



ORCHARD THERAPEUTICS PLC
(the "Company")

108 Cannon Street
London EC4N 6EU
United Kingdom

(Incorporated and registered in England and Wales under the Companies Act 2006 with registered number 11494381)

THIS DOCUMENT IS IMPORTANT AND REQUIRES YOUR IMMEDIATE ATTENTION. If you are in any doubt as to the action to be taken, please seek your own financial advice from your stockbroker, solicitor, accountant or other appropriately authorised independent financial adviser.

If you have sold or transferred all of your holding of ordinary shares in the Company, you should hand this document and all accompanying documents to the purchaser or transferee of those shares, or to the stockbroker, bank or other agent through whom the sale or transfer was effected for transmission to the purchaser or transferee.



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

April 28, 2021

Dear Shareholder:

2021 Annual General Meeting of Orchard Therapeutics plc (the "AGM")

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 22, 2021 (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**"). However, this letter, the Notice and associated materials will also be available to holders of American Depositary Shares ("**ADS**") and contain information relevant to holders of ADSs.

Our AGM will take place at **2:00 p.m. London time (9:00 a.m. Eastern Time) on Wednesday, June 16, 2021 at Goodwin Procter (UK) LLP, 100 Cheapside, London EC2V 6DY**. The Notice is set out in this document, and it contains the resolutions to be proposed at the AGM (the "**Resolutions**").

Impact of COVID-19

In light of the Covid-19 pandemic and the UK Government's current guidance regarding social distancing and the prohibition of public gatherings, the arrangements and format of the AGM have been altered this year in order to protect the health and wellbeing of shareholders and other attendees.

Accordingly, the Company will make arrangements such that the legal requirements to hold the AGM can be satisfied through the attendance of the minimum number of people required to form a quorum. It is with regret that shareholders are therefore requested not to attend the Meeting.

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 ⅓ 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.

This means that, as things currently stand, ordinary shareholders are respectfully asked not to attend the AGM in person, and all shareholders should appoint a proxy to ensure that the AGM is quorate and to vote on the proposed Resolutions. If the UK Government's current guidance regarding social distancing and the prohibition of public gatherings are continuing at the time of the AGM, any shareholder seeking to attend the AGM in person will be refused entry. We strongly encourage you to vote by proxy as described below so that your vote can be counted.

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 AGM. 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.

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 allowed to attend the AGM.**

You are advised to complete and return the form of proxy in accordance with the instructions printed on it and so as to arrive at the Company’s registrar, Equiniti Limited, Aspect House, Spencer Road, Lancing, West Sussex, BN99 6DA, England as soon as possible but in any event by no later than **2:00 p.m. London time (9:00 a.m. Eastern Time) on Monday, June 14, 2021.**

In order to attend and vote at the AGM as an ordinary shareholder, you must continue to be registered as a holder of ordinary shares in the Company’s register of members as of 6:30 p.m. London time (1:30 p.m. Eastern Time) on Monday, June 14, 2021.

Therefore, if you sell or transfer your ordinary shares in the Company on or prior to June 14, 2021, 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 John Ilett, 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 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., **by 5:00 p.m. Eastern Time on Wednesday, April 28, 2021 (the record date for ADS holders).**

If you hold ADSs through a bank, broker or nominee on April 28, 2021, 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 10:00 a.m. Eastern Time on Thursday, June 10, 2021.**

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 John Ilett, Company Secretary, by telephone at +44 (0) 203 808 8286.

Recommendation

You will find an explanatory note in relation to each of the Resolutions set out below and in the attached proxy statement. Your Directors consider that each Resolution is in the best interests of the Company and its shareholders as a whole and is likely to promote the success of the Company. Accordingly, your Directors unanimously recommend that you vote in favor of the Resolutions as each of the Directors with personal holdings of equity interests in the Company intends to do in respect of their own beneficial holdings.

Thank you for your ongoing support of Orchard Therapeutics.

Yours sincerely,

/s/ JAMES GERAGHTY

James Geraghty

Chairman, Orchard Therapeutics plc

EXPLANATORY NOTES TO THE BUSINESS OF THE AGM

Resolutions 1 to 9 (inclusive) will be proposed as ordinary resolutions and 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. Resolution 10 will be proposed as a special resolution. Special resolutions require the affirmative vote of not less than 75% of the votes cast by shareholders present (in person or by proxy) at the meeting and entitled to vote. On a poll, a special resolution is passed if it is approved by holders representing not less than 75% of the total voting rights of shareholders present (in person or by proxy) who (being entitled to vote) vote on the resolution.

ORDINARY BUSINESS

Resolutions 1 and 2: Re-election of directors

Our Board of Directors currently consists of nine 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 annual general meeting to be held in 2022;
- 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, Jon Ellis and Charles A. Rowland Jr., and their terms will expire at the forthcoming AGM.

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 Joanne T. Beck and Charles A. Rowland Jr for election as the Class III directors at the AGM. 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. Jon Ellis will not stand for re-election.

In connection with Resolutions 1 and 2, 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* in the Company's 2021 Proxy Statement.

Resolution 1

Charles A. Rowland Jr

Non-Executive Director

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 Viking Therapeutics, Inc. Since January 2015, he has served as a member of the board of directors and audit committee 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.

Resolution 2

Joanne T. Beck

Non-Executive Director

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.

The Board of Directors recommend a vote for the approval of Resolutions 1 and 2.

Resolution 3: Re-appointment of PricewaterhouseCoopers LLP as the Company's U.K. statutory auditors

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. Resolution 3 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 recommend a vote for the approval of Resolution 3.

Resolution 4: Ratification of the appointment of PricewaterhouseCoopers LLP as the Company's independent registered public accounting firm

Resolution 4 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, 2021.

Background to Resolution 4

The Audit Committee is solely responsible for selecting the Company's independent registered public accounting firm for the fiscal year ending December 31, 2021. Our Audit Committee has selected PwC USA as our independent registered public accounting firm for the fiscal year ending December 31, 2021, and has further directed that we submit the selection of PwC USA for ratification by our shareholders at the forthcoming AGM. 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 AGM, 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 AGM 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, 2020 and December 31, 2019, 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, December 31,	
	2020	2019
	(\$)	(\$)
Audit Fees ⁽¹⁾	1,421	1,680
Audit related fees	—	—
Tax fees	—	—
All Other Fees ⁽²⁾	3	3
Total	<u>1,424</u>	<u>1,683</u>

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

(2) "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.

Change in Independent Registered Public Accounting Firm

On June 26, 2019, the Audit Committee dismissed PwC UK as the Company's independent registered public accounting firm and separately approved the engagement of PwC USA as the Company's new independent registered public accounting firm effective immediately. This decision was made by the Audit Committee in connection with the Company's centralization of its accounting and finance functions to the Company's Boston, Massachusetts office.

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

- no “disagreements” (as that term is defined in Item 304(a)(1)(iv) of Regulation S-K and the instructions to Item 304) between the Company and PwC UK on any matters of accounting principles or practices, financial statement disclosure, or auditing scope or procedures, which disagreements, if not resolved to PwC UK’s satisfaction would have caused PwC UK to make reference to the subject matter of the disagreement(s) in connection with its report, and
- no “reportable events” (as that term is defined in Item 304(a)(1)(v) of Regulation S-K), except for: (i) the material weakness in the Company’s internal control over financial reporting related to the recognition and accrual of research and development related expenses and reimbursements, and (ii) the restatement of the Company’s interim condensed consolidated financial statements as of June 30, 2018 and the six month period then ended for an error in accounting for contingent assets and the related material weakness in internal control over financial reporting which has since been remediated, each as disclosed in the Company’s prior filings with the U.S. Securities and Exchange Commission (“SEC”).

During the Company’s fiscal years ended December 31, 2018 and 2017 and the subsequent interim period through June 26, 2019, neither the Company nor anyone on the Company’s behalf consulted with PwC USA regarding any of the matters or events set forth in Item 304(a)(2)(i) and (ii) of Regulation S-K.

We have furnished the foregoing disclosure to PwC UK and PwC USA.

The Board of Directors recommend a vote for the approval of Resolution 4.

Resolution 5: Authorisation for the Audit Committee to determine the auditors’ remuneration

Resolution 5 authorises the Audit Committee to determine our auditors’ remuneration for the fiscal year ending December 31, 2021. Fees for PwC USA, our independent registered public accounting firm, and PwC UK, our statutory auditor, in respect of the years ended December 31, 2020 and December 31, 2019, are set forth in the notes to Resolution 4 above.

The Board of Directors recommend a vote for the approval of Resolution 5.

Resolution 6: Receipt of the reports and accounts

At the AGM, our Board of Directors will present our U.K. statutory annual accounts and reports for the period January 1, 2020 through December 31, 2020, 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 recommend a vote for the approval of Resolution 6.

Resolution 7: Advisory (non-binding 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 2020 Summary Compensation Table and the related compensation tables, notes, and narrative in the Company’s 2021 Proxy Statement.

Resolution 7, known as a “Say-on-Pay” resolution, gives our shareholders the opportunity to express their views on our named executive officers’ compensation as a whole. 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 the Company’s 2021 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 the Company’s 2021 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 2020 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 Resolution 7 is advisory, and therefore not binding on the Company, the Board or our Compensation Committee. However, our Board of Directors and Compensation Committee values 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 forthcoming AGM to approve the following resolution pursuant to this Resolution 7:

“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 recommend a vote for the approval of Resolution 7.

Resolution 8: Advisory vote on U.K. statutory directors’ annual report on remuneration

Our U.K. statutory directors’ remuneration report is set forth as Annex A to the Company’s 2021 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 upcoming AGM, 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 AGM, 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 recommend a vote for the approval of Resolution 8.

SPECIAL BUSINESS

Background to Resolutions 9 and 10

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

In practice, the operation of such pre-emption rights is onerous and can result in significant delay and additional expense to the cost of an equity fundraising. It is therefore customary for the Board of Directors to seek authority from our shareholders to dis-apply statutory pre-emption rights for cash issues of up to a limit approved by the Company’s shareholders. With the Company solely listed on Nasdaq, and the Company’s peers, key shareholders and primary target market being the United States, the Board of Directors is mindful of the fact that equivalent United States incorporated companies are not required to offer shares to existing shareholders on a pre-emptive basis in the event they are pursuing an equity fundraising. The Board of Directors considers that this may place the Company at a competitive disadvantage.

Our Board of Directors anticipate that there may be occasions when they need flexibility to finance business opportunities and growth, or otherwise act in the best interests of the Company, by the issuance of shares

or grant of rights over shares without a pre-emptive offer to existing shareholders. To ensure our continued ability to respond to market conditions and address business needs, our Board of Directors considers it appropriate that they be authorized to allot shares up to an aggregate nominal amount of £13,023,851.50 and within this amount be empowered to allot shares or grant rights over shares up to an aggregate nominal amount of £13,023,851.50 on a non-pre-emptive basis. This authority to allot shares and power to allot shares on a non-pre-emptive basis will replace all of the existing authorities and powers granted by our shareholders.

Resolutions 9 and 10 (the “Share Authority Resolutions”) ask our shareholders to renew the same share issuance authorities to those which were adopted at last year’s annual general meeting and, in our Board of Directors’ view, are appropriate again this year in order to avoid us potentially being at a competitive disadvantage as compared to our peer companies, many of whom are incorporated in the United States. In particular, the requirement to first offer shares that we propose to issue for cash to all of our existing shareholders in time-consuming pro-rata rights offerings would considerably reduce the speed at which we could complete capital-raising activities undertaken in furtherance of our growth strategy and will potentially make it difficult for us to complete such transactions. Many of our strategic competitors are incorporated in the United States where they are not subject to restrictions on their ability to issue shares.

We are aware that certain proxy advisory firms have in recent proxy seasons applied their United Kingdom voting guidelines in formulating their voting recommendations on share issuance authorities proposals for English-incorporated companies listed in the United States. These firms have applied or otherwise taken into account United Kingdom market practice for companies whose share capital is listed on the London Stock Exchange in formulating their voting recommendations on share issuance authorities proposals for companies incorporated in England, even if their shares are not (and never have been) listed on the London Stock Exchange or any United Kingdom exchange. Market practice for English companies listed on the London Stock Exchange is that resolutions to dis-apply pre-emption rights are typically limited to 10% of issued share capital, irrespective of the cash flows and funding needs of the business. In practice, this means that Resolution 10 may attract a negative voting recommendation from certain proxy advisory firms. For the reasons given above, we respectfully disagree with the historical position taken by such firms.

The Share Authority Resolutions are fully compliant with English company law, consistent with United States capital markets practice and governance standards, and, if approved, will keep us on an equal footing with our peer companies who are incorporated in the United States. Further, approval of the Share Authority Resolutions by shareholders will not exempt the Company from any Nasdaq corporate governance or other requirements, including those limiting the issuance of shares. For these reasons we therefore consider that the Share Authority Resolutions are appropriate to the needs of the Company and in the interests of shareholders.

We are asking you to approve the Share Authority Resolutions to allow us to continue to execute on our business and growth strategy in a timely and competitive manner.

The full details of the Share Authority Resolutions are set forth below.

The Board of Directors strongly recommend a vote for the approval of the Share Authority Resolutions.

Resolution 9: Directors’ authority to issue shares

The Directors currently have an existing authority to allot shares in the Company and to grant rights to subscribe for or convert any securities into shares in the Company. We therefore propose to renew the existing authority at the forthcoming AGM by proposing that the Board of Directors are granted authority to allot new shares or to grant rights to subscribe for or to convert any security into shares in the Company up to a maximum aggregate nominal amount of £13,023,851.50. This is the same level of limitation as proposed and approved at the Company’s annual general meeting last year and if approved at the forthcoming AGM it will replace the existing authority.

Resolution 9 will allow the Directors to allot shares up to a maximum aggregate nominal amount of £13,023,851.50.

If approved by the shareholders, the authority will expire on June 15, 2026, being the date five years after the date on which this Resolution is passed (in accordance with the CA 2006).

The Board of Directors have no present intention of exercising this authority, except in relation to the Company's share incentive schemes, but believe it is in the interests of shareholders for the Board of Directors to have this flexibility to allot shares otherwise than just in relation to the Company's share incentive schemes should circumstances and their intentions change.

Resolution 9 is an ordinary resolution and must receive the affirmative vote of a majority of the votes cast in person or by proxy at the forthcoming AGM in order to be approved.

The Board of Directors recommend a vote for the approval of Resolution 9.

Resolution 10: Renew Directors' authority to issue shares for cash without first offering shares to existing shareholders

As a UK incorporated company, the Company's ordinary shareholders are entitled, under Section 561 of the CA 2006 to pre-emption rights, whereby, in the event that the Company wishes to allot new equity securities for cash, those securities must first be offered to existing shareholders in proportion to the number of ordinary shares they each hold before they can be offered to new shareholders.

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

The Board has therefore decided to seek the disapplication of pre-emption rights over equity securities up to a maximum aggregate nominal amount of £13,023,851.50 at the forthcoming AGM. The Board considers that, at this stage of development of the Company, the ability to raise new equity funds at relatively short notice and at low cost is vital to the continuing financial health of the business. We believe that it is in the best interests of the Company and our shareholders for the Board to seek to retain the ability to readily raise new equity funds at the appropriate time.

Resolution 10 authorises the Directors to allot equity securities in the capital of the Company pursuant to the authority conferred by Resolution 9 for cash without complying with the pre-emption rights in the CA 2006 in certain circumstances. Apart from offers or invitations in proportion to the respective number of shares held, the authority will be limited to the allotment of equity securities for cash up to a maximum aggregate nominal value of £13,023,851.50.

If approved by shareholders, the authority will expire on June 15, 2026, being the date five years after the date on which this Resolution is passed (in accordance with the CA 2006).

The Board of Directors have no present intention of exercising this power, except in relation to the Company's share incentive schemes, but believe it is in the interests of shareholders for the Directors to have this flexibility to allot shares for cash otherwise than just in relation to the Company's share incentive schemes should circumstances and their intentions change.

Resolution 10 is a special resolution and must receive the affirmative vote of at least 75% of the votes cast in person or by proxy at the forthcoming AGM in order to be approved.

The Board of Directors recommend a vote for the approval of Resolution 10.

SHAREHOLDER NOTES

VOTING – ADS Holders

You are entitled to exercise your vote as a holder of an interest in the capital of the Company represented by ADSs if you or your brokerage firm, bank or nominee is registered as a holder of ADSs in the ADS register maintained by Citibank, N.A. **as of 5:00 p.m. Eastern Time on Wednesday, April 28, 2021 (the record date for ADS holders).**

If you hold ADSs through a brokerage firm, bank or nominee on April 28, 2021, 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 10:00 a.m. Eastern Time on Thursday, June 10, 2021.**

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 John Ilett, Company Secretary, by telephone at +44 (0) 203 808 8286.

VOTING – Ordinary Shareholders

When is your voting entitlement fixed?

In order for your vote to be cast at the AGM you must be a registered holder of ordinary shares as recorded in the Company's register of members at 6:30 p.m. (UK time) on Monday, June 14, 2021. Your voting entitlement will depend on the number of shares you hold at that time.

The holders of ordinary shares are entitled to one vote per share on all matters that are subject to shareholder vote. Holders of non-voting ordinary shares have no right to receive notice of, or to attend or vote, at the forthcoming AGM.

If you can't attend but want to vote – what can you do?

If you are a holder of ordinary shares in the Company, please vote on the Resolutions by appointing a proxy. You can appoint a proxy and submit voting instructions either (i) via CREST (see below) or (ii) by completing and returning the paper proxy card (enclosed). Please read the instructions carefully to ensure you have completed and signed the card correctly. Any alterations must be initialed. **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 allowed to attend the AGM.**

By when do you have to submit your vote?

You are advised to complete and return the form of proxy in accordance with the instructions printed on it and so as to 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 **2:00 p.m. London time (9:00 a.m. Eastern Time) on Monday, June 14, 2021.**

If you already voted but have changed your mind – can you change your vote?

You can submit a new instruction at any time before the time and date above. If you wish to amend a paper instruction, you must do so in writing and sign your new instruction. The voting instruction received last will be the one that is followed.

If you hold shares on behalf of several others – can you vote part of the holding separately?

You can appoint more than one proxy using a paper form provided it is in relation to different shares. Corporate shareholders may either appoint one or more proxies using the paper form or via CREST, or alternatively appoint one or more corporate representatives in relation to different shares.

You are a CREST member – can you use the CREST system to vote?

CREST members who wish to appoint a proxy or proxies through the CREST electronic proxy appointment service may do so by using the procedures described in the CREST Manual (available via www.euroclear.com).

CREST ID: RA19

CREST Personal Members or other CREST Sponsored Members, and those CREST members who have appointed a voting service provider(s), should refer to their CREST sponsor or voting service provider(s), who will be able to take the appropriate action on their behalf.

You have a power of attorney from a shareholder – how can you vote?

You can vote using the paper proxy card only. You must ensure that the valid power of attorney and the proxy card have been deposited with the Registrar by 2:00 p.m. (UK time) on Monday, June 14, 2021.

OTHER INFORMATION

A copy of this Notice of AGM and other information required by section 311A of the UK Companies Act 2006 (the "Act") can be found at <https://ir.orchard-tx.com>, including the Company's 2021 Proxy Statement, the Annual Report on Form 10-K, the 2020 U.K. Annual Report and the form of proxy (all available in the Investors & Media section of the website).

Information rights

Under the Act, there are a number of rights that may now be available to indirect investors of the Company, including the right to be nominated by the registered holder to receive general shareholder communications direct from the Company.

The rights of indirect investors who have been nominated to receive communications from the Company in accordance with Section 146 of the Act ("nominated persons") do not include the right to appoint a proxy. However, nominated persons may have a right under an agreement with the registered shareholder who holds the shares on their behalf to be appointed (or to have someone else appointed) as a proxy. Alternatively, if nominated persons do not have such a right or do not wish to exercise it, they may have a right under such an agreement to give instructions to the person holding the shares as to the exercise of voting rights.

If you have been so nominated to receive general shareholder communications direct from the Company, it is important to remember that your main contact in terms of your investment remains with the registered shareholder or custodian or broker, or whoever administers the investment on your behalf. You should also deal with them in relation to any rights that you may have under agreements with them to be appointed as a proxy and to attend, participate in, and vote at the AGM, as described above.

Any changes or queries relating to your personal details and holding (including any administration thereof) must continue to be directed to your existing contact at your investment manager or custodian. The Company cannot guarantee dealing with matters that are directed to us in error. The only exception to this is where the Company is exercising one of its powers under the Act and writes to you directly for a response.

Statements related to the audit

Members satisfying the thresholds in section 527 of the Act can require the Company to publish a statement on its website setting out any matter relating to:

- a. 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 meeting; and
- b. any circumstances connected with an auditor of the Company ceasing to hold office since the last annual general meeting, that the members propose to raise at the meeting.

The Company cannot require the members requesting the publication to pay its expenses in connection with the publication. The company must forward a copy of the statement to the auditors when it publishes the statement on the website. The business which may be dealt with at the meeting includes any such statement that the company has been required to publish on its website.

Shareholder requisition rights

Members satisfying the thresholds in sections 338 and 338A of the Act can require the Company:

- a. to give, to members of the Company entitled to receive notice of the annual general meeting, notice of a resolution which may properly be moved, and which those members intend to move, at the meeting; and
- b. to include in the business to be dealt with at the meeting any matter (other than a proposed resolution) which may properly be included in the business at the meeting, provided in each case that the requirements of those sections are met and provided that the request is received by the company not later than six clear weeks before the meeting or if later the time at which notice is given of the meeting.

Total voting rights and share capital

As of April 22, 2021 (being the last practicable date before the publication of this document) there were 120,553,939 ordinary shares issued and outstanding and entitled to vote.

ORCHARD THERAPEUTICS PLC
(the “Company”)

(Incorporated and registered in England and Wales under the Companies Act 2006 with registered number 11494381)

NOTICE OF 2021 ANNUAL GENERAL MEETING OF SHAREHOLDERS
TO BE HELD ON WEDNESDAY, JUNE 16, 2021

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 Wednesday, June 16, 2021, at 2:00 p.m. London time (9:00 a.m. Eastern Time), at Goodwin Procter (UK) LLP, 100 Cheapside, London EC2V 6DY, for transaction of the following business:

Ordinary resolutions

1. To re-elect as a director Charles A. Rowland, Jr., who retires by rotation in accordance with the Company’s Articles of Association.
2. To re-elect as a director Joanne T. Beck, who retires by rotation in accordance with the Company’s Articles of Association.
3. 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.
4. 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, 2021.
5. To authorize the Audit Committee to determine the Company’s auditors’ remuneration for the fiscal year ending December 31, 2021.
6. To receive the U.K. statutory annual accounts and reports for the fiscal year ended December 31, 2020 and to note that the Company’s directors do not recommend the payment of any dividend for the year ended December 31, 2020.
7. To approve, on a non-binding, advisory basis, the compensation of the Company’s named executive officers for the year ended December 31, 2020.
8. To receive and approve on an advisory basis the Company’s U.K. statutory directors’ remuneration report for the year ended December 31, 2020, which is set forth as Annex A to the attached proxy statement.
9. To authorize the Board of Directors, generally and unconditionally for the purpose of s551 of the U.K. Companies Act 2006 to allot shares in the Company or to grant rights to subscribe for or to convert any security into shares in the Company (“Rights”) up to a maximum aggregate nominal amount of £13,023,851.50. This authority shall expire (unless previously renewed, varied or revoked) on June 15, 2026, but the Company may at any time before the expiration of this authority make an offer or agreement which would or might require shares to be allotted, or Rights to be granted, pursuant to this authority after its expiration, and the Board of Directors may allot shares or grant Rights in pursuance of that offer or agreement as if the authority conferred by this resolution had not expired.

The authority referred to in this resolution is in substitution for the authority conferred on the Board of Directors under s551 of the U.K. Companies Act 2006 at the Company’s annual general meeting held on June 17, 2020, but the Board of Directors may allot shares or grant Rights pursuant to an offer made or agreement entered into by the Company before the expiry of the authority pursuant to which that offer was made or agreement entered into.

Special resolution

10. Subject to the passing of Resolution 9, to empower the Board of Directors generally pursuant to s570(1) of the U.K. Companies Act 2006 to allot equity securities (as defined in s560 of the U.K. Companies Act 2006) for cash pursuant to the general authority conferred on them by Resolution 9 as if s561(1) of the U.K. Companies Act 2006 did not apply to that allotment. This power:
- (a) shall be limited to the allotment of equity securities up to a maximum aggregate nominal amount of £13,023,851.50;
 - (b) expires (unless previously renewed, varied or revoked) on June 15, 2026, but the Company may at any time before the expiration of this authority make an offer or agreement which would or might require equity securities to be allotted after that expiry and the Board of Directors may allot equity securities pursuant to any of those offers or agreements as if this power had not expired; and
 - (c) applies in relation to a sale of shares which is an allotment of equity securities by virtue of s560(3) of the U.K. Companies Act 2006 as if in the first paragraph of this resolution the words “pursuant to the general authority conferred on them by Resolution 9” were omitted.

For the purposes of this resolution, references to the allotment of equity securities shall be interpreted in accordance with s560 of the U.K. Companies Act 2006.

Proposals 1 through 9 will be proposed as ordinary resolutions and 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. Proposal 10 will be proposed as a special resolution. Special resolutions require the affirmative vote of not less than 75% of the votes cast by shareholders present (in person or by proxy) at the meeting and entitled to vote. On a poll, a special resolution is passed if it is approved by holders representing not less than 75% of the total voting rights of shareholders present (in person or by proxy) who (being entitled to vote) vote on the resolution.

The result of the shareholder votes on the ordinary resolutions in proposals 3, 4, 6, 7, and 8 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, 2021, receipt of our U.K. statutory annual accounts and reports for the year ended December 31, 2020, approval of the compensation of our named executive officers for the year ended December 31, 2020, and approval of our U.K. statutory directors' annual report on remuneration for the year ended December 31, 2020 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 3, 4, 6, 7, and 8.

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/ JOHN ILETT

John Ilett

Company Secretary

April 28, 2021

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 p.m. London time (1:30 p.m. Eastern Time) on June 14, 2021 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/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 2:00 p.m. London time (9:00 a.m. Eastern Time) on June 14, 2021. Completion and return of the appropriate proxy form does not prevent a member from attending and voting in person if he/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 which 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.
- (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 2:00 p.m. London time (9:00 a.m. Eastern Time) on June 14, 2021. 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) As of April 22, 2021 (being the last practicable date before circulation of this Notice), the Company’s issued ordinary share capital consisted of 120,553,939 ordinary shares, carrying one vote each, and 3,215,424 non-voting ordinary shares. Therefore, the total voting rights in the Company as of that date are 120,553,939.
- (g) Under s527 of the U.K. Companies Act 2006, members meeting the threshold requirement set out in that section have the right to require the Company to publish on a website a statement setting out any matter relating to: (i) the audit of the Company’s accounts (including the auditor’s report and the conduct of the audit) that are to be laid before the AGM; or (ii) any circumstance connected with an auditor of the Company ceasing to hold office since the previous meeting at which annual accounts and reports were laid in accordance with s437 of the U.K. Companies Act 2006. The Company may not require the shareholders requesting any such website publication to pay its expenses in complying with ss527 or 528 of the U.K. Companies Act 2006. Where the Company is required to place a statement on a website under s527 of the U.K. Companies Act 2006, it must forward the statement to the Company’s auditor not later than the time when it makes the statement available on the website. The business which may be dealt with at the AGM includes any statement that the Company has been required, under s527 of the U.K. Companies Act 2006, to publish on a website.
- (h) 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.

- (i) 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 week day (public holidays excepted) and at the place of the AGM for one hour before the meeting and at the meeting itself.
- (j) 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.
- (k) **As a result of the Covid-19 pandemic and the UK Government's current guidance regarding social distancing and restrictions on public gatherings, other than the presence of the minimum number of people required to form a quorum to be arranged by the Company at the Meeting and notwithstanding the foregoing Notes, members may not be allowed to attend the Meeting in person. Members' attention is drawn to the letter from the Chairman of the Company dated April 28, 2021.**

