximum Shares Covered	Exercise Price	Vest Terms
Bobby Gaspar	Combination of FMV options and premium-priced share options	1 June 2022	850,000	On a fair value basis 50% of the award will be granted as market value options. The remaining 50% to be granted with an exercise price at a 25% premium to the closing price on the date of grant.	(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.

DIRECTORS' REMUNERATION REPORT

continued

Non-Executive Directors' fees for 2022

Non-Executive Directors are eligible to receive the following cash compensation annually. The cash fees remain unchanged for 2022.

	<u>2022 Fee in \$'000</u>	<u>2021 Fee in \$'000</u>
Base fee:		
Board Chair	\$ 85	\$ 85
Board Member	\$ 45	\$ 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	\$ 10	\$ 10
Science and Technology Committee Member	\$ 7.5 ¹	\$ 5

(1) The increase in the Science and Technology Committee fee was effective 1 April 2021.

The Company provides an initial, one-time equity award of 92,000 stock options 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 46,000 stock options to each Non-Executive Director at the 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.

From 2022, and subject to shareholder approval, our Directors' Remuneration Policy will allow Non-Executive Directors the provision to 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 (2020: \$2,500) 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 behalf of the Board
Charles Rowland, Jr.
Chair of the Compensation Committee

25 April 2022

ORCHARD THERAPEUTICS PLC
Form of Proxy for the 2022 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 Chairman 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 Goodwin Procter LLP, 100 Northern Avenue, Boston, Massachusetts, 02210 on Tuesday, June 7, 2022 at 1 pm London time (8 am Eastern time) and at any adjournment 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 as a director, John T. Curnutte, who retires by rotation in accordance with the Company’s Articles of Association	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. To re-elect as a director, Bobby Gaspar, who retires by rotation in accordance with the Company’s Articles of Association	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. To re-elect as a director, Alicia Secor, who retires by rotation in accordance with the Company’s Articles of Association	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
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	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
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, 2022	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. To authorize the Audit Committee to determine the Company’s auditors’ remuneration for the fiscal year ending December 31, 2022	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. To receive the U.K. statutory annual accounts and reports for the fiscal year ended December 31, 2021 and to note that the Company’s directors do not recommend the payment of any dividend for the year ended December 31, 2021	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. To approve the compensation of the Company’s named executive officers for the year ended December 31, 2021 on an advisory basis	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. To receive and approve the Company’s U.K. statutory directors’ remuneration report for the year ended December 31, 2021 on an advisory basis	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. To approve the Company’s U.K. directors’ remuneration policy, which, if approved, will take effect upon the conclusion of the Annual General Meeting	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Signature _____ Dated _____ 2022

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Notes:

1. You may if you wish strike out the words “Chairman 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 Chairman 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 Chairman is appointed as a proxy, the member appointing him or her is responsible for ensuring that he or she attends the Meeting and are 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 Chairman 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/her rights to attend, speak and to vote at the Meeting instead of him/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.
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 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 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 which 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 Chairman as one of your multiple proxies, simply write “the Chairman 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 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 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 6:30 pm London time (1:30 pm Eastern Time) on June 3, 2022 or, in the event that the meeting is adjourned, in such register not later than 48 hours before the time of the adjourned 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, this proxy will be voted in accordance with the Board of Directors’ recommendations.