

**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

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
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-

PROTHENA CORPORATION PUBLIC LIMITED COMPANY
(Name of registrant as specified in its charter)

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

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

- ☒ No fee required.
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 - ☐ 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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Notice of Annual General Meeting of Shareholders 2022



To the Shareholders of Prothena Corporation plc:

NOTICE IS HEREBY GIVEN that the Annual General Meeting of Shareholders (the "Annual Meeting") of Prothena Corporation plc, an Irish public limited company (the "Company"), will be held on Tuesday, May 17, 2022, at 4:00 p.m. local time, at The Merrion Hotel, Upper Merrion Street, Dublin 2, D02 KF79, Ireland for the following purposes:

1. To re-elect, by separate resolutions, Paula K. Cobb, Lars G. Ekman, and Sanjiv K. Patel, as directors, to hold office until no later than the annual general meeting of shareholders in 2025;
2. To ratify, in a non-binding vote, the appointment of KPMG LLP as the Company's independent registered public accounting firm for its fiscal year ending December 31, 2022, and to authorize, in a binding vote, the Company's Board of Directors, acting through its Audit Committee, to approve the remuneration of that auditor;
3. To approve, in a non-binding advisory vote, the compensation of the Company's executive officers named in the Proxy Statement accompanying this Notice;
4. To approve, in a non-binding advisory vote, the frequency of future advisory votes by shareholders on the compensation of the Company's named executive officers;
5. To approve an amendment to the Company's 2018 Long Term Incentive Plan to increase the number of ordinary shares available for issuance under that Plan by 2,000,000 ordinary shares;
6. To renew our Board of Directors' existing authority under Irish law to allot and issue ordinary shares;
7. To renew our Board of Directors' existing authority under Irish law to allot and issue ordinary shares for cash without first offering those shares to existing shareholders pursuant to the statutory pre-emption right that would otherwise apply;
8. To approve any motion to adjourn the Annual Meeting, or any adjournment thereof, to another time and place in order to solicit additional proxies if there are insufficient votes at the time of the Annual Meeting to approve Proposal No. 7; and
9. To transact such other business as properly comes before the Annual Meeting or any adjournment or postponement thereof.

The foregoing items of business are more fully described in the Proxy Statement accompanying this Notice. The Company's Irish statutory financial statements for its fiscal year 2021, including the reports of the directors and auditors thereon, will be presented at the Annual Meeting. There is no requirement under Irish law that those statutory financial statements be approved by shareholders and no such approval will be sought at the Annual Meeting. The Annual Meeting will also include a review of the Company's affairs.

Under our Constitution and Irish law, Proposal Nos. 1, 2, 3, 5, 6, and 8 are deemed to be ordinary resolutions requiring the approval of a simple majority of the votes cast at the Annual Meeting. For Proposal No. 4, the option receiving the greatest number of votes cast at the Annual Meeting will be considered the frequency recommended by our shareholders. Proposal No. 7 is deemed to be a special resolution requiring the approval of 75 percent of the votes cast at the Annual Meeting.

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Only shareholders who owned our ordinary shares at the close of business on March 7, 2022, may vote at the Annual Meeting. Each shareholder of record will be entitled to one vote per ordinary share on each matter submitted to a vote of the shareholders, as long as those shares are represented at the Annual Meeting, either in person or by proxy. Shareholders who are entitled to attend and vote at the Annual Meeting are entitled to appoint a proxy or proxies to attend and vote on their behalf at the Annual Meeting; such proxy is not required to be a shareholder of the Company.

Our Board of Directors unanimously recommends that you vote as follows on the matters to be presented to shareholders at the Annual Meeting:

1. **FOR** the re-election of Paula K. Cobb, Lars G. Ekman, and Sanjiv K. Patel, as directors, as described in Proposal No. 1;
2. **FOR** the ratification, in a non-binding vote, of the appointment of KPMG LLP as the Company's independent registered public accounting firm for its fiscal year 2022 and authorization, in a binding vote, of the Board of Directors, acting through its Audit Committee, to approve the remuneration of that auditor, as described in Proposal No. 2;
3. **FOR** the approval, in a non-binding advisory vote, of the compensation of the Company's named executive officers, as described in Proposal No. 3;
4. **ONE YEAR** as the frequency of future advisory votes by shareholders to approve the compensation of the Company's name executive officers, as described in Proposal No. 4.
5. **FOR** the approval of the amendment to the Company's 2018 Long Term Incentive Plan to increase the number of ordinary shares available for issuance under that Plan by 2,000,000 ordinary shares, as described in Proposal No. 5;
6. **FOR** the renewal of our Board of Directors' existing authority under Irish law to allot and issue shares, as described in Proposal No. 6;
7. **FOR** the renewal of our Board of Directors' existing authority under Irish law to allot and issue shares for cash without first offering those shares to existing shareholders pursuant to the statutory pre-emption right that would otherwise apply, as described in Proposal No. 7; and
8. **FOR** the approval of any motion to adjourn the Annual Meeting, or any adjournment thereof, to another time and place in order to solicit additional proxies if there are insufficient votes at the time of the Annual Meeting to approve Proposal No. 7, as described in Proposal No. 8.

For the Annual Meeting, we have elected to use the internet as the primary means of providing our proxy materials to shareholders. Consequently, some shareholders may not receive paper copies of our proxy materials. We intend to send shareholders a Notice of Internet Availability of Proxy Materials with instructions for accessing the proxy materials and for voting via the internet. The Notice of Internet Availability of Proxy Materials will also provide the date, time, and location of the Annual Meeting; the matters to be acted upon at the meeting and the Board of Directors' recommendation with regard to each matter; a toll-free number, an e-mail address, and a website where shareholders can request a paper or e-mail copy of our Proxy Statement and form of proxy card and our Annual Report on Form 10-K for fiscal year 2021; information on how to access their proxy card; and information on how to attend the meeting and vote in person.

You are cordially invited to attend the Annual Meeting, but whether or not you expect to attend in person, you are urged to complete, sign, and date your proxy card and return it by mail or follow the alternative voting procedures described in the Notice of Internet Availability of Proxy Materials or the proxy card.

The Annual Meeting and COVID-19 Pandemic:

The well-being of all attendees and participants at the Annual Meeting is a primary concern for the Company and in this context we are monitoring developments in relation to the COVID-19 pandemic. While all shareholders are invited to attend the Annual Meeting, the meeting will proceed subject to the guidance provided by the Irish Government and the Irish Department of Health or any other governmental agency in place at the time of the meeting and such other measures as the Board of Directors considers appropriate to address health and safety concerns. As a result, there may be restrictions on travel and/or gatherings that affect or prohibit travel to and in-person attendance at the Annual Meeting. Due to the ongoing risks posed by the COVID-19 pandemic, the members of our Board of Directors and senior management may not be physically present at the Annual Meeting in Ireland and may instead participate remotely. Furthermore, to promote the health and safety of attendees, we may impose additional procedures or limitations on meeting attendance based on applicable governmental requirements or recommendations or facility requirements. Such additional procedures or limitations may include, but are not limited to, thorough screenings of attendees (including temperature checks), limits on the number of attendees to promote social distancing, and requiring the use of face masks.

In the event that any alternative arrangements may be advisable or required due to public health recommendations regarding containment of COVID-19, which may include the closure of, or restrictions on, access to the meeting venue, we will promptly communicate this to shareholders by an announcement in a press release, on the investor relations page of the Company's website found at <https://ir.prothena.com/investor-relations>, and a filing with the Securities and Exchange Commission. We advise shareholders to monitor these sources regularly, as circumstances may change on short notice. In the event it is not possible or advisable to hold the Annual Meeting at a physical location, we may host a virtual-only Annual Meeting.

Whether or not you expect to attend in person, we strongly encourage all shareholders to vote their shares by proxy in advance of the Annual Meeting to ensure you can vote and be represented at the Annual Meeting if attending in person is not feasible or not recommended. This can be done in advance of the Annual Meeting by using one of the voting options detailed in the accompanying proxy statement.

By Order of the Board of Directors



Yvonne M. Tchraikian
Company Secretary
Dublin, Ireland
March 31, 2022

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Proxy Statement For The Annual General Meeting Of Shareholders To Be Held On May 17, 2022



GENERAL INFORMATION

The Board of Directors of Prothena Corporation plc is soliciting your proxy to vote at the Annual General Meeting of Shareholders to be held on Tuesday, May 17, 2022, at 4:00 p.m. local time, and any adjournment or postponement of that meeting (the "Annual Meeting"). The Annual Meeting will be held at The Merrion Hotel, Upper Merrion Street, Dublin 2, D02 KF79, Ireland.

We have elected to use the internet as our primary means of providing our proxy materials to shareholders. Accordingly, on or about March 31, 2022, we are making this Proxy Statement and the accompanying form of proxy card, the accompanying Notice of Annual General Meeting of Shareholders, and our Annual Report on Form 10-K for our fiscal year 2021 available on the internet and mailing a Notice of Internet Availability of Proxy Materials to shareholders of record as of March 7, 2022 (the "Record Date"). Brokers and other nominees who hold shares on behalf of beneficial owners will be sending their own similar notice. All shareholders as of the Record Date will have the ability to access our proxy materials on the website referred to in the Notice of Internet Availability of Proxy Materials or request to receive a printed set of the proxy materials. Instructions on how to request a printed copy by mail or electronically may be found in the Notice of Internet Availability of Proxy Materials and on the website referred to in the notice, including an option to request paper copies on an ongoing basis. We intend to mail this Proxy Statement, together with the accompanying form of proxy card and Notice of Annual General Meeting of Shareholders, to those shareholders entitled to vote at the Annual Meeting who have properly requested paper copies of such materials.

The only voting securities of Prothena are ordinary shares, \$0.01 par value per share ("ordinary shares"). There were 46,741,333 ordinary shares issued and outstanding as of the Record Date. A quorum of shareholders is necessary to hold a valid meeting and requires that the shareholders holding a majority of the issued and outstanding ordinary shares entitled to vote are present in person or represented by proxy at the Annual Meeting.

In this Proxy Statement, we refer to Prothena Corporation plc as the "Company," "Prothena," "our," "we," or "us" and the Board of Directors as the "Board." When we refer to Prothena's fiscal year, we mean the 12-month period ending December 31 of the stated year. The contents of our website are not intended to be incorporated by reference in this Proxy Statement, and any references to our website herein are intended for textual references only.

THE PROXY PROCESS AND SHAREHOLDER VOTING QUESTIONS AND ANSWERS ABOUT THESE PROXY MATERIALS AND VOTING

1. Who can vote at the Annual Meeting?

Only shareholders of record at the close of business on the Record Date will be entitled to vote at the Annual Meeting. At the close of business on the Record Date, there were 46,741,333 ordinary shares issued and outstanding and entitled to vote.

Shareholder of Record: Shares Registered in Your Name

If, on the Record Date, your shares were registered directly in your name with the transfer agent for our ordinary shares, Computershare Trust Company, N.A., then you are a shareholder of record. As a shareholder of record, you may vote in person at the Annual Meeting or vote by proxy. Whether or not you plan to attend the Annual Meeting, we urge you to fill out and return the enclosed proxy card or vote by proxy over the telephone or on the internet as instructed below to ensure your vote is counted.

Beneficial Owner: Shares Registered in the Name of a Broker, Bank, or Other Agent

If, on the Record Date, your shares were not held in your name, but rather in an account at a brokerage firm, bank, dealer, or other similar organization, who in turn hold through The Depository Trust Company ("DTC"), then you are the beneficial owner of shares held in "street name" and these proxy materials are being forwarded to you by that organization. The organization holding your account is considered the shareholder of record for purposes of voting at the Annual Meeting. As a beneficial owner, you have the right to direct your broker or other agent on how to vote the shares in your account. You are also invited to attend the Annual Meeting. However, since you are not the shareholder of record, you may not vote your shares in person at the Annual Meeting unless you request and obtain a valid proxy card from your broker or other agent who is the record holder of the shares authorizing you to vote at the Annual Meeting.

2. What am I being asked to vote on?

You are being asked to vote **FOR**:

- Re-election, by separate resolutions, of Paula K. Cobb, Lars G. Ekman, and Sanjiv K. Patel as directors, to hold office until no later than our annual general meeting of shareholders in 2025;
- Ratification, in a non-binding vote, of the appointment of KPMG LLP as our independent registered public accounting firm for our fiscal year 2022 and authorization, in a binding vote, of our Board, acting through its Audit Committee, to approve the remuneration of that auditor;
- Approval, in a non-binding advisory vote, of the compensation of our executive officers named in this Proxy Statement;
- One Year, in a non-binding advisory vote, as the frequency of future advisory votes by shareholders on the compensation of our executive officers named in this Proxy Statement;
- Approval of an amendment to our 2018 Long Term Incentive Plan to increase the number of ordinary shares available for issuance under that Plan by 2,000,000 ordinary shares;
- Renewal of our Board of Directors' existing authority under Irish law to allot and issue ordinary shares;
- Renewal of our Board of Directors' existing authority under Irish law to allot and issue ordinary shares for cash without first offering those shares to existing shareholders pursuant to the statutory pre-emption right that would otherwise apply; and

- Approval of any motion to adjourn the Annual Meeting, or any adjournment thereof, to another time and place in order to solicit additional proxies if there are insufficient votes at the time of the Annual Meeting to approve Proposal No. 7.

In addition, you are entitled to vote on any other matters that are properly brought before the Annual

Meeting. We are not aware of any other matter that will be presented for consideration at the Annual Meeting. If any other matter is properly brought before the Annual Meeting, the Board intends that one of the individuals named in the accompanying form of proxy card will vote on such matter in accordance with his or her discretion.

3. How do I vote?

You may vote by mail or follow any alternative voting procedure described on the proxy card or the Notice of Internet Availability of Proxy Materials. To use an alternative voting procedure, follow the instructions on each proxy card that you receive or on the Notice of Internet Availability of Proxy Materials.

For proposals 1, 2, 3, 5, 6, 7, and 8, you may vote “FOR” or “AGAINST” or abstain from voting. For proposal No. 4, you may vote “ONE YEAR” or “TWO YEARS” or “THREE YEARS” or abstain from voting.

The procedures for voting are as follows:

Shareholder of Record: Shares Registered in Your Name

If you are a shareholder of record, you may vote in person at the Annual Meeting. Alternatively, you may vote by proxy by mail, over the internet, or by telephone. Whether or not you plan to attend the Annual Meeting, we urge you to vote by proxy to ensure your vote is counted. Even if you have submitted a proxy before the Annual Meeting, you may still attend the Annual Meeting and vote in person. In such case, your previously submitted proxy will be disregarded.

- To vote in person, come to the Annual Meeting and we will give you a ballot when you arrive.
- To vote using the proxy card, simply complete, sign, and date the proxy card and return it

promptly in the envelope provided. If you return your signed proxy card to us before the Annual Meeting, we will vote your shares as you direct.

- To vote by proxy over the internet, follow the instructions provided on the proxy card or in the Notice of Internet Availability of Proxy Materials.
- To vote by telephone if you request printed copies of the proxy materials by mail, you may vote by proxy by calling the toll-free number found on the proxy card.

Beneficial Owner: Shares Registered in the Name of Broker, Bank, or Other Agent

If you are a beneficial owner of shares registered in the name of your broker, bank, or other agent, who in turn hold through DTC, you should have received a voting instruction card and voting instructions with these proxy materials from that organization rather than from us. Simply complete and mail the voting instruction card to ensure that your vote is counted, or follow such instructions to submit your vote by the internet or telephone, if the instructions provide for internet and telephone voting. To vote in person at the Annual Meeting, you must obtain a valid proxy from your broker, bank, or other agent. Follow the instructions from your broker, bank, or other agent included with these proxy materials, or contact your broker, bank, or other agent to request a proxy form.

4. Who counts the votes?

Broadridge Financial Solutions, Inc. (“Broadridge”) has been engaged as our independent agent to tabulate shareholder votes.

5. How are votes counted?

With respect to each of Proposal Nos. 1, 2, 3, 5, 6, and 8, an affirmative vote of a simple majority of the votes cast in person or by proxy at the Annual Meeting is required for approval. With respect to Proposal No. 7, an affirmative vote of 75 percent of the votes cast in person or by proxy at the Annual Meeting is required for approval. With respect to Proposal No. 4, shareholders are not being asked to approve or disapprove the Board's recommendation, but rather to indicate their choice among the following frequency options: one year, two years, or three years, or to abstain from voting on this item. If none of the frequency alternatives - one year, two years, or three years - receives a majority of the votes cast, we will consider the highest number of votes cast by shareholders to be the frequency that has been selected by shareholders, and our board of directors will review the voting results and take them into consideration in determining the frequency of future non-binding advisory votes on the compensation of our named executive officers.

If your shares are held by a broker on your behalf (that is, in "street name"), please instruct your broker on how to vote your shares. If you do not provide voting instructions, your shares will not be voted on any proposal for which the broker does not have discretionary authority to vote. This is called a "broker non-vote." In these cases, the broker can regis-

ter your shares as being present at the Annual Meeting for purposes of determining the presence of a quorum, and exercise its discretionary authority to vote on Proposal 2, but will not be able to vote on those proposals for which specific authorization from you is required under applicable rules. Accordingly, while broker non-votes will *not* be counted as having been voted on a particular proposal, broker non-votes will be considered present and entitled to vote at the Annual Meeting and will be counted towards determining whether or not a quorum is present. We strongly encourage you to provide voting instructions to your broker to ensure that your vote is counted on all of the proposals.

If shareholders abstain from voting, including brokers holding their clients' shares of record who cause abstentions to be recorded, these shares will be considered present and entitled to vote at the Annual Meeting and will be counted towards determining whether or not a quorum is present. Abstentions will not, however, be considered votes cast at the Annual Meeting.

Because the approval of each of the proposals is based on the votes cast at the Annual Meeting, abstentions and broker non-votes will not have any effect on the outcome of voting on any of the proposals.

6. How many votes do I have?

On each matter to be voted upon, you have one vote for each ordinary share you own as of the Record Date.

7. Why did I receive a notice in the mail regarding the internet availability of proxy materials instead of a full set of proxy materials?

Pursuant to rules of the U.S. Securities and Exchange Commission (the "SEC"), Irish law, and our Constitution, we have elected to provide access to our proxy materials on the internet. Accordingly, we are sending a Notice of Internet Availability of Proxy Materials to our shareholders. All shareholders will have the ability to access the proxy materials on the website referred to in the Notice of Internet Availability of Proxy Materials or request to receive a printed set of the proxy materials. Instructions on

how to access the proxy materials on the internet or to request a printed copy may be found in the Notice of Internet Availability of Proxy Materials. In addition, shareholders may request to receive proxy materials in printed form by mail or electronically by email on an ongoing basis. We encourage shareholders to take advantage of the availability of the proxy materials on the internet to help reduce the environmental impact of the Annual Meeting.

8. How do I vote via internet or telephone?

You may vote by proxy on the internet by following the instructions provided on the proxy card or in the Notice of Internet Availability of Proxy Materials. If you request printed copies of the proxy materials by mail, you may vote by proxy by calling the toll-free number found on the proxy card. Please be aware that if you vote on the internet, you may incur costs such as internet access or telephone charges for which you will be responsible. The internet and telephone voting facilities for eligible shareholders of record will close at 11:59 p.m. Eastern Time on May 16, 2022. The giving of such a proxy by internet

or telephone will not affect your right to vote in person should you decide to attend the Annual Meeting.

The internet and telephone voting procedures are designed to authenticate shareholders' identities, to allow shareholders to give their voting instructions and to confirm that shareholders' instructions have been recorded properly. If you vote by internet or telephone, that vote authorizes your proxy in the same manner as if you signed, dated, and returned a written proxy card by mail.

9. What if I return a proxy card but do not make specific choices?

If we receive a signed and dated proxy card and the proxy card does not specify how your shares are to be voted, your shares will be voted as follows:

- FOR the re-election, by separate resolutions, of Paula K. Cobb, Lars G. Ekman, and Sanjiv K. Patel as directors, to hold office until no later than our annual general meeting of shareholders in 2025;
- FOR the ratification, in a non-binding vote, of the appointment of KPMG LLP as our independent registered public accounting firm for our fiscal year 2022 and authorization, in a binding vote, of our Board, acting through its Audit Committee, to approve the remuneration of that auditor;
- FOR the approval, in a non-binding advisory vote, of the compensation of our named executive officers;
- ONE YEAR, as the frequency in which future non-binding advisory votes on the compensation of our named executive officers will be held;

- FOR the approval of the amendment to our 2018 Long Term Incentive Plan to increase the number of ordinary shares available for issuance under that Plan by 2,000,000 ordinary shares.
- FOR the renewal of our Board of Directors' existing authority under Irish law to allot and issue shares;
- FOR the renewal of our Board of Directors' existing authority under Irish law to allot and issue shares for cash without first offering those shares to existing shareholders pursuant to the statutory pre-emption right that would otherwise apply; and
- FOR the approval of any motion to adjourn the Annual Meeting, or any adjournment thereof, to another time and place in order to solicit additional proxies if there are insufficient votes at the time of the Annual Meeting to approve Proposal No. 7.

If any other matter is properly presented at the Annual Meeting, your proxy (one of the individuals named on your proxy card) will vote your shares using his or her discretion.

10. Who is paying for this proxy solicitation?

We will pay for the entire cost of soliciting proxies. In addition to these mailed proxy materials, our directors, officers, and employees may also solicit proxies in person, by telephone, or by other means of communication. Directors, officers, and employees will not be paid any additional compensation for soliciting proxies. We may also reimburse brokerage firms,

banks, and other agents for the cost of forwarding proxy materials to beneficial owners. In addition, we have retained Alliance Advisors, a proxy solicitation firm, to assist in the solicitation of proxies for a fee of approximately \$25,000, plus reimbursement of expenses.

11. What does it mean if I receive more than one set of materials?

If you receive more than one set of materials, your shares are registered in more than one name or are registered in different accounts. In order to vote all the shares you own, you must either sign and return

all of the proxy cards or follow the instructions for any alternative voting procedure on each of the proxy cards or Notice of Internet Availability of Proxy Materials you receive.

12. Can I change my vote after submitting my proxy?

Yes. You may revoke your proxy at any time before commencement of the Annual Meeting. If you are the record holder of your shares, you may revoke your proxy in any one of three ways:

- You may submit a new vote on the internet or by telephone or submit another properly completed proxy card with a later date than your original proxy card, but no later than 11:59 p.m. Eastern Time on May 16, 2022.
- You may deliver a written notice that you are revoking your proxy to our Company Secretary at Prothena Corporation plc, 77 Sir John Rogerson's

Quay, Block C, Grand Canal Docklands, Dublin 2, D02 VK60, Ireland, which notice must be delivered no later than 11:59 p.m. Eastern Time on May 16, 2022.

- You may attend the Annual Meeting and either vote or revoke your proxy in person. Simply attending the Annual Meeting will not, by itself, revoke your proxy.

If your shares are held by your broker, bank, or other agent, you must contact the broker, bank, or other agent and follow the instructions provided by them.

13. When are shareholder proposals and nominations due for next year's annual meeting?

In accordance with Rule 14a-8 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), shareholders may submit to us proposals on matters appropriate for shareholder action at meetings of our shareholders. In order to be considered for inclusion in next year's proxy materials, your proposal must comply with the requirements of Rule 14a-8 of the Exchange Act and other SEC rules and be submitted in writing no later than December 1, 2022, to our Company Secretary at Prothena Corporation plc, 77 Sir John Rogerson's Quay, Block C, Grand Canal Docklands, Dublin 2, D02 VK60, Ireland; provided that if the date of next year's annual general meeting of shareholders is greater than 30 days from May 17, 2023, the deadline is a reasonable time before we begin to print and send our proxy materials for next year's annual general meeting.

For a shareholder to make any formal nomination of a director candidate for election to the Board at

the 2023 annual general meeting of shareholders, the shareholder must provide notice to the Company not earlier than November 1, 2022, and not later than December 31, 2022, and must otherwise comply with the requirements set forth in our Constitution. You are advised to review our Constitution, which contains additional requirements about advance notice of director nominations. For more information, see below under the heading *Corporate Governance and Board Matters - Board Committees - Nominating and Corporate Governance Committee*.

In addition to satisfying the requirements regarding director nominations in our Constitution, 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 March 18, 2023.

14. What is the quorum requirement?

A quorum of shareholders is necessary to hold a valid meeting. A quorum will be present if the holders of not less than one-half of the ordinary shares issued and outstanding and entitled to vote are present in person or represented by proxy at the Annual Meeting. On the Record Date, there were 46,741,333 ordinary shares issued and outstanding and entitled to vote. Accordingly, 23,370,667 ordinary shares must be represented in person or by proxy at the Annual Meeting to have a quorum.

Your shares will be counted towards the quorum if you submit a valid proxy vote or vote at the Annual Meeting. Abstentions and broker non-votes will also be counted towards the quorum requirement. If there is no quorum, either the chairperson of the Annual Meeting or a majority in voting power of the shareholders entitled to vote at the Annual Meeting, present in person or represented by proxy, may adjourn the Annual Meeting to another time or place.

15. How can I find out the results of the voting at the Annual Meeting?

Voting results will be announced by the filing with the SEC of a Current Report on Form 8-K within four business days after the Annual Meeting.

16. Where can I find directions to the Annual Meeting?

To obtain directions to the Annual Meeting, which will be held at The Merrion Hotel, Upper Merrion Street, Dublin 2, D02 KF79, Ireland, you may send a request to our Company Secretary at Prothena Cor

poration plc, 77 Sir John Rogerson's Quay, Block C, Grand Canal Docklands, Dublin 2, D02 VK60, Ireland.

17. What are the Irish statutory financial statements?

Since we are an Irish company, we are required to prepare Irish statutory financial statements, including the respective reports of the directors and the auditors thereon, under applicable Irish company law; to deliver those statutory financial statements to our shareholders of record prior to the Annual Meeting; and to present those statutory financial statements at the Annual Meeting. The Irish statutory financial statements cover the results of operations and financial position of the Company for our fiscal year 2021, and are prepared in accordance with generally accepted accounting principles in the United States to the extent the use of such principles does not contravene any provision of the Irish Com

panies Act 2014 or any regulation thereunder. There is no requirement under Irish law that our Irish statutory financial statements be approved by our shareholders and no such approval will be sought at the Annual Meeting. Our Irish statutory financial statements are available on our website at <https://ir.prothena.com/financial-information/irish>. We will mail without charge, upon written request, a copy of our Irish statutory financial statements to beneficial owners of our shares. Such requests should be sent to our Company Secretary at Prothena Corporation plc, 77 Sir John Rogerson's Quay, Block C, Grand Canal Docklands, Dublin 2, D02 VK60, Ireland.

PROPOSAL NO. 1

ELECTION OF DIRECTORS

The Company's Constitution requires that at least one-third (which, if not a round number, is rounded to the number which is nearest to and less than one-third) of the directors (excluding any director who wishes to retire and does not wish to offer themselves for re-appointment, and any director appointed by the Board to fill a vacancy since the last annual general meeting) must stand for re-election at each annual general meeting of shareholders, and that directors must stand for re-election no later than the third annual general meeting subsequent to their election or appointment to the Board. Generally, vacancies on the Board may be filled only by ordinary resolution of the Company's shareholders or the affirmative vote of a majority of the remaining directors. A director appointed by the Board to fill a vacancy will serve until the subsequent annual general meeting and must stand for election at that time.

As of the date of this Proxy Statement, we have ten directors serving on our Board. Dr. Henney, whose current term will expire at the Annual Meeting, is not standing for re-election at the Annual Meeting. The Board plans to reduce the size of the Board to nine members immediately after the Annual Meeting. Our Board currently is divided into the following groups:

- Dr. Henney and Dr. Patel, whose current terms will expire at the Annual Meeting;
- Ms. Cobb, Dr. Ekman, Dr. Kinney, Mr. Nodelman, and Dr. Selkoe, whose current terms will expire no later than the annual general meeting of shareholders to be held in 2023; and
- Mr. Collier, Mr. Cooke, and Dr. Härfstrand, whose current terms will expire no later than the annual general meeting of shareholders to be held in 2024.

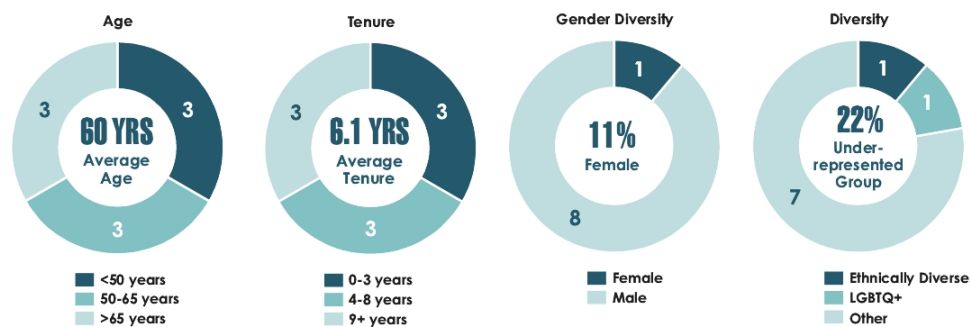
Ms. Cobb, Dr. Ekman, and Dr. Patel have been nominated by the Board to stand for re-election. The Board nominated Ms. Cobb and Dr. Ekman to stand for re-election even though their three-year terms will not expire until 2023, because the Company's Constitution requires that one-third of the directors (not including any director appointed to the Board since the last annual general meeting or a director who wishes to retire and does not wish to be re-appointed) stand for election at each annual general meeting and that a director longest in office since being appointed or last elected must be nominated to complete such slate of directors. The Board nominated Dr. Patel to stand for re-election because he was appointed by the Board in 2021 and the Company's Constitution requires that any director appointed by the Board stand for election at the next annual general meeting of shareholders following that appointment. If re-elected by our shareholders at the Annual Meeting, Ms. Cobb, Dr. Ekman, and Dr. Patel will each hold office from the date of their election until no later than the third subsequent annual general meeting of shareholders (i.e., in 2025), or until their earlier death, resignation, or removal.

In order to be elected as a director, each nominee must receive the affirmative vote of a majority of the votes cast in person or by proxy at the Annual Meeting; if a director nominee does not receive this majority vote, such nominee will not be elected to our Board. In the event that any nominee becomes unavailable for election as a result of an unexpected occurrence, the proxy holders may vote your shares for the election of any substitute nominee whom the Board proposes. Each person nominated for election has consented to being named as a nominee in this Proxy Statement and agreed to serve if elected, and management has no reason to believe that any nominee will be unable to serve.

The table below is provided to highlight the specific skills, qualifications, and other attributes of our director nominees and continuing directors. The lack of a mark for a particular item for a particular director does not mean the director lacks that skill or qualification; rather, a mark indicates a specific area of focus or expertise for which the Board relies on such director most. Also provided are summary statistics regarding the composition of the Board.

The table required by Nasdaq Stock Market Listing Rule 5605(f) is provided at Appendix A. Following the table is certain biographical information for each nominee for director and each director whose term as a director will continue after the Annual Meeting, which includes information regarding each person's individual experience, qualifications, attributes, or skills that led the Board to conclude that such person should serve as a director, in light of our business and structure.

Skills and Qualifications									
	Lars G. Ekman	Paula K. Cobb	Richard T. Collier	Shane M. Cooke	K. Anders O. Hattis/Stand	Gene G. Kinney	Oleg Nodelman	Sanjiv K. Patel	Dennis J. Seikoe
Science & Research Scientific expertise in biopharmaceutical research and/or in relevant medical fields	•				•	•			•
Clinical Development and Operations Experience in the design and implementation of clinical studies in support of drug development	•			•	•	•			•
Regulatory Experience with the regulation in the healthcare industry	•	•	•		•	•			•
Drug Commercialization Experience with bringing drugs to market		•		•	•	•		•	•
Business Strategy/Operations Experience overseeing and driving strategic direction and growth of an organization	•	•	•	•	•	•	•	•	•
Finance/Accounting Experience or expertise in financial accounting and reporting processes or the financial management of an organization	•	•	•	•	•	•		•	
Legal/Ethics/Public Policy Experience with legal and ethical and public policy issues in the healthcare industry			•			•			•
Public Company Governance Service on a public company board other than Prothena's	•	•		•	•		•	•	•
Capital Markets & M&A Experience Experience in capital market transactions or mergers and acquisitions	•		•	•	•	•	•	•	•
Human Capital Management Experience in attracting and retaining top talent and building organizational culture	•	•			•	•		•	•
Basic Information (as of 3/31/2022)									
Independent	•	•	•	•	•		•	•	•
Age	72	49	68	59	65	53	45	48	78
Tenure (Years)	9.3	2.8	9.3	9.3	6.8	5.5	2.3	0.8	8.7



Nominees for Election to Terms Expiring No Later than the Annual General Meeting of Shareholders in 2025

Paula K. Cobb is the Chief Business Officer at Affinia Therapeutics, Inc., a biotechnology company developing gene therapies, a position she has held since 2020. From 2016 to 2019, Ms. Cobb held positions as Executive Vice President, Corporate Development, and Chief Operating Officer of Decibel Therapeutics, Inc. From 2003 to 2016, Ms. Cobb held numerous positions with Biogen, Inc., including Senior Vice President, Rare Disease Group (from 2015 to 2016), Senior Vice President, MS Franchise Strategy (from 2014 to 2015), and Vice President, Program Leadership & Management (from 2010 to 2014). She also served on the Board of Directors of Nightstar Therapeutics plc (a biotechnology company) from 2018 until it was acquired by Biogen in 2019. Ms. Cobb earned her B.A. from Amherst College and her M.B.A. from Harvard University's Graduate School of Business Administration. She has served on our Board since 2019. Age: 49

The Board concluded that Ms. Cobb should continue to serve as a director given her significant operational, business development, and management experience from serving in a range of senior executive positions with several biotechnology/biopharmaceutical companies. The Board also considered her experience serving on the board of directors of another biotechnology company.

Lars G. Ekman, M.D., Ph.D., is Chair of our Board of Directors, a position he has held since 2012. He is an executive partner at Sofinnova Ventures, Inc. (a venture capital firm), a position he has held since 2008. Dr. Ekman is also chair of the board of Amarin Corporation plc, and serves as a director of Ultragenyx Pharmaceutical Inc. He also served as a director of Intermune (from 2006 to 2013), as a director of Ocera Therapeutics, Inc. (from 2009 to 2015), as a director of Spark Therapeutics, Inc. (from 2014 to 2019), and as Chair of the Board of Sphiris Bio Inc. (from 2010 to 2020). Dr. Ekman co-founded Cebix Incorporated, where he served as Chief Executive Officer from 2009 to 2012. He was President of Research & Development at Elan Corporation, plc (from 2001 to 2007), where he also served as a director (from 2005 to 2012). From 1997 to 2001, Dr. Ekman was Executive Vice President, Research & Development, at Schwarz Pharma AG. Prior to that, he held various

senior positions at Pharmacia Corporation. Dr. Ekman is a board-certified surgeon with a Ph.D. in experimental biology and has held several clinical and academic positions in both the United States and Europe. He earned his Ph.D. and M.D. from the University of Gothenburg, Sweden. Dr. Ekman has served on our Board since 2012. Age: 72

The Board concluded that Dr. Ekman should continue to serve as a director given his significant scientific, operational, and management experience gained as a research scientist and in managing research and development functions engaged in drug discovery with a number of companies in the pharmaceutical industry. The Board also considered his clinical background, his venture capital experience in the life science industry, and his experience serving on the boards of directors at a number of public and private companies in the pharmaceutical/biotechnology industry.

Sanjiv K. Patel, MBBS, is President, Chief Executive Officer and a director of Relay Therapeutics, Inc., a clinical-stage precision medicines company, a position he has held since 2017. Before joining Relay Therapeutics, Dr. Patel served in various roles at Allergan, Inc. from 2006 to 2017, including Chief Strategy Officer (from 2015 to 2017) and Corporate Vice President, Global Strategic Marketing & Global Health Outcomes (from 2013 to 2015). Prior to this, he was a management consultant at The Boston Consulting Group and practiced as a surgeon within the UK's National Health Service. Dr. Patel earned his MBBS from University of London, his M.A. in Medical Sciences from the University of Cambridge, his MRCS from the Royal College of Surgeons of England, and his M.B.A. from INSEAD. He has served on our board since 2021. Age: 48.

The Board concluded that Dr. Patel should continue to serve as a director given his significant operational and management experience from serving as a CEO of a public biopharmaceutical company. The Board also considered his experience as a senior executive at and as a management consultant to pharmaceutical companies, as well as his clinical training and background.

THE BOARD OF DIRECTORS UNANIMOUSLY RECOMMENDS THAT SHAREHOLDERS VOTE FOR THE RE-ELECTION, BY SEPARATE RESOLUTIONS, OF MS. COBB, DR. EKMAN, AND DR. PATEL AS DIRECTORS.

Directors Continuing in Office Until No Later than the Annual General Meeting of Shareholders in 2023

Gene G. Kinney, Ph.D., has served as our President and Chief Executive Officer since 2016. Prior to that, he was our Chief Operating Officer for part of 2016, and prior to that he was our Chief Scientific Officer and Head of Research and Development from 2012 to 2016. From 2009 to 2012, Dr. Kinney was Vice President, Pharmacology and then Senior Vice President of Pharmacological Sciences at Elan Pharmaceuticals, Inc.; while in those positions, he also served as Head of Nonclinical Research for Janssen Alzheimer Immunotherapy R&D. From 2001 to 2009, Dr. Kinney was Senior Director, Head of Central Pharmacology and acting lead for Bioanalytics & Pathology at the Merck Research Laboratories, where he contributed to the strategic direction and oversight of drug discovery activities and led a number of non-clinical discovery and clinical development programs targeted for the treatment of neurodegenerative and psychiatric conditions. Dr. Kinney also held positions at Bristol Myers Squibb and was an Assistant Professor at the Emory University School of Medicine, Department of Psychiatry and Behavioral Sciences. He earned his B.A. from Bloomsburg University and his M.A. and Ph.D. from Florida Atlantic University. Dr. Kinney has served on our Board since 2016. Age: 53

The Board concluded that Dr. Kinney should continue to serve as a director given his role as the Company's President and Chief Executive Officer and his extensive scientific and operational knowledge of our business and its drug discovery and development programs, from his tenure with the Prothena business when it was a part of Elan as well as since its separation from Elan. The Board also considered his significant experience in neuroscience and drug development programs encompassing immunotherapy, vaccine and small molecule approaches, as well as his experience gained from serving in key research and development leadership roles in other biotechnology companies.

Oleg Nodelman is the Founder and Portfolio Manager of EcoR1 Capital, LLC, a biotechnology-focused investment advisory firm established in 2013, which invests in companies in all stages of research and development. From 2001 to 2012, he held various roles including Portfolio Manager at BVF Partners. Mr. Nodelman also serves as a director of Nuvation Biosciences, Inc. and AnaptysBio, Inc. (both biotechnology companies whose boards he joined in 2021), and Panacea Acquisition Corp. II (a blank check company whose board he joined in 2021).

Mr. Nodelman earned his B.S. in Foreign Service with a concentration in Science and Technology from Georgetown University. He has served on our Board since 2019. Age: 45

The Board concluded that Mr. Nodelman should continue to serve as a director given his significant experience in venture capital investment in the life science industry. The Board also considered his experience serving on the boards of directors of public and private companies in the pharmaceutical/biotechnology industry, as well as his role as Founder and Portfolio Manager of EcoR1 Capital, LLC, a significant shareholder of the Company.

Dennis J. Selkoe, M.D., is the Vincent and Stella Coates Professor of Neurologic Diseases at Harvard Medical School and co-director of the Ann Romney Center for Neurologic Diseases at Brigham and Women's Hospital in Boston, positions he has held since 2000 and 1985, respectively. He has served on the faculty at Harvard Medical School since 1978. Dr. Selkoe was the principal founding scientist and served as a director of Athena Neurosciences, Inc. until it was acquired by Elan Corporation, plc in 1996. He has received numerous honors, including the Mathilde Soloway Award in the Neurosciences (NIH), the Potamkin Prize (American Academy of Neurology), the A.H. Heineken Prize for Medicine (The Netherlands), the Pioneer Award and the Lifetime Achievement Award (Alzheimer's Association), the George C. Cotzias Lecture of the American Academy of Neurology, and the Ulysses Medal of University College Dublin. Dr. Selkoe is a Fellow of the American Academy of Neurology, the American Association for the Advancement of Science and the American College of Physicians, an elected member of the National Academy of Medicine and a director of the Foundation for Neurologic Diseases. He served as a director of Elan Corporation, plc from 1996 to 2013. Dr. Selkoe earned his B.A. from Columbia University and his M.D. from the University of Virginia. He has served on our Board since 2013. Age: 78

The Board concluded that Dr. Selkoe should continue to serve as a director given his significant experience as both a research scientist and a practicing clinician, and in particular his expertise in the preclinical and clinical features of neurodegenerative diseases, especially Parkinson's disease and Alzheimer's disease. The Board also considered his lengthy experience as a director of a global public company in the pharmaceutical/biotechnology industry.

Directors Continuing in Office Until No Later than the Annual General Meeting of Shareholders in 2024

Richard T. Collier is the former Executive Vice President and General Counsel of Elan Corporation, plc, a position he held from 2004 to 2010. Prior to that, he served as Senior Vice President and General Counsel of Rhone-Poulenc Rorer Inc., Pharmacia & Upjohn Company, and Pharmacia Corporation. Mr. Collier was an Adjunct Professor of Law at the Temple University Beasley School of Law, where he taught drug and medical device law, from 2004 to 2017. He also practiced law at two leading Philadelphia-based law firms and with the U.S. Federal Trade Commission and U.S. Department of Justice. Mr. Collier earned both his B.A. and his J.D. from Temple University. He has served on our Board since 2012. Age: 68

The Board concluded that Mr. Collier should serve as a director given his extensive legal and management experience as a senior executive with a number of global pharmaceutical companies. The Board also considered his extensive knowledge of and experience with laws and regulations applicable to the pharmaceutical industry.

Shane M. Cooke is the former President of Alkermes plc (a biopharmaceutical company), a position he held from 2011 to 2018. Prior to that, he served as Head of Elan Drug Technologies and Executive Vice President of Elan Corporation, plc (from 2007 to 2011), where he also served as Chief Financial Officer (from 2001 to 2011) and as a director (from 2005 to 2011). Mr. Cooke has also held a number of senior positions in finance in the banking and aviation industries. He is a director of Alkermes plc and Endo International plc (both biopharmaceutical companies, whose boards he joined in 2018 and 2014, respectively). He served as a director (from 2019 to 2020) and board chair (from 2020 to 2021) of UDG Healthcare plc (a biopharmaceutical company). Mr. Cooke earned his Bachelor of Commerce and Master of Accounting degrees from University College Dublin, Ireland, and is a chartered accountant. He has served on our Board since 2012. Age: 59

The Board concluded that Mr. Cooke should serve as a director given his significant operational, financial, commercial, and management experience in the biotechnology industry, as well as his qualification as a chartered accountant. The Board also considered his Irish residency and experience as a director and an executive officer of other Irish companies traded on U.S. stock exchanges.

K. Anders O. Härfstrand, M.D., Ph.D., is Chair of Härfstrand Consulting AG (a pharmaceutical/biotechnology consulting firm), which he founded in 2010. Dr. Härfstrand also served as Chief Executive Officer of BBB Therapeutics BV (a biopharmaceutical company) from 2014 to 2015. Prior to that, he was President and Chief Executive Officer, Europe of Makhteshim Agan Industries Ltd. (an agrichemicals company) from 2013 to 2014; President and Chief Executive Officer of Humabs BioMed SA (a biotechnology company) from 2011 to 2012; and Chief Executive Officer of Nitec Pharma AG (a biopharmaceutical company) from 2007 to 2010. He also served in various executive and management roles at Serono, Pfizer, and Pharmacia, and in non-executive roles on a number of Supervisory Boards in Europe. Dr. Härfstrand is chair of the board of Oasmia Pharmaceutical AB and Diurnal Group, plc. He served as a director of Karolinski Development AB (a biopharmaceutical investment company) from 2017 to 2019. Dr. Härfstrand earned his M.D. and Ph.D. in neuropharmacology endocrinology from Karolinska Institute in Sweden. He has served on our Board since 2015. Age: 65

The Board concluded that Dr. Härfstrand should serve as a director given his significant management, operational, and commercial experience from serving in executive positions with a number of biopharmaceutical companies. The Board also considered his scientific background and work experience in a broad range of geographies.

CORPORATE GOVERNANCE AND BOARD MATTERS

Overview

We are committed to exercising good corporate governance practices. In furtherance of this commitment, we regularly monitor developments in the area of corporate governance and review our processes, policies, and procedures in light of such developments. Key information regarding our corporate governance can be found on our website at <http://ir.prothena.com/corporate-governance>, including in our Corporate Governance Guidelines;

the charters for our Audit, Compensation, and Nominating and Corporate Governance Committees; and our Code of Conduct. We believe that our corporate governance policies and practices are adequately designed to ensure that our independent directors effectively oversee our management - including the performance of our Chief Executive Officer - and provide an effective and appropriately balanced Board governance structure.

Independence of Directors

Rules of The Nasdaq Stock Market ("Nasdaq") require that a majority of the members of a listed company's board of directors must qualify as "independent directors" as defined by Nasdaq rules and affirmatively determined by the board of directors.

Our Board has determined that, with the exception of Dr. Kinney, all members of our Board are "independent directors" as defined by Nasdaq rules. Dr. Kinney is not an independent director because he is our President and Chief Executive Officer.

Board Role in Risk Oversight

Our Board is responsible for the oversight of risk, while management is responsible for the day-to-day management of risk. The Board fulfills this oversight role directly and through certain of its committees. In particular, our Board reviews strategic as well as operational risks as an element of its review of strategic and operational plans and programs. The Audit Committee of the Board periodically

reviews the Company's major risk exposures and the steps management has undertaken to control them; oversees internal controls and other activities to manage financial risks; and periodically reviews the Company's policies, programs, and systems intended to ensure compliance with applicable laws and ethical standards.

Board Leadership Structure

Our Chair of the Board and our Chief Executive Officer are currently separate individuals. Dr. Ekman serves as Chair of the Board, and Dr. Kinney serves as our President and Chief Executive Officer. In his role as Chair, Dr. Ekman provides leadership to the Board; approves Board meeting schedules and agendas; presides over all Board meetings, including regular executive sessions of the independent directors; and

serves as the primary liaison between the independent directors and our Chief Executive Officer and other members of management. Our Board has concluded that our current leadership structure is appropriate at this time. However, our Board will continue to periodically review our leadership structure and may make changes as it deems appropriate.

Board Committees

Our Board has the following standing committees: the Audit Committee, the Compensation Committee, and the Nominating and Corporate Governance Committee. The current composition and responsibilities of each of these committees are described below. Members serve on these committees until their resignation or until otherwise determined by our Board.

Director	Audit Committee	Compensation Committee	Nominating and Corporate Governance Committee
Lars G. Ekman			
Paula K. Cobb ⁽¹⁾		C	
Richard T. Collier	✓		C
Shane M. Cooke	C		
K. Anders O. Härfstrand ⁽²⁾	✓		✓
Christopher S. Henney	✓	✓	
Gene G. Kinney			
Oleg Nodelman ⁽³⁾		✓	✓
Sanjiv K. Patel ⁽⁴⁾		✓	
Dennis J. Selkoe			
C Committee Chair	✓ Member		

(1) Ms. Cobb stepped down from the Nominating and Corporate Governance Committee on May 18, 2021.

(2) Mr. Härfstrand was appointed to the Audit Committee on May 18, 2021.

(3) Mr. Nodelman was appointed to the Nominating and Governance Committee on May 18, 2021.

(4) Dr. Patel was appointed to the Compensation Committee on May 18, 2021.

Audit Committee

Our Audit Committee's primary purposes are to oversee our corporate accounting and financial reporting processes and the audits and reviews of our financial statements, as well as our legal and ethical compliance activities. Among other matters, the Audit Committee is responsible for the appointment, compensation, retention, and oversight of our independent registered public accounting firm (the "auditor"); reviewing and confirming the auditor's independence; periodically reviewing the adequacy and effectiveness of the Company's internal control over financial reporting; reviewing with the management and the auditor the audited and reviewed financial statements to be included in the Company's annual and quarterly reports, respectively, filed with the SEC; reviewing the Company's major risk exposures and steps to control them; and reviewing the Company's policies, programs, and

systems intended to ensure compliance with applicable laws and ethical standards.

The current members of our Audit Committee are Mr. Collier, Mr. Cooke, Dr. Härfstrand, and Dr. Henney. Mr. Cooke serves as chair of the Committee. Each member of the Committee is an "independent director" and meets the heightened independence requirements and also meets the financial literacy requirements under Nasdaq rules. Our Board has determined that Mr. Cooke and Dr. Henney are each an "audit committee financial expert" as defined under SEC rules and each has the requisite additional financial sophistication required under Nasdaq rules. The Audit Committee operates under a written charter, a copy of which is available on our website at <http://ir.prothena.com/corporate-governance>.

Compensation Committee

Our Compensation Committee's primary purposes are to consider and approve all compensation of our executive officers other than our chief executive officer (our "CEO") and consider and recommend to the Board all compensation of our CEO; consider and recommend to the Board all director compensation; and administer or oversee our compensation plans (including equity compensation plans).

The current members of our Compensation Committee are Ms. Cobb, Dr. Henney, Mr. Nodelman, and Dr. Patel. Ms. Cobb serves as chair of the Committee. Each member of the Committee is an "independent director" and otherwise meets the independence requirements under Nasdaq rules and is a "non-employee director" as defined in Rule 16b-3 under the Exchange Act. The Committee operates under a written charter, a copy of which is available on our website at <http://ir.prothena.com/corporate-governance>.

Our CEO makes recommendations to the Compensation Committee on compensation to executive officers other than himself. He also makes recommendations to the Board and the Compensation Committee on what should be the Company objectives that drive annual performance-based incentive compensation (cash bonuses). Following completion of the fiscal year, he provides his assess

ment of the Company's performance relative to those objectives, as well as the individual performance of executive officers other than himself. Certain of our executive officers and other members of management provide data and other information to the Committee's compensation consultant (discussed below), as requested by that consultant. Our executive officers do not determine or recommend the amount or form of director compensation.

The Compensation Committee utilizes a compensation consultant to provide advice and recommendations to the Committee on the amounts and forms of executive and director compensation. The Committee is directly responsible for the appointment, compensation, and oversight of its compensation consultants, and is responsible for assessing the independence of those consultants after consideration of the independence factors prescribed by Nasdaq rules.

The Compensation Committee directly engaged Radford (an Aon Company) to act as an independent consultant and provide advice and recommendations on executive officer as well as non-employee director compensation for our fiscal year 2021. The Committee assessed Radford's independence prior to that engagement.

Nominating and Corporate Governance Committee

Our Nominating and Corporate Governance Committee's primary purposes are to identify individuals qualified to become Board members and recommend to the Board qualified individuals to be nominated for election or appointment to the Board; make recommendations to the Board regarding composition of the Board and its committees; develop and implement annual evaluations of the Board; develop and implement regular performance evaluations of our CEO; develop a succession plan for our CEO; and develop corporate governance guidelines applicable to the Company.

The current members of our Nominating and Corporate Governance Committee are Mr. Collier, Dr. Härfstrand, and Mr. Nodelman. Mr. Collier serves as chair of the Committee. Each member of the Committee is an "independent director" under Nasdaq rules. The Committee operates under a written charter, a copy of which is available on our website at <http://ir.prothena.com/corporate-governance>.

The Nominating and Corporate Governance Committee is responsible for determining the qualifications of nominees for election and candidates for appointment as directors, and for identifying, evaluating, and then recommending to the Board such nominees or candidates. The Committee reviews periodically the composition and size of the Board and makes recommendations to the Board as it deems necessary or appropriate so that the Board has the requisite expertise and that its membership consists of persons with sufficiently diverse and independent backgrounds.

In 2020, in response to proposed actions by Nasdaq, developments in various state laws, and other attention to the issue, the Board, upon a recommendation by the Committee, adopted an amendment to the Committee's charter that the Committee ensures that the Board's membership consists of persons with sufficiently diverse and independent backgrounds (including consideration of gender, ethnicity, geography and other characteristics) when identifying and evaluating qualified individuals for nomination or appointment to the Board. In 2021, the Board, upon a recommendation by the Committee, adopted a further amendment to the Committee's charter to require that diverse candidates, including candidates who are women and candidates from underrepresented communities, be

included in any pool from which nominees or candidates are selected.

Nominees or candidates are expected to possess and have demonstrated breadth and depth of management and leadership experience, financial and/or business acumen, and relevant industry or scientific experience, high integrity, sufficient time to devote to the Company's business, and a demonstrated ability to think independently but work collaboratively with other members of the Board and the Company's management. In recommending candidates for election or appointment to the Board, the Committee considers each nominee's or candidate's knowledge, skills, and experience, according to the foregoing criteria, as well as his or her independence under Nasdaq and SEC rules. The Committee evaluates each nominee or candidate in the context of the Board as a whole, with the objective of assembling a group that can best maximize the success of the business and represent shareholder interests through the exercise of sound judgment using its diversity of experience.

To assist the Nominating and Corporate Governance Committee in identifying potential directors who meet the criteria and priorities established from time to time and facilitate the evaluation of such potential directors, the Committee may retain third-party search firms.

The Nominating and Corporate Governance Committee will consider director candidates recommended by shareholders. Recommendations should be directed to the Company's registered office (Prothena Corporation plc, 77 Sir John Rogerson's Quay, Block C, Grand Canal Docklands, Dublin 2, D02 VK60, Ireland, Attention: Company Secretary). The Nominating and Corporate Governance Committee will apply the same standards in considering director candidates recommended by shareholders as it applies to other candidates. Once the Nominating and Corporate Governance Committee receives a recommendation from a shareholder, it may request additional information from the candidate about the candidate's independence, qualifications and other information that would assist the Nominating and Corporate Governance Committee in evaluating the candidate, as well as certain information that must be disclosed about the candidate in the Company's proxy statement, if nominated.

For a shareholder to make any formal nomination of a director candidate for election to the Board at an annual general meeting of shareholders, please

see the requirements described above in response to “When are shareholder proposals and nominations due for next year’s annual meeting?”

Meetings of the Board and Committees, Meeting Attendance and Shareholder Meeting Attendance

During our fiscal year 2021, our Board met eight times, our Audit Committee met eight times, our Compensation Committee met four times, and our Nominating and Corporate Governance Committee met four times.

During our fiscal year 2021, each of our directors attended at least 75% of all meetings of the Board and committees of the Board of which the director was a member.

We encourage all of our directors and nominees for director to attend our annual general meetings of shareholders, although attendance is not mandatory. In 2021, due to travel restrictions related to the COVID-19 pandemic, eight of our nine directors attended our annual general meeting of shareholders via videoconference and were available to answer questions.

Other Corporate Governance Matters

Corporate Governance Guidelines. As a part of our Board’s commitment to enhancing shareholder value over the long term, our Board has adopted Corporate Governance Guidelines. Our Corporate Governance Guidelines cover, among other topics, board composition, director independence, new director orientation and continuing education, annual Board performance evaluations, Board and director responsibilities, director access to management and independent advisors, Board committees and director compensation. Our Corporate Governance Guidelines are available on our website at <http://ir.prothena.com/corporate-governance>.

Majority Voting for Election of Directors. Our directors are elected by the affirmative vote of a majority of the votes cast by our shareholders at an annual general meeting. Any nominee for director who does not receive a majority of the votes cast is not elected to our Board. Accordingly, there is no “holdover” rule under Irish law or our Constitution.

Staggered Board. Our Board is divided into three groups and our Constitution requires that at least one-third (which, if not a round number, is rounded to the number which is nearest to and less than one-third) of the directors must stand for re-election at each annual general meeting, and that directors must stand for re-election no later than the third annual general meeting subsequent to their election or appointment to the Board. However, under Irish law and our Constitution, our directors may be removed at any time with or without cause by the affirmative vote of a majority of the votes cast by

shareholders. Under Irish law, shareholders holding 10% or more of the total voting rights of the Company can at any time requisition an extraordinary general meeting (i.e., a special meeting) to vote on the removal of any or all of our directors and, if desired, the appointment of replacement directors.

Shareholder Ability to Call Extraordinary Meetings. As noted above, Irish law provides that shareholders holding 10% or more of the total voting rights can at any time request that the directors call an extraordinary general meeting. The shareholders who wish to request an extraordinary general meeting must deliver to our registered office (set forth above) a written notice, signed by the shareholders requesting the meeting and stating the purposes of the meeting. If the directors do not, within 21 days of the date of delivery of the request, proceed to convene a meeting to be held within two months of that date, those shareholders (or any of them representing more than half of the total voting rights of all of them) may themselves convene a meeting within a specified period, but any meeting so convened cannot be held after the expiration of three months from the date of delivery of the request.

Compensation Governance. We are committed to having strong governance standards with respect to our compensation programs, procedures, and practices. Our key compensation governance practices are described in this Proxy Statement under the heading *Compensation Discussion and Analysis - Compensation Governance and Best Practices*.

Code of Conduct. We have a Code of Conduct that applies to all of our directors, executive officers, and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. Our Code of Conduct is available on our website at <http://ir.prothena.com/corporate-governance>. We will provide to any person without charge, upon request, a copy of that Code of Conduct; such a request may be made by sending it to our Company Secretary at Prothena Corporation plc, 77 Sir John Rogerson's Quay, Block C, Grand Canal Docklands, Dublin 2, D02 VK60, Ireland. If we make any amendment to, or waiver from, a provision of our Code of Conduct that we are required to disclose under SEC rules, we intend to satisfy that disclosure requirement by posting such information on our website at <http://ir.prothena.com/corporate-governance>. The contents of our websites are not intended to be incorporated by reference into this Proxy Statement or in any other report or document we file with the SEC, and any references to our websites are intended to be inactive textual references only.

Anti-Hedging/Pledging Policies. Our Code of Conduct expressly prohibits our directors, executive officers, and employees from engaging in speculative transactions in Company securities, including short sales, transactions in put or call options, hedging transactions, and other inherently speculative transactions. We also have an Insider Trading Compliance Policy that further prohibits our directors, executive officers, and employees from entering into any form of hedging or monetization transaction with respect to Company securities and from pledging such securities as collateral for any loans, including purchasing any Company securities on margin.

Shareholder Communications with the Board. Any shareholder who desires to communicate with the Board or any specified individual director may do so by directing such correspondence to the attention of our Company Secretary at Prothena Corporation plc, 77 Sir John Rogerson's Quay, Block C, Grand Canal Docklands, Dublin 2, D02 VK60, Ireland. The Company Secretary will forward the communication to the Board members or individual director as appropriate.

DIRECTOR COMPENSATION - FISCAL YEAR 2021

The Compensation Committee, with the assistance of its independent consultant, evaluates the compensation of the Board each year and recommends the amount of cash and equity compensation. After considering the input of the Compensation Committee's independent compensation consultant, the Compensation Committee and Board

approved the fiscal year 2021 compensation program, with the cash compensation levels remaining at the same levels as approved with respect to 2020 and an adjustment to the annual and initial equity grant levels due to the changes in the Company's stock price and market data.

Our non-employee directors, other than the Chair of the Board, each received an annual cash retainer fee of \$60,000. Our Chair received an annual cash retainer fee of \$90,000. In addition, all of our non-employee directors who serve on or chair a Board committee received the following annual committee fees:

Committee	Chair	Other Member
Audit Committee	\$20,000	\$9,000
Compensation Committee	15,000	6,000
Nominating and Corporate Governance Committee	10,000	5,000

All of these fees were paid in quarterly installments.

Each of our non-employee directors is awarded annually, on the first business day following each annual general meeting of the shareholders, a nonqualified stock option to acquire a specified number of the Company's ordinary shares. As noted above, in 2021, after considering input from the Compensation Committee's independent consultant, the number of shares subject to the annual option awards was reduced to 15,000 shares (from 17,500). These options vest on the earlier of the first anniversary of the grant date or the day of the next annual general meeting of shareholders (subject to continuous service as a director until such vesting date, except in the event of certain terminations of service) and have a ten-year term.

Any new non-employee director is awarded, on the first business day following the date of initial appointment or election to the Board, a nonqualified stock option to acquire a specified number of the Company's ordinary shares. As noted above, in 2021, after considering input from the Compensation Committee's independent consultant, the number of shares subject to the initial option awards was reduced to 30,000 shares (from 35,000). This option vests in equal annual installments over three years following the grant date with the final year vesting date being the earlier of the third anniversary of the grant date or the day of the annual general meeting of shareholders for that year (subject to continuous service as a director until each such vesting date, except in the event of certain terminations of service) and has a ten-year term.

All of these options are awarded under our 2018 Long Term Incentive Plan, as amended (the "2018 LTIP"), and have a per share exercise price equal to the closing market price of our ordinary shares on the date of grant.

Mr. Nodelman, although a non-employee director, has declined to receive any cash or equity compensation for his service on our Board or any of its committees.

Our sole non-independent director, Dr. Kinney (our President and Chief Executive Officer), does not receive any additional compensation for his service on our Board. Please see the *Summary Compensation Table - Fiscal Year 2021* for a summary of the compensation received by Dr. Kinney with respect to fiscal year 2021.

At their annual general meeting in 2020, our shareholders approved a "value-for-value" option exchange program. Pursuant to this approval, we offered the option exchange to eligible employees and directors in an issuer tender offer that closed on February 12, 2021. Under the terms of the program, eligible employees and directors could surrender outstanding options for ordinary shares granted prior to April 23, 2018, and with exercise prices equal to or greater than \$17.63, in exchange for a new option award. Members of the Board holding eligible grants were eligible to participate in the option exchange program.

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DIRECTOR COMPENSATION - FISCAL YEAR 2021

The following table sets forth the compensation paid to our non-employee directors in our fiscal year 2021.

Name	Fees Earned or Paid in Cash ⁽¹⁾ (\$)	Option Awards ⁽²⁾ (\$)	All Other Compensation (\$) ⁽³⁾	Total (\$)
Lars G. Ekman	90,000	249,273	—	339,273
Paula K. Cobb	76,877	249,273	—	326,150
Richard T. Collier	79,000	249,273	—	328,273
Shane M. Cooke	80,000	249,273	—	329,273
K. Anders O. Härfstrand	70,622	249,273	—	319,895
Christopher S. Henney	75,000	249,273	—	324,273
Oleg Nodelman ⁽⁴⁾	—	—	—	—
Sanjiv K. Patel ⁽⁵⁾	41,227	498,546	—	539,773
Dennis J. Selkoe	60,000	249,273	11,500	320,773

- (1) Consists of Board retainer, committee chair, and committee service fees, as described in the narrative above.
- (2) Consists of nonqualified stock options awarded under the 2018 LTIP. These amounts do not reflect compensation actually received. Rather, these amounts represent the grant date fair value of the options awarded in 2021, calculated in accordance with Financial Accounting Standards Board ASC Topic 718. For a discussion of the assumptions made in calculating the values reflected, see Note 9 of the Consolidated Financial Statements included in our Annual Report on Form 10-K for our fiscal year 2021, filed with the SEC on February 25, 2022 (our "Form 10-K"). Except in the case of Dr. Patel, the amounts reported represent the grant date fair value of options granted on May 19, 2021, to acquire 15,000 of the Company's ordinary shares, which options have an exercise price of \$23.97 per share (the fair market value per share on the date of grant), vest on the earlier of the first anniversary of the grant date or the day of the next annual general meeting of shareholders (subject to continuous service as a director until such vesting date), and have a ten-year term. In the case of Dr. Patel, the amount reported represents the grant date fair value of options granted on May 19, 2021, to acquire 30,000 of the Company's ordinary shares, which option has an exercise price of \$23.97 per share (the fair market value per share on the date of grant), vests in equal annual installments over three years following the grant date with the final year vesting date being the earlier of the third anniversary of the grant date or the day of the annual general meeting of shareholders for that year (subject to continuous service as a director until each such vesting date, except in the event of certain terminations of service), and has a ten-year term. Dr. Ekman, Mr. Collier, Mr. Cooke, Dr. Härfstrand, Dr. Henney, and Dr. Selkoe received replacement options in the "value-for-value" option exchange program described above. Based on the exchange ratio in relation to the price of the Company's ordinary shares at the time of the exchange, there was no aggregate incremental fair value associated with the "value-for-value" option exchange program and, thus, no additional amounts are reflected in this table due to the exchange.
- (3) Consists of consulting fees paid under a Consulting Agreement entered into on July 15, 2020, and subsequently amended and restated on September 30, 2021, between Dr. Selkoe and the Company's wholly-owned subsidiary Prothena Biosciences Inc under which Dr. Selkoe provides consulting services in connection with the Company's assessment of potential business development opportunities and matters related to partnered collaboration programs.
- (4) Mr. Nodelman has declined to receive any cash or equity compensation for his service as a director.
- (5) Dr. Patel was appointed to the Board on May 18, 2021, and his cash compensation was pro-rated for his service as a director in 2021.

As of the end of our fiscal year 2021, the total number of shares subject to outstanding option awards held by each non-employee director were as set forth in the following table. No other equity awards were held by our non-employee directors as of the end of our fiscal year 2021. Awards made prior to 2018 were made under our Amended and Restated 2012 Long Term Incentive Plan.

Name	Outstanding Option Awards (Shares)
Lars G. Ekman	181,544
Paula K. Cobb	67,500
Richard T. Collier	136,544
Shane M. Cooke	136,544
K. Anders O. Härfstrand	92,614
Christopher S. Henney	53,644
Oleg Nodelman	—
Sanjiv K. Patel	30,000
Dennis J. Selkoe	80,044

PROPOSAL NO. 2

RATIFICATION, IN A NON-BINDING VOTE, OF THE APPOINTMENT OF KPMG LLP AS OUR INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM FOR OUR FISCAL YEAR 2022 AND AUTHORIZATION, IN A BINDING VOTE, OF OUR BOARD OF DIRECTORS, ACTING THROUGH ITS AUDIT COMMITTEE, TO APPROVE THE REMUNERATION OF THAT AUDITOR

The Audit Committee is responsible for the appointment of our independent accounting firm. The Audit Committee has appointed KPMG LLP, a registered public accounting firm, as our independent accounting firm to audit our consolidated financial statements for our fiscal year ending December 31, 2022, and our shareholders are being asked to ratify that appointment and authorize the Board of Directors, acting through its Audit Committee, to approve the remuneration of KPMG LLP as our auditor. Neither our Constitution nor Irish law requires shareholder ratification of the appointment of KPMG LLP as our independent registered public accounting firm. Our Board is nonetheless submitting the appointment of KPMG LLP to our shareholders for ratification, in a non-binding vote, as a matter of good governance. The Board is also requesting that shareholders authorize, in a binding vote, the Board, acting through its Audit Committee, to approve the remuneration of KPMG LLP as our auditor.

If our shareholders fail to ratify such appointment of KPMG LLP, the Audit Committee will reconsider whether or not to retain KPMG LLP, but may still determine to maintain its appointment of KPMG LLP as our independent registered public accounting firm for our fiscal year 2022. Even if the appointment of KPMG LLP is ratified by our shareholders, the Audit Committee may appoint a different independent registered public accounting firm at any time if the Committee determines that such a change would be in the best interests of the Company and its shareholders.

KPMG LLP has audited our financial statements since the year ended December 31, 2012. Representatives of KPMG LLP are expected to attend the Annual Meeting. They will have an opportunity to make a statement if they so desire and will be available to respond to appropriate questions.

Fees Paid to KPMG

The following table sets forth fees paid to KPMG LLP for services provided to the Company for our fiscal years ended December 31, 2021 and 2020.

	Year Ended December 31,	
	2021	2020
Audit Fees ⁽¹⁾	\$1,043,267	\$613,543
Audit-Related Fees	—	—
Tax Fees ⁽²⁾	168,092	253,214
All Other Fees	—	—
Total Fees	\$1,211,359	\$866,757

(1) Consists of fees and out-of-pocket expenses for services rendered (a) for the audits of our annual financial statements, reviews of our quarterly financial statements, and audits of our Irish statutory financial statements, and (b) for the reviews of our registration statements, including the provision of comfort letters and consents.

(2) Consists of fees and out-of-pocket expenses incurred in connection with international tax compliance and tax consultation services.

Pre-Approval Policies and Procedures

The Audit Committee has adopted policies and procedures requiring that the Company obtain the Committee's pre-approval of all audit and permissible non-audit services to be provided by the Company's independent registered public accounting firm. Under those policies and procedures, all such services must be pre-approved by the Committee (although certain services may be pre-approved by the chair of the Committee followed by Committee

ratification at the next Committee meeting). Before pre-approving services, the Committee considers the estimated fees for those services and whether those services might impair KPMG LLP's independence. Pursuant to these policies and procedures, the Audit Committee pre-approved all services provided by KPMG LLP for our fiscal years 2021 and 2020.

THE BOARD OF DIRECTORS UNANIMOUSLY RECOMMENDS THAT SHAREHOLDERS VOTE FOR RATIFICATION, IN A NON-BINDING VOTE, OF THE APPOINTMENT OF KPMG LLP AS OUR INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM FOR OUR FISCAL YEAR 2022 AND AUTHORIZATION, IN A BINDING VOTE, OF OUR BOARD OF DIRECTORS, ACTING THROUGH ITS AUDIT COMMITTEE, TO APPROVE THE REMUNERATION OF THAT AUDITOR.

REPORT OF THE AUDIT COMMITTEE OF THE BOARD OF DIRECTORS

The information in this report is not "soliciting material," is not deemed "filed" with the SEC and is not to be incorporated by reference into any filing by the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether before or after the date hereof and irrespective of any general incorporation language in any such filing.

The primary purpose of the Audit Committee is to oversee the Company's financial reporting processes on behalf of our Board. The Audit Committee's functions are more fully described in its charter, which is available on our website at <http://ir.prothena.com/corporate-governance>. Management has the primary responsibility for our financial statements and reporting processes including our systems of internal controls. In fulfilling its oversight responsibilities, the Audit Committee reviewed and discussed with management the Company's audited consolidated financial statements as of and for the year ended December 31, 2021.

The Audit Committee reviewed and discussed with KPMG LLP, the Company's independent registered public accounting firm, the matters required to be discussed by the applicable requirements of the Public Company Accounting Oversight Board (the "PCAOB") and the U.S. Securities and Exchange Commission. In addition, the Audit Committee discussed with KPMG LLP their independence, and received from KPMG LLP and reviewed the written disclosures and the letter required by Ethics and Independence Rule 3526 of the PCAOB. Finally, the Audit Committee discussed with KPMG LLP, with and without management present, the scope and results of KPMG LLP's audit of such financial statements.

Based on these reviews and discussions, the Audit Committee recommended to our Board that such audited financial statements be included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2021, for filing with the U.S. Securities and Exchange Commission.

Shane M. Cooke (Committee Chair)
Richard T. Collier
K. Anders O. Härfstrand
Christopher S. Henney

PROPOSAL NO. 3

APPROVAL, IN A NON-BINDING ADVISORY VOTE, OF THE COMPENSATION OF OUR EXECUTIVE OFFICERS NAMED IN THIS PROXY STATEMENT ("SAY-ON-PAY")

Summary

We are providing our shareholders with the opportunity to vote on a resolution to approve, on an advisory (non-binding) basis, the compensation of our named executive officers - our Chief Executive Officer, our Chief Financial Officer, and our other three most highly compensated executive officers. This advisory shareholder vote pursuant to the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010 - commonly known as "Say-on-Pay" - gives our shareholders the opportunity to endorse or not endorse the named executive officer compensation as described and explained in the *Compensation Discussion and Analysis*, compensation tables, and accompanying narrative disclosures in this Proxy Statement. We encourage you to carefully review that information.

We believe that the compensation of our named executive officers for fiscal year 2021 was aligned with the Company's performance during 2021 and its go-forward strategy. As is described in the *Compensation Discussion and Analysis*:

2021 Performance Highlights. We are a late-stage clinical company with a robust pipeline of investigational therapeutics with the potential to change the course of devastating neurodegenerative and rare peripheral amyloid diseases. Our executive compensation programs are designed to reward superior performance and provide consequences for under-performance. We believe that compensation of our named executive officers for fiscal year 2021 was aligned with the Company's performance during 2021 and its go-forward strategy. Highlights of that performance include:

- **We Made Significant Advances in our Neurodegenerative Diseases Portfolio.**

- PRX012, a potential best-in-class treatment for Alzheimer's disease (AD), is an investigational monoclonal antibody targeting a key epitope at the N-terminus of amyloid beta (A β) with high binding potency. We presented preclinical results demonstrating that

PRX012 significantly cleared both pyroglutamate-modified and -unmodified A β plaque in post-mortem brain tissue of late-stage AD patients.

- PRX005, a potential best-in-class treatment for AD, is an investigational antibody that specifically targets a key epitope within the microtubule binding region (MTBR) of tau, a protein implicated in diseases including AD, frontotemporal dementia (FTD), progressive supranuclear palsy (PSP), chronic traumatic encephalopathy (CTE), and other tauopathies. PRX005 is part of the global neuroscience research and development collaboration with Bristol Myers Squibb. We filed an Investigational New Drug (IND) application for PRX005, received \$80 million option payment from Bristol Myers Squibb for execution of a U.S. license agreement, and initiated a Phase 1 study.
- Dual A β -tau vaccine, a potential first-in-class prevention and treatment for AD, is a dual-target vaccine targeting key epitopes within the A β and tau proteins to promote amyloid clearance and blockade of pathogenic tau. We presented preclinical data demonstrating that the dual A β -tau vaccine generated appropriate and balanced antibody titers promoting both phagocytosis of A β plaque and blockade of tau transmission *in vitro*.
- Prasinezumab (PRX002/RG7935), a potential first-in-class treatment for Parkinson's disease, is an investigational humanized monoclonal antibody designed to target key epitopes within the C-terminus of alpha-synuclein and is the focus of the worldwide collaboration with Roche. We earned a \$60 million clinical milestone payment upon dosing of the first patient in the global Phase 2b PADOVA study for prasinezumab.

• **We Made Significant Advances in our Rare Peripheral Amyloid Diseases Portfolio.**

- Birtamimab, a potential best-in-class amyloid depleter treatment for AL amyloidosis, is an investigational humanized monoclonal antibody designed to directly neutralize soluble toxic aggregates and promote clearance of amyloid that causes organ dysfunction and failure. We reached a Special Protocol Assessment (SPA) agreement with the U.S. Food and Drug Administration (FDA) to advance birtamimab into a confirmatory Phase 3 study in Mayo Stage IV patients. We then initiated AFFIRM-AL, a global, registration-enabling Phase 3 study that will be conducted with a primary endpoint of all-cause mortality at $p \leq 0.10$ under the SPA agreement with FDA.
- PRX004, a potential first-in-class treatment for ATTR amyloidosis, is an investigational humanized monoclonal antibody designed

to deplete the pathogenic, non-native forms of the TTR protein. We announced the Novo Nordisk acquisition of our ATTR amyloidosis business, under which we are eligible to receive a total aggregate of up to \$1.23 billion, and we received a \$60 million upfront payment from Novo Nordisk.

- **We Carefully Managed and Increased our Cash Balance.** During fiscal year 2021, we carefully managed our capital. While progressing all of our development programs described above, our cash provided by operating and investing activities was \$92 million, in the middle of our revised guidance range of \$85 to \$95 million. We finished 2021 with \$580.4 million in cash, cash equivalents, and restricted cash, including cash provided by operating and financing activities, at the top end of our revised guidance range of \$570 to \$580 million, providing a solid financial foundation for continuing to advance the Company’s discovery and clinical programs.

Board Recommendation

Our Board believes that the information provided above and in the *Compensation Discussion and Analysis*, compensation tables, and accompanying narrative disclosures in this Proxy Statement demonstrate that our executive compensation programs were designed appropriately and are working to align the interests of our management team with the interests of our shareholders and support long-term value creation, and that those interests were well-served in fiscal year 2021. Accordingly, we are asking shareholders to approve the following non-binding advisory resolution at the Annual Meeting:

RESOLVED, that the shareholders of Prothena Corporation plc (the “Company”) approve, on an advisory basis, the compensation of the Company’s named executive officers, as disclosed in the *Compensation Discussion and Analysis*, compensation tables, and accompanying narrative disclosures set forth in this Proxy Statement.

The vote on this Proposal No. 3 is advisory, and, therefore, not binding on the Company, our Board, or its Compensation Committee. Although non-binding, our Board and its Compensation Committee will review and consider the voting on this Proposal No. 3 when making future decisions regarding compensation of our named executive officers.

THE BOARD OF DIRECTORS UNANIMOUSLY RECOMMENDS THAT SHAREHOLDERS VOTE FOR THE NON-BINDING ADVISORY RESOLUTION APPROVING THE COMPENSATION OF OUR NAMED EXECUTIVE OFFICERS.

PROPOSAL NO. 4

APPROVAL, IN A NON-BINDING ADVISORY VOTE, OF THE FREQUENCY OF FUTURE SAY ON PAY VOTES BY SHAREHOLDERS OF THE COMPENSATION OF EXECUTIVE OFFICERS NAMED IN THE PROXY STATEMENT

Summary

The Dodd-Frank Act enables our shareholders to indicate how frequently they believe we should seek an advisory (non-binding) vote from shareholders on the compensation of our named executive officers, i.e., how frequently to request future “Say-on-Pay” votes from shareholders. We are accordingly seeking a non-binding advisory vote from shareholders as to the frequency with which our shareholders should have an opportunity to provide an advisory approval of our named executive officer compensation. We are providing our shareholders with the choice of selecting a frequency of one, two, or three years.

The Company currently holds an advisory “Say-on-Pay” vote from shareholders every year. We believe that this frequency is appropriate because it will enable our shareholders to vote, on an advisory basis, on the most recent executive compensation information that is presented in each of our proxy statements, leading to a more meaningful and regular communication between the Company and our shareholders on the compensation of our named executive officers.

Board Recommendation

Based on these factors, the Board recommends that future advisory votes by shareholders on named executive officer compensation continue to occur every year, at least until the next advisory vote on the frequency of future “Say-on-Pay” votes. Shareholders are not being asked to approve or disapprove the Board’s recommendation, but rather to indicate their choice among the following frequency options: one year, two years or three years, or to abstain from voting on this item. If none of the frequency alternatives - one year, two years or three years - receives a majority of the votes cast, we will consider the highest number of votes cast by shareholders to be the frequency that has been selected by shareholders. Accordingly,

we are asking shareholders to approve the following non-binding advisory resolution at the Annual Meeting:

RESOLVED, that the compensation of named executive officers of Prothena Corporation plc (the “Company”) be submitted to an advisory vote by the Company’s shareholders every (a) year, (b) two years, or (c) three years, with such alternative that receives the highest number of votes cast representing the vote of shareholders.

The vote on this resolution is advisory, and therefore not binding on the Company, our Board, or its Compensation Committee. The Board may decide that it is in the best interests of the Company and its shareholders to hold future advisory “Say-on-Pay” votes more or less frequently than the frequency indicated by shareholders in voting on this proposal.

THE BOARD OF DIRECTORS RECOMMENDS THAT SHAREHOLDERS APPROVE, IN A NON-BINDING ADVISORY VOTE, THAT FUTURE ADVISORY VOTES BY SHAREHOLDERS ON THE COMPENSATION OF OUR NAMED EXECUTIVE OFFICERS BE REQUESTED EVERY YEAR.

PROPOSAL NO. 5

APPROVAL OF AN AMENDMENT TO THE PROTHENA CORPORATION PLC 2018 LONG TERM INCENTIVE PLAN TO INCREASE THE NUMBER OF ORDINARY SHARES AVAILABLE FOR ISSUANCE UNDER THAT PLAN BY 2,000,000 ORDINARY SHARES

Summary

On February 23, 2022, our Board adopted, subject to shareholder approval, a further amendment (the “Amendment”) to the Prothena Corporation plc 2018 Long Term Incentive Plan, as amended (the “2018 LTIP” and, as proposed to be amended by the Amendment, the “Amended 2018 LTIP”) to increase the number of shares available under the 2018 LTIP by 2,000,000 shares. The effectiveness of the Amendment is subject to approval by our shareholders.

The 2018 LTIP was adopted by our Board on February 21, 2018, and approved by our shareholders on May 15, 2018, and subsequently amended by our Board and approved by our shareholders in 2020 and 2021. The 2018 LTIP superseded and replaced in its entirety our Amended and Restated 2012 Long Term Incentive Plan (the “2012 LTIP”). The number of our ordinary shares available for issuance under the 2018 LTIP, prior to approval of the Amendment, is equal to the sum of (a) 5,100,000 shares, (b) 1,177,933 shares, which is the number of shares that were available for issuance under the 2012 LTIP as of May 15, 2018, the effective date of the 2018 LTIP, and (c) any shares subject to issued and outstanding awards under the 2012 LTIP that expired, were cancelled or otherwise terminated, or that in the future expire, are cancelled or otherwise terminate, following the effective date of the 2018 LTIP.

We are proposing the Amendment solely to increase the number of ordinary shares available for issuance under the 2018 LTIP by 2,000,000 ordinary shares, which we believe is necessary to help ensure that the Company has a sufficient reserve of ordinary shares available to attract and retain the services of key individuals essential to the Company's long-term growth and success.

Employees and consultants of the Company and its subsidiaries and affiliates, as well as members of our Board, are eligible to receive awards under the 2018 LTIP. The 2018 LTIP provides for the grant of options, including incentive stock options (“ISOs”) and nonqualified stock options (“NQSOs”), share appreciation rights (“SARs”), restricted shares, restricted share units (“RSUs”), performance bonus awards, performance share units awards, other share or cash-based awards, and dividend equivalents to eligible individuals.

If shareholders do not approve this Proposal No. 4, the Amended 2018 LTIP will not become effective, and the current 2018 LTIP, without the share increase proposed in the Amendment, will continue in full force and effect subject to the limitations set forth therein.

Key Features of the 2018 LTIP

The 2018 LTIP reflects a broad range of compensation and governance best practices, including the following:

- **Automatic acceleration of awards only if not assumed or substituted.** The 2018 LTIP provides that awards will automatically accelerate upon a change in control only if not assumed or substituted, and further that any such performance-based awards will vest based on the higher of (a) actual performance as of the change in control,

or (b) target performance, prorated based on a shortened performance period as of the change in control.

- **Prohibition of liberal share recycling on all awards.** The 2018 LTIP prohibits any shares withheld for taxes on all awards from being added back to the share reserve, in addition to prohibiting other practices considered to be liberal share recycling with respect to options and SARs.

- **Minimum vesting requirements.** Subject to limited exceptions, no awards granted under the 2018 LTIP may vest until the first anniversary of the date of grant, and awards other than options and SARs made to our employees or consultants must become vested over a period of not less than three years.
- **Payment of dividends only if underlying awards vest.** Dividends and dividend equivalents may only be paid to the extent the underlying award vests.
- **No dividends on options or SARs.** The 2018 LTIP prohibits the payment of dividends with respect to options and SARs.
- **No repricing or exchange of awards without shareholder approval.** Awards may not be repriced, replaced, exchanged, or re-granted through cancellation or modification without shareholder approval if the effect would be to reduce the exercise price for the shares under the award.
- **No transferability.** Equity awards may only be transferred under limited circumstances and in any event without consideration.
- **Fungible share counting; limit on full value awards.** Shares issued as full-value awards (awards other than options, SARs, or any other award for which the holder pays the intrinsic value existing as of the date of grant) will have the effect of reducing the aggregate number of shares available for issuance on a 1.5-to-1 basis. Accordingly, if shareholders approve the Amendment adding 2,000,000 ordinary shares available for issuance under the 2018 LTIP, the maximum number of those shares that may be issued as full-value awards under the Amended 2018 LTIP will be 2,000,000.
- **No evergreen feature/shareholder approval required for share reserve increases.** The 2018 LTIP does not provide for an annual increase in the share reserve, and the 2018 LTIP may not be amended to increase the share reserve without shareholder approval.

Outstanding Awards Under our Equity Incentive Plans

As of March 7, 2022, under the 2018 LTIP and the 2012 LTIP:

- 9,006,763 of our ordinary shares were subject to outstanding option awards, with a weighted average exercise price of \$20.87 and a weighted average remaining term of 7.13 years;
- No ordinary shares were subject to any other types of outstanding awards; and
- 1,410,367 ordinary shares remained available for future grant under only the 2018 LTIP.

The 1,410,367 ordinary shares available for future grant under the 2018 LTIP as of March 7, 2022, includes 741,818 ordinary shares returned to the 2018 LTIP as a result of our “value-for-value” option exchange program approved by our shareholders on May 19, 2020, and implemented through a tender offer that closed on February 12, 2021.

On February 25, 2020, our Board approved our 2020 Employment Inducement Incentive Plan, and subsequently adopted a series of amendments to increase the ordinary shares available for issuance (as amended, the “2020 EIIP”). Since adoption, we have used the 2020 EIIP to induce our Chief Business Officer (now our Chief Operating Officer), our Chief

Medical Officer, and 19 other employees at the director level and above to join the Company in 2020 and 2021. As of March 7, 2022, under the 2020 EIIP:

- 1,317,508 of our ordinary shares were subject to new-hire option awards, with a weighted average exercise price of \$25.65, and a weighted average remaining term of 8.78 years;
- No ordinary shares were subject to any other types of outstanding awards; and
- No ordinary shares remained available for future grant under the 2020 EIIP, but the Board and the Compensation Committee reserve the right to further amend the 2020 EIIP from time-to-time to increase the number of ordinary shares available for issuance and to make additional awards to key new-hires.

Thus, as of March 7, 2022, under the 2018 LTIP, the 2012 LTIP, and the 2020 EIIP:

- 10,324,271 of our ordinary shares were subject to outstanding option awards, with a weighted average exercise price of \$21.48 and a weighted average remaining term of 7.34 years;

- No ordinary shares were subject to any other types of outstanding awards; and
- 1,410,367 ordinary shares remained available for future grant under only the 2018 LTIP.

The closing price of our ordinary shares on March 7, 2022, was \$30.27 per share.

Why You Should Vote FOR the Amendment to the 2018 LTIP

In its determination to approve the Amendment, our Board considered an analysis prepared by Radford (an Aon Company), the compensation consultant for the Compensation Committee of our Board, which included an analysis of our historical share usage, certain burn rate metrics, and the costs of the 2018 LTIP. Specifically, our Board considered the following:

- We need the additional 2,000,000 shares requested in the Amendment to retain and hire the talent deemed necessary to execute on our research and development objectives and long-term strategy. We expect that share authorization, used in conjunction with our 2020 EIIP where appropriate, to provide us with enough shares for awards for at least one year (until the annual meeting of our shareholders in 2023).
- In determining the reasonableness of the Amendment, our Board considered our historic equity “burn rate.” Equity burn rate is calculated by dividing the number of shares subject to equity awards granted during the fiscal year (without adjusting for forfeitures) by the weighted average ordinary shares outstanding during the fiscal year. In 2021, 2020, and 2019, we granted stock options representing a total of 3,530,477 shares (1,372,587 of which were replacement options granted pursuant to the Option Exchange), 2,108,950 shares, and 1,315,975 shares, respectively, under the 2018 LTIP and the 2020 EIIP. This level of option awards represents a three-year average burn rate of approximately 5.5% of weighted average ordinary shares outstanding.

Unlike over two-thirds of our peer group, we do not have an evergreen provision in our 2018 LTIP.

- Our Compensation Committee considers option awards to be a particularly effective incentive and retention tool because they motivate our employees to increase shareholder value and

remain with the Company. Options link compensation directly to increases in the price of our ordinary shares, which directly reflects increased shareholder value; and our options have generally required continued employment for four years in order to fully vest. All of the companies in the peer group used by the Compensation Committee used option awards for at least a portion of equity compensation.

- Our use of option awards is broad-based across our organization. All of our employees participate in the 2018 LTIP and/or the 2020 EIIP and we currently expect to continue this approach.

In light of the factors described above, and that the ability to continue to grant equity compensation is vital to our ability to continue to attract and retain employees in the highly competitive labor markets in which we compete, our Board has determined that the size of the share reserve under the Amended 2018 LTIP, as proposed to be augmented pursuant to the Amendment, is reasonable and appropriate at this time.

A summary of the principal provisions of the Amended 2018 LTIP is set forth below. This summary is qualified by reference to the Amendment, which is attached as Appendix B to this Proxy Statement; the Prothena Corporation plc 2018 Long Term Incentive Plan, which is available as Exhibit 10.1 of the Company's Current Report on Form 8-K filed with the SEC on May 18, 2018; the First Amendment to the Prothena Corporation plc 2018 Long Term Incentive Plan, which is available as Exhibit 10.1 of the Company's Current Report on Form 8-K filed with the SEC on May 22, 2020; and the Second Amendment to the Prothena Corporation plc 2018 Long Term Incentive Plan, which is available as Exhibit 10.1 of the Company's Current Report on Form 8-K filed with the SEC on May 21, 2021.

Administration

The Amended 2018 LTIP may be administered by our Board, its Compensation Committee, or such other

committee of the Board (the “Committee”) as is designated by the Board. To the extent required to

comply with Rule 16b-3 of the U.S. Exchange Act, it is intended that each member of the Committee will be a “non-employee director” within the meaning of Rule 16b-3. The Committee or our Board may delegate its powers under the Amended 2018 LTIP to one or more members of the Board or one or more directors, officers, or managers of the Company or any subsidiary, provided that no officer may be delegated the authority to grant awards to or amend awards held by senior executives of the Company who are subject to Section 16 of the Exchange Act or any officer or director to whom authority to grant or amend awards has been del

egated. The Board, the Committee, or a delegate thereof, as applicable, are referred to herein as the “plan administrator.”

The plan administrator has the authority to administer the Amended 2018 LTIP, including the power to determine eligibility, the types and sizes of awards, the price and vesting schedule of awards, the methods for settling awards, the method of payment for any exercise or purchase price, any rules and regulations the plan administrator deems necessary to administer the Amended 2018 LTIP, and the acceleration or waiver of any vesting restriction.

Eligibility

Persons eligible to participate in the Amended 2018 LTIP include all members of our Board, which as of March 7, 2022, was comprised of nine non-employee directors, and as of the same date approximately

92 employees (including nine executive officers) and approximately 31 consultants of the Company and its subsidiaries, in each case, as determined by the plan administrator.

Limitation on Awards and Shares Available

If our shareholders approve the Amendment, the number of ordinary shares authorized for issuance under the Amended 2018 LTIP will be equal to the sum of (a) 7,100,000 shares, (b) 1,177,933 shares, which is the number of shares that were available for issuance under the 2012 LTIP as of May 15, 2018, the effective date of the 2018 LTIP, (c) 5,514,183 shares, which is the number of shares that were subject to issued and outstanding awards under the 2012 LTIP that as of March 7, 2022, had expired, been cancelled, or otherwise terminated following May 15, 2018 (the effective date of the 2018 LTIP), and (d) any shares subject to issued and outstanding awards under the 2012 LTIP that expire, are cancelled, or otherwise terminate subsequent to March 7, 2022; provided, that no more than 2,500,000 shares may be issued pursuant to the exercise of ISOs. In addition, the aggregate number of shares available for issuance under the Amended 2018 LTIP will be reduced by 1.5 shares (the “Fungible Share Counting Ratio”) for each share delivered in settlement of any awards other than an option, SAR, or any other award for which the holder pays the intrinsic value existing as of the date of grant (each, a “Full Value Award”). The ordinary shares distributed pursuant to an award under the Amended 2018 LTIP may be (a) authorized but unissued shares, (b) shares purchased by the Company on the open market, or (c) treasury shares.

If any shares subject to an award under the Amended 2018 LTIP or any award under the 2012 LTIP are forfeited, expire, or are settled for cash, any shares deemed subject to such award (taking into account the Fungible Share Counting Ratio with respect to Full Value Awards granted under the Amended 2018 LTIP) may, to the extent of such forfeiture, expiration, or cash settlement, be used again for new grants under the Amended 2018 LTIP. However, the following shares may not be used again for grants under the Amended 2018 LTIP: (1) shares tendered or withheld to satisfy the exercise price of an option; (2) shares tendered or withheld to satisfy the tax withholding obligations with respect to an award; (3) shares subject to an SAR that are not issued in connection with the share settlement of the SAR on its exercise; and (4) shares purchased on the open market with the cash proceeds from the exercise of options. Awards granted under the Amended 2018 LTIP in connection with the assumption or substitution of outstanding equity awards previously granted by a company or other entity in the context of a corporate acquisition or merger will not reduce the shares authorized for grant under the Amended 2018 LTIP.

Under the Amended 2018 LTIP, Full Value Awards (as defined in the Amended 2018 LTIP) granted to employees or consultants of the Company, other than options and SARs, must vest over a period of not less than three years measured from the date of

grant or, in the case of performance-vesting awards, a period of not less than one year measured from the beginning of the applicable performance period, provided that the award agreement may provide that such vesting restrictions may lapse or be waived upon a participant's termination of service. The Company has committed to applying this minimum vesting requirement to members of our Board if they are to receive such awards.

In addition, all awards (or any portion thereof) granted under the Amended 2018 LTIP must vest no earlier than one year measured from the date of grant and no award agreement shall reduce or

eliminate such minimum vesting requirement, provided that an award may provide that such minimum vesting restrictions may lapse or be waived upon a participant's termination of service. In addition, up to an aggregate of five percent of the number of shares available for issuance under the Amended 2018 LTIP as of its effective date may be granted without regard to the foregoing minimum vesting requirement. For the purposes of awards to non-employee directors, a vesting period shall be deemed to be one year if it runs from the date of one annual meeting of our shareholders to the next annual meeting of our shareholders.

Awards

The Amended 2018 LTIP provides for the grant of ISOs, NQSOs, SARs, restricted shares, RSUs, performance bonus awards, performance share units awards, other share or cash-based awards, and dividend equivalents. All

awards under the Amended 2018 LTIP are set forth in award agreements, which detail all terms and conditions of the awards, including any applicable vesting and payment terms and post-termination exercise limitations. No fractional shares may be issued or delivered pursuant to the Amended 2018 LTIP or any award thereunder.

Options. Options provide for the purchase of ordinary shares in the future at an exercise price set on the grant date. ISOs, by contrast to NQSOs, may provide tax deferral beyond exercise and favorable capital gains tax treatment to their holders if certain holding period and other requirements of the U.S. Internal Revenue Code of 1986, as amended (the "Code") are satisfied. The exercise price of an option may not be less than 100% of the fair market value of the underlying share on the date of grant (or 110% in the case of ISOs granted to certain significant shareholders), except with respect to certain substitute options granted in connection with a corporate transaction. The term of an option may not be longer than ten years (or five years in the case of ISOs granted to certain significant shareholders). Vesting conditions determined by the plan administrator may apply to options and may include continued service, performance and/or other conditions.

Share Appreciation Rights. SARs entitle their holder, upon exercise, to receive an amount equal to the appreciation of the shares subject to the award between the grant date and the exercise date. The

exercise price of an SAR may not be less than 100% of the fair market value of the underlying share on the date of grant (except with respect to certain substitute SARs granted in connection with a corporate transaction) and the term of an SAR may not be longer than ten years. Vesting conditions determined by the plan administrator may apply to SARs and may include continued service, performance and/or other conditions. SARs will be settled in cash or ordinary shares, or in a combination of both, as determined by the plan administrator.

Restricted Shares. A restricted share award is an award of nontransferable ordinary shares that remain forfeitable unless and until specified vesting conditions are met. Vesting conditions applicable to restricted shares may be based on continuing service, the attainment of performance goals and/or such other conditions as the plan administrator may determine. In general, restricted shares may not be sold or otherwise transferred until restrictions are removed or expire. Participants holding restricted shares will have voting rights and will have the right to receive dividends; however, dividends may not be paid until the applicable restricted shares vests.

Restricted Share Units. RSUs are contractual promises to deliver ordinary shares (or the fair market value of such shares in cash) in the future, which may also remain forfeitable unless and until specified vesting conditions are met. RSUs generally may not be sold or transferred until vesting conditions are removed or expire. The shares underlying RSUs will not be issued until the RSUs have vested, and recipients of RSUs generally will have no voting or dividend rights prior to the time the RSUs are settled in shares. Delivery of the shares underlying RSUs may be deferred under the terms of the award or at the election of the participant, if the plan administrator

permits such a deferral. On the settlement date or dates, we will issue to the participant one unrestricted, fully transferable ordinary share (or the fair market value of one such share in cash) for each vested and non-forfeited RSU.

Performance Share Units and Performance Bonus Awards. Performance share unit awards are denominated in shares or unit equivalents, and performance bonus awards are denominated in cash. Each may be linked to one or more performance or other criteria as determined by the plan administrator.

Other Share or Cash Based Awards. Other share or cash based awards are awards of cash, fully vested ordinary shares, and other awards valued wholly or partially by referring to, or otherwise based on, our ordinary shares. Other share or cash based awards

may be granted to participants and may also be available as a payment form in the settlement of other awards, as standalone payments or as payment in lieu of base salary, bonus, fees, or other cash compensation otherwise payable to any individual who is eligible to receive awards. The plan administrator will determine the terms and conditions of other share or cash based awards, which may include vesting conditions based on continued service, performance, and/or other conditions.

Dividend Equivalents. Dividend equivalents represent the right to receive the equivalent value of dividends paid on our ordinary shares and may be granted alone or in tandem with awards other than options or SARs. Dividend equivalents may accrue on awards, but are not be payable unless and until the applicable award vests.

Amendment and Termination

Our Board may amend or terminate the Amended 2018 LTIP at any time; however, except in connection with certain changes in our capital structure, shareholder approval will be required for any amendment that increases the aggregate number of shares available under the Amended 2018 LTIP, “reprices” any option or SAR, or cancels any option or SAR in exchange for cash or another award when the option or SAR price per share exceeds the fair

market value of the underlying shares. In addition, no amendment, suspension, or termination of the Amended 2018 LTIP may, without the consent of the affected participant, materially and adversely affect the participant’s rights. No award may be granted pursuant to the Amended 2018 LTIP after the tenth anniversary of the date the 2018 LTIP was adopted by our Board (which was February 21, 2018).

Corporate Transactions

The plan administrator has broad discretion to take action under the Amended 2018 LTIP, as well as make adjustments to the terms and conditions of existing and future awards, to prevent the dilution or enlargement of intended benefits and facilitate necessary or desirable changes in the event of certain transactions and events affecting our ordinary shares, such as share dividends, share splits, mergers, acquisitions, consolidations and other corporate transactions. In addition, in the event of certain non-reciprocal transactions with our shareholders known as “equity restructurings,” the plan administrator will make equitable adjustments to the 2018 LTIP and outstanding awards.

If a “Change in Control” of the Company occurs (as defined in the Amended 2018 LTIP), all outstand

ing options and SARs that are not exercised shall be assumed or substituted by the surviving corporation and other outstanding awards shall be converted into similar awards of the surviving corporation. If the surviving corporation refuses to assume or substitute for an award, the award shall accelerate and become fully vested and exercisable upon the Change in Control and all restrictions on the award shall lapse, provided that any awards subject to performance-based vesting will vest based on the greater of (a) actual performance as of the Change in Control, or (b) target performance, prorated based on a shortened performance period ending as of the Change in Control.

U.S. Federal Income Tax Consequences

The following is a brief summary of certain United States federal income tax consequences generally arising with respect to awards under the Amended 2018 LTIP. This discussion does not address all aspects of the United States federal income tax consequences of participating in the Amended 2018 LTIP that may be relevant to participants in light of their personal investment or tax circumstances and does not discuss any state, local, or non-United States tax consequences of participating in the Amended 2018 LTIP. Each participant is advised to consult their particular tax advisor concerning the application of the United States federal income tax laws to such participant's particular situation, as well as the applicability and effect of any state, local, or non-United States tax laws before taking any actions with respect to any awards.

With respect to NQSOs, the Company (or the applicable employer) is generally entitled to deduct and the recipient of the option recognizes ordinary income in an amount equal to the difference between the option exercise price and the fair market value of the shares at the time of exercise, subject to the deduction limitations under Section 162(m) of the Code. The gain or loss (in an amount equal to the difference between the fair market value on the date of sale and the exercise price) upon disposition of such shares will be treated as a long-term capital gain or loss, and neither the Company nor the applicable employer will be entitled to any deduction.

With respect to ISOs, if applicable holding period requirements are met (*i.e.*, the shares acquired upon exercise of an ISO is held for a minimum of two years from the date of grant and one year from the date of exercise), the participant will not recognize taxable income at the time of exercise of the ISO. However, the excess of the fair market value of the

ordinary shares received over the exercise price is an item of tax preference income potentially subject to the alternative minimum tax. The gain or loss (in an amount equal to the difference between the fair market value on the date of sale and the exercise price) upon disposition of such shares will be treated as a long-term capital gain or loss, and neither the Company nor the applicable employer will be entitled to any deduction. If the holding period requirements described above are not met, the ISO will be treated as one which does not meet the requirements of the Code for ISOs and the tax consequences described for NQSOs will apply in the year of disposition, although the amount of income recognized by the participant will be the lesser of (a) the excess of the fair market value of the shares at the time of exercise over the exercise price, or (b) the excess of the amount realized on the disposition over the exercise price.

The current federal income tax consequences of other awards authorized under the Amended 2018 LTIP generally follow certain basic patterns: SARs are taxed and deductible in substantially the same manner as NQSOs; nontransferable restricted shares subject to a substantial risk of forfeiture will result in income recognition equal to the excess of the fair market value over the price paid, if any, only at the time the restrictions applicable to such awards lapse (unless the recipient elects to accelerate recognition as of the date of grant); RSUs, share-based performance awards, dividend equivalents, and other types of awards are generally subject to tax at ordinary income rates at the time of payment. In each of the foregoing cases, the Company will generally have a corresponding deduction at the time the participant recognizes income, subject to Section 162(m) of the Code with respect to covered employees.

New Plan Benefits

The Amended 2018 LTIP does not require set benefits or amounts to be granted to participants, but instead awards are subject to the discretion of the plan administrator. Therefore, it is not possible to determine the benefits that will be received in the future by other participants in the Amended 2018 LTIP. Information regarding awards granted in 2021 under the Amended 2018 LTIP to the named executive

officers is provided in the *Summary Compensation Table – Fiscal Year 2021* and the *Grants of Plan-Based Awards – Fiscal Year 2021* table. Information regarding awards granted in 2021 under the Amended 2018 LTIP to non-employee directors is provided in the *Director Compensation – Fiscal Year 2021* table.

Equity Award Grants Under the 2018 LTIP and the 2020 EIIP Since Inception

The following table provides summary information concerning the number of shares of our ordinary shares subject to awards granted under the 2018 LTIP and the 2020 EIIP to our named executive offi

cers, directors, and employees since the 2018 LTIP's effective date through March 7, 2022, and also shows the impact of participation in the option exchange.

Name and Position	Number of Shares Underlying Option Grants (#)	Weighted Average Exercise Price of Options (\$)
Gene G. Kinney, Ph.D., President and Chief Executive Officer, Director	2,009,700	18.87
Tran B. Nguyen, Chief Strategy Officer and Chief Financial Officer	808,837	18.94
Hideki Garren, M.D., Ph.D., Chief Medical Officer	335,000	26.82
Brandon S. Smith, Chief Operating Officer	406,000	20.84
Carol D. Karp, Chief Regulatory Officer	507,394	19.73
All current executive officers as a group	5,641,423	19.33
All current directors who are not executive officers as a group	622,834	17.07
Paula K. Cobb, Director and director nominee	67,500	13.46
Lars G. Ekman, Director and director nominee	86,544	17.07
Sanjiv K. Patel, Director and director nominee	30,000	23.97
Each associate of any such executive officer, director or director nominee	—	—
Each other person who received or is to receive 5 percent of such options, warrants or rights	—	—
All employees, including all current officers who are not executive officers, as a group	5,342,345	22.45

Vote Required; Recommendation of the Board

The affirmative vote of a simple majority of the votes cast in person or by proxy at the Annual Meeting is required for approval of this proposal. Abstentions

and broker non-votes will not have any effect on the outcome of voting on any of this proposal.

THE BOARD OF DIRECTORS UNANIMOUSLY RECOMMENDS THAT SHAREHOLDERS VOTE FOR APPROVAL OF THE AMENDMENT TO THE COMPANY'S 2018 LONG TERM INCENTIVE PLAN TO INCREASE THE NUMBER OF ORDINARY SHARES AVAILABLE FOR ISSUANCE UNDER THAT PLAN BY 2,000,000 ORDINARY SHARES.

BACKGROUND DISCUSSION ON PROPOSAL NOS. 6 AND 7

Introduction

Why we are presenting Proposal Nos. 5 and 6. As a matter of Irish law, directors of an Irish public limited company must have specific authority from shareholders to allot and issue any of the company's shares (other than pursuant to employee equity compensation plans). In addition, when the directors of an Irish public limited company determine that it is in the best interests of the company to issue shares for cash, the company must first offer those shares on the same or more favorable terms to existing shareholders of the company on a pro-rata basis (commonly referred to as the statutory pre-emption right) unless the directors opt out of - i.e., "dis-apply" - the statutory pre-emption right under an authority conferred by the constitution of the company or approved by shareholders. Companies incorporated in the U.S. are not subject to similar share issuance restrictions.

Why we are incorporated in Ireland and listed in the U.S. Prothena was formerly substantially all of the drug discovery business of Elan Corporation, plc ("Elan"), an Irish public limited company formed in 1969. In connection with the planned separation of the drug discovery business from Elan - in what is commonly referred to as a "spin off" transaction - Prothena was formed on September 26, 2012, under the laws of Ireland. Elan's drug discovery business was then distributed to Prothena on December 20, 2012, and Prothena commenced trading the next day on The Nasdaq Global Market. Both Elan and Prothena were at all times Irish companies, i.e., neither became an Irish company through an "inversion" transaction. In preparing for becoming a separate publicly-traded company, Prothena's management and Board of Directors determined to list its shares only on The Nasdaq Global Market based on their assessment that it would provide the best access to the capital Prothena would require in order to advance the development of its product candidates and otherwise achieve its strategic goals.

Our current share issuance authorities. When it formed on September 26, 2012, Prothena's initial Articles of Association (now referred to as its Constitution) authorized our Board of Directors to allot and issue shares up to a maximum of our authorized but unissued share capital and to opt out of the statu-

tory pre-emption right. These authorizations were renewed by our shareholders in 2017 with the support of approximately 89% of the shares voted. Accordingly, subject to The Nasdaq Stock Market ("Nasdaq") and SEC rules and regulations, our Board is currently authorized to issue shares, without shareholder approval, up to a maximum of our authorized but unissued share capital, and is further authorized to issue those shares for cash without first being required to offer those shares to all of our shareholders on a pro-rata basis. In this Proxy Statement, we refer to our Board's authority to allot and issue shares and our Board's authority to opt out of the statutory pre-emption right collectively as our share issuance authorities. Our current share issuance authorities have, since Prothena was first formed, kept us on an equal footing with our peer companies who are incorporated and listed in the U.S. However, unless renewed by our shareholders, our current share issuance authorities will expire on May 17, 2022.

Renewal of our current share issuance authorities will allow us to continue to execute on our business and growth strategy without competitive disadvantage. Proposal Nos. 5 and 6 ask our shareholders to renew, for another five years, the same share issuance authorities that have been in place and that we have been operating under since Prothena was formed. Approval of these proposals would extend - but would *not* expand - the current share issuance authorities of our Board. We are and will continue to be subject to all of the shareholder approval and other requirements that arise from our ordinary shares being listed exclusively on The Nasdaq Global Select Market and from Prothena being considered a U.S. domestic reporting company under SEC rules. Our Board will also continue to focus on and satisfy its fiduciary duties to our shareholders with respect to share issuances.

Many of the companies with which we compete strategically and for capital are incorporated in the U.S., and are therefore not subject to similar share issuance restrictions. We are asking you to approve Proposal Nos. 6 and 7 to allow us to continue to execute on our business and growth strategy in a timely and competitive manner.

Effect on Authorized Ordinary Shares

Of the 100,000,000 ordinary shares that we currently have authorized for issuance, as of the close of business on March 7, 2022, there were 46,741,333 ordinary shares outstanding and another 1,410,367 ordinary shares reserved for issuance under our shareholder-approved equity compensation plans (the 2012 LTIP and the 2018 LTIP) as well as the 2020 EIIP. Renewal of the current share issuance authorities will *not* increase the number of our authorized ordinary shares or otherwise provide greater

authority than is currently provided for under our existing share issuance authorities, other than to renew the term of the share issuance authorities for an additional five years. In addition, our Board desires to retain the flexibility afforded by the current share issuance authorities in order to allow us to continue to be in a position to act quickly with respect to financing opportunities to further our development programs.

Specific Rationale for Proposing to Renew Our Current Share Issuance Authorities

We need the ability to execute on our business and growth strategy without competitive disadvantage.

The renewal of our Board's share issuance authorities is fundamental to the way we intend to advance our business and increase shareholder value. As further described below, our growth strategy depends on our ability to research, develop, and commercialize our product candidates, which requires significant capital. Our Board and management rely heavily on having the flexibility to quickly take advantage of opportunities to raise capital through share issuances for cash. If Proposal No. 6 is not approved, we would be required to obtain shareholder approval prior to issuing any shares after May 17, 2022, even if we would not otherwise be required to obtain shareholder approval under Nasdaq rules. Similarly, even if Proposal No. 6 is approved, if Proposal No. 7 is not also approved, in each case where we propose to issue shares for cash consideration after May 17, 2022, we would first have to offer those shares on the same or more favorable terms to all of our existing shareholders. These limitations, in either case, would put us at a distinct disadvantage in effectively and efficiently raising capital, and in competing for capital vis-à-vis many of our peers because many of the companies with which we compete strategically and for capital are incorporated in the U.S., and are therefore not subject to similar share issuance restrictions. These limitations would make it more difficult and costly for us to complete capital raising transactions in furtherance of our growth strategy, thus potentially limiting our ability to raise the capital necessary to execute on the strategy that we believe is in the best interests of our shareholders.

While we would still retain the ability to seek shareholder approval in connection with a specific issuance of shares should our shareholders not approve

Proposal Nos. 5 and 6, we do not believe that convening an extraordinary general meeting of shareholders to approve each specific share issuance (and the corresponding dis-application of the statutory pre-emption right) we seek to undertake would be a workable alternative to obtaining approval of Proposal Nos. 6 and 7. The uncertainty of whether we could obtain such shareholder approval in the context of a specific issuance, as well as the delays we would experience in seeking such approval, would preclude us from taking advantage of opportunistic market windows and could preclude our ability to raise capital altogether. A case-by-case shareholder approval approach ignores market dynamics and competitive realities.

Likewise, even if Proposal No. 6 is approved, if Proposal No. 7 is not also approved, in any capital raising transaction where we propose to issue shares for cash consideration, we would be required to first offer those shares that we propose to issue for cash to all of our existing shareholders in a time-consuming pro-rata rights offering, which would disadvantage us vis-à-vis many of our peers in competing for capital, would significantly encumber the capital-raising process, would significantly increase our costs, and would significantly increase the timetable for completing such a cash financing transaction, thus potentially limiting our ability to advance the development of our product candidates and otherwise achieve strategic goals that we believe are in the best interests of our shareholders.

Our specific growth strategy drives our proposal to renew our current share issuance authorities. We are a late-stage clinical biotechnology company with expertise in protein dysregulation and a pipeline of investigational therapeutics with the potential to change the course of devastating rare peripheral amyloid and neurodegenerative diseases. We

are establishing fully-integrated research, development, and commercial capabilities. As a clinical stage company, we have no products approved for sale and focus substantially all of our efforts on the development and clinical testing of our product candidates, which efforts require significant capital.

Our proposal to renew our share issuance authorities for five years is directly tied to our specific growth strategy. As a clinical stage company, we rely heavily on, and until such time that we successfully obtain regulatory approval of our product candidates and achieve substantial positive cash flows from the commercialization of any approved drug candidates, will continue to rely heavily on, access to the capital markets in order to fund our operations. Likewise, because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, the amounts of increased capital outlays and operating expenses associated with completing the development of our product candidates are inherently uncertain, as is the time horizon for which we expect to rely principally on access to the capital markets to fund the completion of our product candidate development efforts.

Specifically, our future capital requirements will depend on numerous factors, including, without limitation, the timing of initiation, progress, results and costs of our clinical trials; the results of our research and preclinical studies; the costs of clinical manufacturing and of establishing commercial manufacturing arrangements; the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims; the costs and timing of capital asset purchases; our ability to establish research collaborations, strategic collaborations, licensing or other arrangements; the costs to satisfy our obligations under current and potential future collaborations; and the timing, receipt, and amount of revenues or royalties, if any, from any approved drug candidates.

We believe that renewing our current share issuance authorities for an additional five years is in the best interests of our shareholders because renewal of the share issuance authorities provides our Board the flexibility, consistent with its fiduciary duties and subject always to the shareholder approval and other requirements of Nasdaq and the SEC, to efficiently and cost-effectively access the capital markets without the competitive disadvantage and risks associated with seeking deal-specific shareholder approvals. As noted above, we do not believe that

convening an extraordinary general meeting of shareholders to approve each specific share issuance we seek to undertake would be a workable alternative to obtaining approval of Proposal Nos. 5 and 6. In addition, we believe that renewing our current share issuance authorities for an additional five years instead of seeking general re-approval of our share issuance authorities on a more frequent basis is in the best interests of our shareholders because seeking general re-approval of our share issuance authorities on a more frequent basis would still subject us to the competitive disadvantage risk, particularly given the 75% vote threshold required to dis-apply the statutory pre-emption right. Our concern in this regard is that a single shareholder or small number of shareholders, including those with a short-term focus, could defeat a proposal to dis-apply the statutory pre-emption right given the high vote threshold to approve that dis-application, even if a substantial majority of our shareholders who are supportive of our business and long-term growth strategy vote to approve the dis-application of the statutory pre-emption right.

We do not believe that limitations derived from Irish capital market practice should apply to Prothena.

While not required by Irish law, we understand that it has become market practice for companies whose share capital is listed on the primary stock exchange in Ireland, Euronext Dublin, to limit the share allotment and issuance authority to an amount equal to 33% of their issued share capital for a period of 12 to 18 months and to generally limit the dis-application of the statutory pre-emption right to only 5% of their issued share capital for a period of 12 to 18 months. While these limitations in size and duration on share issuance authorities are part of the corporate governance framework applicable to companies whose share capital is listed on the Euronext Dublin (regardless of whether such companies are incorporated in Ireland or elsewhere), our shares are not, and never have been, listed on the Euronext Dublin, and we are not subject to Euronext Dublin share listing rules or corporate governance standards applicable to companies whose share capital is listed on the Euronext Dublin.

We are required to seek shareholder approval to renew our current share issuance authorities because we are incorporated in Ireland. However, the U.S. capital markets are the sole capital markets for our ordinary shares and our ordinary shares are listed solely on The Nasdaq Global Select Market. As such, we believe that our shareholders expect us to, and we are committed to, follow customary U.S. capital markets practices, U.S. corporate governance stan

dards and Nasdaq and SEC rules and regulations. We also believe that applying the standards and market practices of a market where our shares are not listed, and where the institutional shareholder guidance creating such market practices was not intended to be applied to companies listed in the U.S., would be inappropriate and not in the best interests of our Company or our shareholders, especially in circumstances where we are committed to complying with the governance rules and practices of the actual capital market for our shares - The Nasdaq Global Select Market - which imposes its own restrictions on share issuances for the protection of shareholders.

We understand that certain proxy advisory firms have in recent proxy seasons applied their United

Kingdom ("U.K.") and Ireland voting guidelines in formulating their voting recommendations on share issuance authorities proposals for Irish-incorporated U.S.-listed companies, meaning that they have applied or otherwise taken into account the market practice for companies whose share capital is listed on Euronext Dublin in formulating their voting recommendations on share issuance authorities proposals for Irish-incorporated companies, even if their shares are not listed on Euronext Dublin (or any U.K. exchange). For all of the reasons discussed above and below, we respectfully disagree with this approach.

Why Our Shareholders Should Support Our Proposals to Renew Our Current Share Issuance Authorities

We believe we have responsibly used our current share issuance authorities which have been in place for almost a decade. We believe that we have made significant progress in executing on our long-term business plan and growth strategy, while also creating value for our shareholders. We have been deliberately disciplined in deploying our cash and raising additional capital. Our cash management and what we believe to be well-timed and well-executed share issuances that have successfully raised critically needed capital to further our development programs speak to our commitment to deploy and raise capital wisely and in the best interests of our shareholders.

As discussed above, we do not have any products approved for commercial sale, and in order to develop and obtain regulatory approval for our product candidates we will need to raise substantial additional capital. It is therefore critical that we have the ability to efficiently and cost-effectively access the capital markets, including by capitalizing on what can be narrow opportunistic market windows and avoiding unnecessary costs, delays, and uncertainties.

Risks if our current share issuance authorities are not renewed. For all of the foregoing reasons, we believe that the additional restrictions on our ability to raise capital if our share issuance authorities are not renewed would negatively impact our ability to execute on our business and growth strategy. In addition, we operate in a highly competitive industry, and believe that the failure to renew our current

share issuance authorities would put us at a competitive disadvantage; conversely, we believe that the renewal of our current share issuance authorities, as proposed, would keep us on an equal footing with our peer companies who are incorporated and listed in the U.S.

We believe that these typical Irish stock exchange limitations would disadvantage us relative to our U.S.- incorporated U.S.- listed peers. Companies that are incorporated and exchange-listed in the U.S. are not generally required to - and therefore do not - seek shareholder approval to renew their authority to allot and issue shares or to opt out of the statutory pre-emption right. In this regard, companies that are incorporated and publicly-traded in the U.S. generally do not grant all of their shareholders pre-emptive rights on new issuances of shares for cash. Instead, U.S. investors generally appear to accept that companies often need to access capital markets quickly, and that potential concerns associated with affording management flexibility in this respect are adequately protected against by other factors, including the shareholder approval requirements of U.S. exchanges with respect to share issuances.

Shareholder approval of Proposal Nos. 6 and 7 would NOT mean that our Board would have no limits on future share issuances. To the contrary, Prothena is considered to be a U.S. domestic reporting company under SEC rules and is subject to the same shareholder approval rules with respect to share issuances as all other U.S.-incorporated companies

listed on The Nasdaq Global Select Market. For example, Nasdaq rules generally require shareholder approval prior to our issuing shares at a discount in connection with a transaction other than a public offering where the number of shares to be issued is or will be equal to or in excess of 20% of the number of our ordinary shares outstanding before the issuance. Likewise, shareholder approval is required under the Nasdaq rules prior to our issuing shares when the issuance would result in a change of control of the Company (which would generally be deemed to occur under Nasdaq rules if a share issuance transaction results in an investor or group of investors obtaining a 20% or greater ownership position in our Company on a post-transaction basis, and that ownership position would be the largest position in the Company). Moreover, with limited exceptions, our Board must also seek shareholder approval of equity compensation plans, including material revisions of such plans. In addition, our shareholders will also continue to benefit from our directors' duties under Irish law, including their principal fiduciary duties to act in good faith and in the best interests of the company.

Our shareholders are supportive of our business and growth strategy that drives our proposal to renew our current share issuance authorities. A priority for our Board is listening to the views of our shareholders on a variety of topics, including our business and growth strategy and corporate governance practices. This year, we have solicited the views of institutional investors representing approximately 62% of our outstanding shares and spoke with institutional investors representing approximately 52% of our shares. These discussions have been productive and informative, and have helped ensure that our Board's decisions are aligned with shareholder objectives. In discussions we have had with shareholders about the share issuance authorities that must be renewed as a matter of Irish law, shareholders have generally understood that renewing our existing share issuance authorities would allow us to continue to execute on our business and growth strategy in a timely and competitive manner.

Summary

The renewal of our Board's share issuance authorities is fundamental to the way we intend to advance our business and increase shareholder value. Proposal Nos. 6 and 7, if approved, will maintain the status quo, allowing our Board continued flexibility to issue ordinary shares that are already within our authorized share capital, subject to the shareholder approval and other requirements of Nasdaq and the SEC. The renewal of the share issuance authorities, as proposed:

- Will not increase our authorized share capital;
- Will not exempt us from any Nasdaq or other requirements or limitations on our share issuances;

- Will keep us on an equal footing with our peer companies that are incorporated and listed in the U.S., while also fully complying with Irish law;
- Are fully consistent with U.S. capital market practices and governance standards; and
- Will maintain our ability to execute on our business and growth strategies and enable us to advance our pipeline of product candidates.

For the above reasons, our Board strongly recommends that you vote **FOR** both Proposal No. 6 and Proposal No. 7.

PROPOSAL NO. 6

RENEWAL OF OUR BOARD OF DIRECTORS' EXISTING AUTHORITY UNDER IRISH LAW TO ALLOT AND ISSUE ORDINARY SHARES

The directors of an Irish public limited company must have specific authority from shareholders to allot and issue shares (including rights to subscribe for or otherwise acquire any shares) - even shares which are part of the company's authorized but unissued share capital. Currently, our Board of Directors is authorized to allot and issue new shares without shareholder approval up to a maximum of our authorized but unissued share capital.

This authority of our Board to allot and issue shares has been in place since the Company was formed on September 26, 2012, and was renewed with the approval of our shareholders on May 17, 2017, by approximately 89% of the shares voted. Under Irish law, this authority may be granted for a maximum period of five years, at which point it lapses unless renewed by our shareholders. Therefore, our Board's current authority to allot and issue shares is due to expire on May 17, 2022.

We are asking for your approval to renew our Board's authority to allot and issue ordinary shares for an additional five-year period to expire on May 17, 2027 (or such date that is five years after the date shareholders approve this Proposal No. 6). We are *not* asking you to approve an *increase* to our authorized share capital. Your approval of this Proposal No. 6 will simply provide our Board with continued flexibility to issue shares up to the maximum of our existing authorized but unissued share capital, subject to the shareholder approval and other requirements of Nasdaq and the SEC. The renewed authority would apply to the issuance of shares, equity awards under our equity compensation plan and other securities convertible into or exercisable or exchangeable for our shares.

Renewal of this authority would *not* exempt the Company from applicable Nasdaq requirements to obtain shareholder approval prior to certain share issuances or to comply with applicable SEC disclosure and other regulations, and our Board will continue to focus on and satisfy its fiduciary duties to our shareholders with respect to share issuances.

If shareholders do not approve this Proposal No. 6, our Board's existing authority to allot and issue shares up to the amount of our authorized but unissued share capital will continue to apply until May 17,

2022. However, our Board would generally not be able to issue any shares after May 17, 2022 (other than to employees pursuant to our employee equity compensation plans or pursuant to any pre-existing contractual obligation) without first seeking and obtaining shareholder approval for each such issuance. ***This limitation on our ability to issue shares would disadvantage us vis-à-vis many of our peers in competing for capital, would significantly encumber our capital-raising process, would significantly increase our costs, would add significant uncertainty to our ability to complete capital-raising transactions, and would significantly increase the timetable for completing capital-raising transactions undertaken in furtherance of our growth strategy, thus potentially limiting our ability to advance the development of our product candidates and otherwise achieve strategic goals that we believe are in the best interests of our shareholders.***

Please see the *Background Discussion on Proposal Nos. 6 and 7* in this Proxy Statement for additional information regarding this Proposal No. 6.

Accordingly, we are asking shareholders to approve the following ordinary resolution at the Annual Meeting:

RESOLVED, that the Board of Directors (the "Board") of Prothena Corporation plc (the "Company") be and is hereby generally and unconditionally authorized pursuant to Section 1021(1) of the Irish Companies Act 2014 (the "Act") to exercise all powers of the Company to allot relevant securities (within the meaning of section 1021(12) of the Act) up to the amount of the Company's authorized but unissued share capital as at the date of this resolution, provided that this authority shall expire five years from the date of passing of this resolution and provided that the Company may before such expiry make an offer or agreement which would or might require relevant securities to be allotted after such expiry and the Board may allot relevant securities in pursuance of such an offer or agreement as if the authority conferred by this resolution had not expired.

**THE BOARD OF DIRECTORS RECOMMENDS THAT SHAREHOLDERS VOTE FOR THE
RENEWAL OF OUR BOARD OF DIRECTORS' EXISTING AUTHORITY UNDER IRISH LAW TO
ALLOT AND ISSUE ORDINARY SHARES.**

PROPOSAL NO. 7

RENEWAL OF OUR BOARD OF DIRECTORS' EXISTING AUTHORITY UNDER IRISH LAW TO ALLOT AND ISSUE ORDINARY SHARES FOR CASH WITHOUT FIRST OFFERING THOSE SHARES TO EXISTING SHAREHOLDERS PURSUANT TO THE STATUTORY PRE-EMPTION RIGHT THAT WOULD OTHERWISE APPLY

In general, unless otherwise authorized by shareholders, before an Irish public limited company can issue shares for cash (including rights to subscribe for or otherwise acquire any shares) to any new shareholders, it must first offer those shares or rights to existing shareholders of the company pro-rata to their existing shareholdings - pursuant to what is commonly referred to as the statutory pre-emption right. The statutory pre-emption right, if not dis-applied, affords existing shareholders the right to purchase any new shares that we propose to issue for cash in order to maintain their proportionate ownership interests in Prothena following the issuance of those shares resulting in a time-consuming and expensive pro-rata rights offering which would disadvantage us compared to our peers. Our Board of Directors is currently authorized to issue new shares for cash, up to a maximum of our authorized but unissued share capital, without first offering those shares to existing shareholders, thereby opting out of the statutory pre-emption right.

This authority of our Board to opt out of the statutory pre-emption right has been in place since the Company was formed on September 26, 2012, and was renewed with the approval of our shareholders on May 17, 2017, by approximately 89% of the shares voted. Under Irish law, this authority may be granted for a maximum period of five years, at which point it will lapse unless renewed by our shareholders. Therefore, our Board's current authority to opt out of the pre-emption right is due to expire on May 17, 2022.

We are asking for your approval to renew our Board's authority to opt out of the statutory pre-emption right for an additional five-year period to expire on May 17, 2027 (or such date that is five years after the date shareholders approve this Proposal No. 7). We are *not* asking you to approve an *increase* to our authorized share capital. Your approval of this Proposal No. 7 will simply provide our Board with continued flexibility to issue shares for cash up to the maximum of our existing authorized but unissued share capital without offering those shares to existing shareholders under the statutory pre-emption right.

Renewal of this authority would *not* exempt the Company from applicable Nasdaq requirements to obtain shareholder approval prior to certain share issuances or to comply with applicable SEC disclosure and other regulations, and our Board will continue to focus on and satisfy its fiduciary duties to our shareholders with respect to share issuances.

If our shareholders do not approve this Proposal No. 7, our Board's existing authority to opt out of the statutory pre-emption right up to the amount of our authorized but unissued share capital will continue to apply until May 17, 2022. However, our Board would generally not be able to issue shares for cash after May 17, 2022, to any new shareholders without first offering those shares to existing shareholders pro-rata to their existing shareholdings. ***As a result of this limitation, in any capital raising transaction where we propose to issue shares for cash consideration, we would be required to first offer those shares that we propose to issue for cash to all of our existing shareholders in a time-consuming pro-rata rights offering, which would disadvantage us vis-à-vis many of our peers in competing for capital, would significantly encumber the capital-raising process, would significantly increase our costs, and would significantly increase the timetable for completing such a cash financing transaction, thus potentially limiting our ability to advance the development of our product candidates and otherwise achieve strategic goals that we believe are in the best interests of our shareholders.***

The statutory pre-emption right applies only to share issuances for cash consideration; accordingly, it does not apply where we issue shares for non-cash consideration (such as in a share exchange transaction or in any transaction in which property other than cash is received by us in payment for shares) or where we issue shares pursuant to our employee equity compensation plans.

Please see the Background Discussion on Proposal Nos. 6 and 7 in this Proxy Statement for additional information regarding this Proposal No. 7.

Accordingly, we are asking shareholders to approve the following special resolution at the Annual Meeting:

RESOLVED, subject to and conditional upon Proposal No. 6 being approved, that the Board of Directors (the "Board") of Prothena Corporation plc (the "Company") be and is hereby empowered pursuant to section 1023(3) of the Irish Companies Act 2014 (the "Act") to allot equity securities within the meaning of said section 1023 for cash pursuant to the authority conferred by Proposal No. 6 up to an aggregate nominal amount equal to the authorized but unissued share capital of the Company as at the date of this resolution as if section 1022 of the Act did not apply to any such allotment, provided that this authority shall expire five years from the date of passing of this resolution and provided that the Company may before the expiry of such authority make

an offer or agreement which would or might require equity securities to be allotted after such expiry and the Board may allot equity securities in pursuance of such an offer or agreement as if the power conferred by this resolution had not expired.

As required under Irish law, Proposal No. 7 is a special resolution that requires the affirmative vote of not less than 75% of the votes cast in person or by proxy at the Annual Meeting in order to be approved.

In addition, approval of this Proposal No. 7 is subject to and conditional upon Proposal No. 6 also being approved because Irish law requires that a general authority to allot and issue shares be in place before an authority to opt out of the statutory pre-emption right can be granted. Therefore, unless shareholders approve Proposal No. 6, this Proposal No. 7 will fail and not be implemented, even if shareholders approve this Proposal No. 7.

THE BOARD OF DIRECTORS RECOMMENDS THAT SHAREHOLDERS VOTE *FOR* THE RENEWAL OF OUR BOARD OF DIRECTORS' EXISTING AUTHORITY UNDER IRISH LAW TO ALLOT AND ISSUE ORDINARY SHARES FOR CASH WITHOUT FIRST OFFERING THOSE SHARES TO EXISTING SHAREHOLDERS PURSUANT TO THE STATUTORY PRE-EMPTION RIGHT THAT WOULD OTHERWISE APPLY.

PROPOSAL NO. 8

APPROVAL OF ANY MOTION TO ADJOURN THE ANNUAL MEETING, OR ANY ADJOURNMENT THEREOF, TO ANOTHER TIME AND PLACE IN ORDER TO SOLICIT ADDITIONAL PROXIES IF THERE ARE INSUFFICIENT VOTES AT THE TIME OF THE ANNUAL MEETING TO APPROVE PROPOSAL NO. 7

Shareholders are being asked to vote for approval of any motion to adjourn the Annual Meeting, or any adjournment thereof, to another time and place in order to solicit additional proxies if there are insufficient votes at the time of the Annual Meeting to approve Proposal No. 7.

Under Irish law, Proposal No. 7 must be approved as a special resolution, which means that not less than 75% of the votes cast in person or by proxy at the Annual Meeting must be voted FOR Proposal No. 7 in order for it to be approved. Given this high vote threshold associated with Proposal No. 7, we are requesting authority to adjourn the Annual Meeting to solicit additional proxies if there are insufficient votes at the time of the Annual Meeting to approve Proposal No. 7.

Accordingly, we are asking shareholders to approve the following ordinary resolution at the Annual Meeting:

RESOLVED, that any motion to adjourn the Annual Meeting, or any adjournment thereof, to another time and place in order to solicit additional proxies if there are insufficient votes at the time of the Annual Meeting to approve Proposal No. 7 set forth in this Proxy Statement, be approved.

THE BOARD OF DIRECTORS RECOMMENDS THAT SHAREHOLDERS VOTE FOR THE RESOLUTION TO APPROVE ANY MOTION TO ADJOURN THE ANNUAL MEETING, OR ANY ADJOURNMENT THEREOF, TO ANOTHER TIME AND PLACE IN ORDER TO SOLICIT ADDITIONAL PROXIES IF THERE ARE INSUFFICIENT VOTES AT THE TIME OF THE ANNUAL MEETING TO APPROVE PROPOSAL NO. 7.

SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The following table presents information as to the beneficial ownership of our ordinary shares as of March 7, 2022, for:

- each person, or group of affiliated persons, known by us to beneficially own more than 5% of our ordinary shares;
- each of our directors;
- each of our executive officers named in the *Summary Compensation Table - Fiscal Year 2021* below; and
- all of our directors and executive officers as a group.

Unless otherwise indicated, the address of each beneficial owner named below is c/o Prothena Corporation plc, 77 Sir John Rogerson's Quay, Block C, Grand Canal Docklands, Dublin 2, D02 VK60, Ireland.

Name and Address of Beneficial Owner	Amount and Nature of Beneficial Ownership ⁽¹⁾			
	Shares	Shares Acquirable Within 60 Days ⁽²⁾	Total Shares Deemed Beneficially Owned	Percent of Outstanding Shares ⁽³⁾
5% Shareholders:				
Entities Associated with EcoR1 Capital, LLC ⁽⁴⁾ 357 Tehama Street, #3 San Francisco, CA 94103, USA	11,584,280	—	11,584,280	24.8%
T. Rowe Price Associates, Inc. ⁽⁵⁾ 100 E Pratt St. Baltimore, Maryland, 21202, USA	5,948,861	—	5,948,861	12.7%
BlackRock, Inc. ⁽⁶⁾ 55 East 52nd Street New York, NY 10055, USA	3,872,300	—	3,872,300	8.3%
Entities Associated with Fidelity Investments ⁽⁷⁾ 245 Summer Street Boston, MA 02210, USA	2,641,741	—	2,641,741	5.7%
Directors and Named Executive Officers:				
Lars G. Ekman	243	166,544	166,787	*
Paula K. Cobb	—	40,834	40,834	*
Richard T. Collier	1,219	121,544	122,763	*
Shane M. Cooke	—	121,544	121,544	*
K. Anders O. Härfstrand	—	77,614	77,614	*
Christopher S. Henney	—	38,644	38,644	*
Oleg Nodelman ⁽⁸⁾	11,584,280	—	11,584,280	24.8%
Sanjiv K. Patel	—	—	—	*
Dennis J. Selkoe ⁽⁹⁾	4,208	60,044	64,252	*
Gene G. Kinney	12,793	1,508,147	1,520,940	3.2%
Tran B. Nguyen	3,200	781,003	784,203	1.7%
Hideki Garren	—	67,708	67,708	*
Brandon S. Smith	—	146,333	146,333	*
Carol D. Karp	—	303,976	303,976	*
All 18 directors and executive officers as a group	11,605,943	4,359,942	15,965,885	31.2%

* Represents beneficial ownership of less than one percent of our issued and outstanding ordinary shares.

SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

- (1) Represents ordinary shares. Beneficial ownership is determined in accordance with U.S. Securities and Exchange Commission (the "SEC") rules and generally includes voting or investment power. Unless otherwise indicated below, to our knowledge, the persons and entities named in this table have sole voting and sole dispositive power with respect to all shares beneficially owned, subject to community property laws where applicable.
- (2) For purposes of this table, a person is deemed to have beneficial ownership of our ordinary shares which such person has the right to acquire on or within 60 days after March 7, 2022. The shares reported in this column consist of shares that may be acquired by exercise of NQSOs (nonqualified stock options) granted under our Amended and Restated 2012 Long Term Incentive Plan, our 2018 Long Term Incentive Plan, as amended, or our 2020 Employment Inducement Incentive Plan, as amended.
- (3) The percentage of outstanding shares is based on the 46,741,333 ordinary shares issued and outstanding on March 7, 2022. However, for purposes of computing the percentage of outstanding ordinary shares beneficially owned by each person or group of persons, any shares which such person or group of persons has a right to acquire on or within 60 days after March 7, 2022, are deemed to be outstanding, but are not deemed to be outstanding for the purpose of computing the percentage of beneficial ownership of any other person.
- (4) As reported on Amendment No. 3 to Schedule 13D filed with the SEC on January 14, 2022, by EcoR1 Capital, LLC ("EcoR1"), EcoR1 Capital Fund Qualified, L.P. ("Qualified Fund") and Oleg Nodelman, reporting beneficial ownership as of January 12, 2022. EcoR1 and Mr. Nodelman have shared voting and dispositive power over 11,584,280 ordinary shares, and Qualified Fund has shared voting and dispositive power over 9,785,116 ordinary shares. Mr. Nodelman is the manager and control person of EcoR1 and a member of our Board. EcoR1 is an investment advisor to Qualified Fund. Each of EcoR1, Qualified Fund, and Mr. Nodelman disclaim beneficial ownership of the shares reported herein, except to the extent of such person's pecuniary interest therein.
- (5) As reported on Amendment No. 1 to Schedule 13G filed with the SEC on February 14, 2022, by T. Rowe Price Associates, Inc., reporting beneficial ownership of December 31, 2021. T. Rowe Price has sole voting power over 1,305,737 ordinary shares and sole dispositive power over 5,948,861 ordinary shares. Various persons have the right to receive or the power to direct the receipt of dividends from, or the proceeds from the sale of, the ordinary shares; no one person's interest in those ordinary shares is more than five percent of the total outstanding ordinary shares. We have also received a letter pursuant to the Irish Companies Act 2014 ("Notification Letter") from T. Rowe Price Associates, Inc. reporting a change in its "notifiable interest" in our ordinary shares. The Notification Letter reports that, as of March 4, 2022, certain registered holders associated with T. Rowe Price Associates, Inc. held 6,055,447 of our ordinary shares (or 13.0% of our outstanding ordinary shares as of March 7, 2022). Because the "notifiable interest" reported in the Notification Letter is not necessarily the same as "beneficial ownership" as defined under SEC rules, the table does not reflect the information reported in the Notification Letter.
- (6) As reported on Amendment No. 7 to Schedule 13G filed with the SEC on February 3, 2022, by BlackRock, Inc., reporting beneficial ownership of December 31, 2021. BlackRock, Inc. is a parent holding company/control person that has sole voting power over 3,804,993 ordinary shares and sole dispositive power over 3,872,300 ordinary shares. Various persons have the right to receive or the power to direct the receipt of dividends from, or the proceeds from the sale of, the ordinary shares; no one person's interest in those ordinary shares is more than five percent of the total outstanding ordinary shares. The subsidiaries holding the shares reported herein are BlackRock Life Limited; BlackRock Advisors, LLC; Aperio Group, LLC; BlackRock (Netherlands) B.V.; BlackRock Institutional Trust Company, National Association; BlackRock Asset Management Ireland Limited; BlackRock Financial Management, Inc.; BlackRock Asset Management Schweiz AG; BlackRock Investment Management, LLC; BlackRock Investment Management (UK) Limited; BlackRock Asset Management Canada Limited; BlackRock (Luxembourg) S.A.; BlackRock Investment Management (Australia) Limited; BlackRock Fund Advisors; BlackRock Fund Managers Ltd.
- (7) As reported on Schedule 13G filed with the SEC on February 9, 2022, by FMR LLC ("FMR") and Abigail P. Johnson, reporting beneficial ownership of December 31, 2021. FMR has sole voting power over 841,958 ordinary shares and sole dispositive power over 2,641,741 ordinary shares. Ms. Johnson and members of the Johnson family control 49% of FMR and have shared voting and dispositive power over the shares listed herein. Various persons have the right to receive or the power to direct the receipt of dividends from, or the proceeds from the sale of ordinary shares.
- (8) Consists of the ordinary shares described in footnote 4 above. Mr. Nodelman disclaims beneficial ownership of such shares, except to the extent of his pecuniary interest therein.
- (9) Includes 2,845 ordinary shares held by Dr. Selkoe and 1,363 ordinary shares held by Dr. Selkoe's spouse.

COMPENSATION DISCUSSION AND ANALYSIS

In this section we provide an explanation and analysis of the material elements of the compensation provided to our chief executive officer, our chief financial officer (who also serves as our chief strategy officer) and our other three most highly compensated executive officers who were serving as such at the end of our fiscal year 2021 (collectively referred to as our “named executive officers”). Those named executive officers were:

- Gene G. Kinney, Ph.D., our President and Chief Executive Officer;
- Tran B. Nguyen, our Chief Strategy Officer and Chief Financial Officer;
- Hideki Garren, M.D., Ph.D., our Chief Medical Officer;
- Brandon S. Smith, our Chief Operating Officer; and
- Carol D. Karp, our Chief Regulatory Officer.

Executive Summary: Fiscal Year 2021 Company Performance and Key Pay Decisions

2021 Performance Highlights. We are a late-stage clinical company with a robust pipeline of investigational therapeutics with the potential to change the course of devastating neurodegenerative and rare peripheral amyloid diseases. Our executive compensation programs are designed to reward superior performance and provide consequences for under-performance. We believe that compensation of our named executive officers for fiscal year 2021 was aligned with the Company's performance during 2021 and its go-forward strategy. Highlights of that performance include:

• **We Made Significant Advances in our Neurodegenerative Diseases Portfolio.**

- PRX012, a potential best-in-class treatment for Alzheimer's disease (AD), is an investigational monoclonal antibody targeting a key epitope at the N-terminus of amyloid beta (A β) with high binding potency. We presented preclinical results demonstrating that PRX012 significantly cleared both pyroglutamate-modified and -unmodified A β plaque in post-mortem brain tissue of late-stage AD patients.
- PRX005, a potential best-in-class treatment for AD, is an investigational antibody that specifically targets a key epitope within the microtubule binding region (MTBR) of tau, a protein implicated in diseases including AD, frontotemporal dementia (FTD), progressive supranuclear palsy (PSP), chronic traumatic encephalopathy (CTE), and other tauopathies. PRX005 is part of the global neuroscience research and development collaboration with Bristol Myers Squibb. We filed an Investigational New Drug (IND) application

for PRX005, received \$80 million option payment from Bristol Myers Squibb for execution of a U.S. license agreement, and initiated a Phase 1 study.

- Dual A β -tau vaccine, a potential first-in-class prevention and treatment for AD, is a dual-target vaccine targeting key epitopes within the A β and tau proteins to promote amyloid clearance and blockade of pathogenic tau. We presented preclinical data demonstrating that the dual A β -tau vaccine generated appropriate and balanced antibody titers promoting both phagocytosis of A β plaque and blockade of tau transmission *in vitro*.
 - Prasinezumab (PRX002/RG7935), a potential first-in-class treatment for Parkinson's disease, is an investigational humanized monoclonal antibody designed to target key epitopes within the C-terminus of alpha-synuclein and is the focus of the worldwide collaboration with Roche. We earned a \$60 million clinical milestone payment upon dosing of the first patient in the global Phase 2b PADOVA study for prasinezumab.
- **We Made Significant Advances in our Rare Peripheral Amyloid Diseases Portfolio.**
- Birtamimab, a potential best-in-class amyloid depleter treatment for AL amyloidosis, is an investigational humanized monoclonal antibody designed to directly neutralize soluble toxic aggregates and promote clearance of amyloid that causes organ dysfunction and failure. We reached a Special Protocol Assessment (SPA) agreement with the U.S. Food and Drug Administration (FDA) to

advance birtamimab into a confirmatory Phase 3 study in Mayo Stage IV patients. We then initiated AFFIRM-AL, a global, registration-enabling Phase 3 study that will be conducted with a primary endpoint of all-cause mortality at $p \leq 0.10$ under the SPA agreement with FDA.

- PRX004, a potential first-in-class treatment for ATTR amyloidosis, is an investigational humanized monoclonal antibody designed to deplete the pathogenic, non-native forms of the TTR protein. We announced the Novo Nordisk acquisition of our ATTR amyloidosis business, under which we are eligible to receive a total aggregate of up to \$1.23 billion, and we received a \$60 million upfront payment from Novo Nordisk.

- We Carefully Managed And Increased Our Cash Balance.** During fiscal year 2021, we carefully managed our capital. While progressing all of our development programs described above, our cash provided by operating and investing activities was \$92 million, in the middle of our revised guidance range of \$85 to \$95 million. We finished 2021 with \$580.4 million in cash, cash equivalents, and restricted cash, including cash provided by operating and financing activities, at the top end of our revised guidance range of \$570 to \$580 million, providing a solid financial foundation for continuing to advance the Company's discovery and clinical programs.

2021 Compensation Highlights. We seek to provide fair and competitive compensation for our executive officers, while emphasizing at-risk pay tied to performance in the form of annual bonuses and long-term equity incentives. Highlights of our 2021 executive compensation program reflected this and include the following:

- Modest Base Salary Adjustments.** In 2021, our CEO, Dr. Kinney, and our other named executive officers continuing from 2020 - Mr. Nguyen, Mr. Smith, and Ms. Karp - all received 3.5% increases in their base salaries.
- Annual Bonuses Reflected 2021 Company Performance.** At the beginning of fiscal year 2021, the Committee determined not to change the target bonus opportunities of our named executive officers continuing from 2020 from their respective levels in 2020. Dr. Garren's target bonus level was set at 50% of his annualized base salary at the time of his hire. In connection with Mr. Smith's promotion to Chief Operating Officer in September 2021,

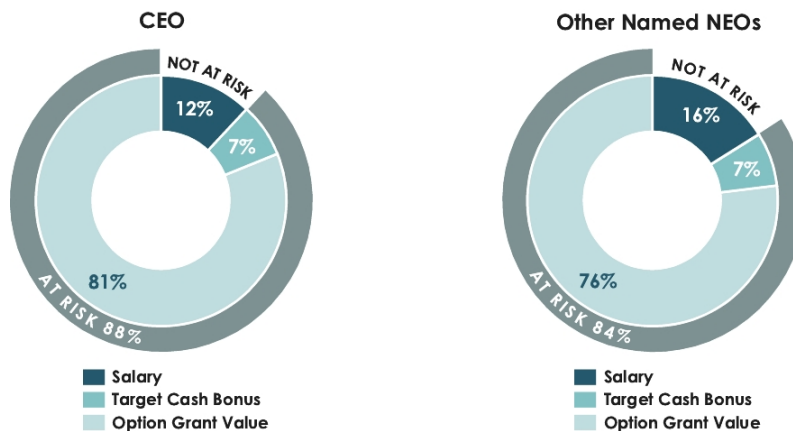
the Committee increased his targeted bonus opportunity from 40% to 50% of his base salary earned in the fourth quarter of the fiscal year 2021. For fiscal year 2021, the Committee and Board established pre-determined corporate objectives that it considered critical to the near- and long-term success of the Company. Following 2021, the Committee and the Board determined that Company performance relative to the corporate objectives was 125%. Based on that corporate performance and the individual performance of each named executive officer other than Dr. Kinney, the Committee approved payouts at 125% of the target bonuses as to the corporate portion of the bonus (75%) for those named executive officers. Dr. Kinney's bonus was based solely on corporate performance, and the Board therefore approved his payout at 125% of his target bonus for 2021.

- Equity as a Key Component of Compensation.** We use stock options to directly link executive officer compensation to increases in the price of our ordinary shares, which directly reflects increased shareholder value. As in past years, we made annual grants of stock options to our then-serving named executive officers early in 2021, which grants were around the 50th percentiles of the market data. At the time he joined the Company in April 2021, Dr. Garren received a new-hire grant of a stock option for 250,000 shares following the Committee's review of peer data for that position and negotiations with Dr. Garren. Mr. Smith received a grant of a stock option for 25,000 shares in connection with his promotion to Chief Operating Officer in September 2021.
- No Adjustments Were Made Due to the Pandemic.** The Committee and Board did not modify any of the fiscal year 2021 pre-determined corporate objectives or make any adjustments to compensation based on the impact of the worldwide COVID-19 pandemic.

Commitment to Pay for Performance. Our executive compensation programs are designed to deliver pay that is tied to our corporate and individual performance. Accordingly, 88% of our CEO's and on average 84% of each of our other named executive officers' total targeted compensation for fiscal year 2021 (based on annual base salary, target annual cash bonus, and grant date fair value of stock option award granted in 2021) was in the form of cash incentives tied to actual performance against pre-determined strategic, operational, and financial objectives; and stock options, which align

our named executive officers' interests with shareholders and foster long-term focus on the Company's objectives as well as retention.

Total Target Direct Compensation Focuses on "At Risk" Compensation. The charts below show the target mix of each element of the total targeted compensation in 2021 for our CEO and for our other named executive officers in the aggregate, which we believe show our strong emphasis on variable pay linked to actual performance.



Compensation Governance and Best Practices

We are committed to having strong governance standards with respect to our compensation programs, procedures, and practices. Our key governance practices include the following:

What We Do	What We <u>Don't</u> Do
✓ Pay for performance. A significant percentage of total target compensation is pay at-risk that is connected to performance.	✗ No guaranteed annual salary increases or bonuses. Our named executive officers' salary increases are assessed individually, and their annual cash incentives are tied to corporate and individual performance.
✓ Strong link between performance measures and strategic objectives. Performance measures for cash incentive compensation are linked to business priorities designed to create long-term shareholder value.	✗ No tax gross-ups. We do not provide any tax gross-ups to our named executive officers.
✓ Independent compensation consultant. The Committee retains an independent compensation consultant to review our executive compensation program and practices.	✗ No perquisites. We do not provide any perquisites or personal benefits to our named executive officers.
✓ Annual comparator peer group review. The Committee, in conjunction with our compensation consultant, determines the makeup of our comparator peer group at least annually.	✗ No executive retirement plans. We do not maintain executive or supplemental retirement plans.
✓ Double-trigger change-in-control severance arrangements. All of our change-in-control severance arrangements have double triggers requiring a qualifying termination.	✗ No option exchange or repricing permitted without shareholder approval. Our equity incentive compensation plan expressly prohibits repricing of equity awards and cash-buyouts of "underwater" awards without shareholder approval.
	✗ No hedging or pledging permitted. We prohibit our executive officers from engaging in speculative transactions in our ordinary shares, including short sales, transactions in put or call options, hedging transactions and other inherently speculative transactions; from entering into any form of hedging or monetization transactions; and from pledging our ordinary shares as collateral for loans.

Shareholder Approval of Executive Compensation

At the annual general meeting of 2021, our shareholders voted to approve the 2020 compensation of our named executive officers, with 80% of the shares cast at the meeting voting to approve that compensation. The Committee reviewed the result

of this advisory vote by shareholders on our executive compensation and did not implement any changes to our executive compensation programs as a result of the vote.

The Objective of Our Executive Compensation Programs

The principal objective of our executive compensation programs is to attract, retain, motivate, and reward individuals with the executive experience and skills necessary for us to achieve our ultimate goal of increasing shareholder value. In order to do this, our executive compensation programs are designed to:

- Attract and retain individuals of superior ability, experience, and management talent;
- Motivate and reward executives whose knowledge, skills, and performance support our continued success;

- Align compensation with corporate strategies, business and financial objectives, operational needs, and the long-term interests of our shareholders;
- Avoid elements of compensation that would encourage excessive risk-taking or otherwise create inappropriate incentives; and
- Provide total compensation that is fair, reasonable, and competitive relative to both internal and external comparison points.

How We Determine Executive Compensation

The Compensation Committee is Responsible for Executive Compensation. The Committee makes all decisions on compensation to our executive officers other than our CEO. In the case of our CEO, the Committee makes recommendations to the Board regarding his compensation, and the Board (excluding the CEO) makes all final decisions on his compensation. Information on the Committee is provided in this Proxy Statement under the heading *Corporate Governance and Board Matters - Board Committees - Compensation Committee*.

The Committee Utilizes a Compensation Consultant. The Committee annually retains an independent executive compensation consultant to assist the Committee in making informed decisions on executive officer compensation. The compensation consultant engaged by the Committee for the purpose of establishing fiscal year 2021 compensation was Radford. Radford was engaged directly by the Committee, after the Committee assessed Radford's independence from the Company and its management. This process is repeated annually before the Committee selects its executive compensation consultant for that year.

Radford was engaged by the Committee to prepare and present a data-based assessment of compensation programs for our executive officers, with comparisons to those of "peer" companies and input on their appropriateness in accomplishing the Committee's objectives. Radford was also asked to provide to the Committee specific recommendations on our executive compensation programs generally.

The Committee Selects a Peer Group. For purposes of their annual compensation assessments and decisions for 2021, the Committee approved a "peer group" of companies to assist the Committee in its review of executive compensation. At the Committee's instruction, Radford used criteria based on (a) industry sector, stage of development and geography (biotechnology companies in Phase 1 to 3 of clinical development, and companies located in the San Francisco, California area or other biotechnology hub markets that reflect Prothena's talent market), (b) market capitalization between \$250 million and \$1.5 billion (based on the Company's then-market capitalization of approximately \$504 million which was at the 31st percentile), and (c) number of employees (generally under 200 employees). These criteria were used to develop a recommended list of peer companies, which Radford presented to the Committee. As a result of this analysis, 89bio, Alector, AnaptysBio, Celldex Therapeutics, Concert Pharmaceuticals, Cortexyme, Crinetics Pharmaceuticals, Geron, Kura Oncology, MEI Pharma, Protagonist Therapeutics, and Replimune Group were added to our peer group; Aduro Biotech, ChemoCentryx, Corvus Pharmaceuticals, Fate Therapeutics, Five Prime Therapeutics, Jounce Therapeutics, Pieris Pharmaceuticals, Synlogic, and TG Therapeutics were removed from our peer group. The peer group companies identified by Radford and considered, discussed, and approved by the Committee to assist the Committee in its evaluation of 2021 compensation decisions were:

89 bio
Adverum Biotechnologies
Alector

Concert Pharmaceuticals
Cortexyme
Crinetics Pharmaceuticals

MEI Pharma
Mersana Therapeutics
Protagonist Therapeutics

AnaptysBio
Assembly Biosciences
Atara Biotherapeutics, Inc.
Calithera Biosciences
Celldex Therapeutics

Cytokinetics
CytomX Therapeutics
Geron
Kura Oncology

Replimune Group
Syros Pharmaceuticals
Voyager Therapeutics
ZIOPHARM Oncology

For competitive assessment purposes, Radford used executive compensation data publicly reported by these peer group companies (*i.e.*, proxy statement data), as well as data from Radford's Global Life Science Survey for other publicly-traded pre-commercial biotechnology companies with characteristics (*e.g.*, market capitalization, stage of development, and number of employees) comparable to these peer group companies and the Company.

Radford's reports to the Committee included a review of our existing executive compensation programs, practices, levels, and arrangements; each executive officer's compensation relative to the market data; and our equity grant practices for all employees (not just executive officers) relative to the market data. Radford's reports also provided recommendations on changes that might be made to our executive compensation programs generally and to each executive officer's compensation. Radford provided its written report in advance of Committee meetings, at which the Radford consultant presented and responded to questions from the Committee.

The CEO Makes Recommendations. For fiscal year 2021, Dr. Kinney presented to the Committee his recommendations on compensation for the executive officers other than himself. Following completion of fiscal year 2021, Dr. Kinney provided his assessment of the performance of executive officers other than himself, both in general and with specific reference to the corporate objectives pre-established by the Committee for 2021.

The Committee or Board Makes Compensation Decisions. At the beginning of 2021, the Committee determined the structure of our executive officer compensation programs for that year, after receiving Radford's report and recommendations and receiving Dr. Kinney's recommendations on compensation for executive officers other than himself. Specifically, the Committee determined for each executive officer other than Dr. Kinney (a) any adjustment to his or her base salary, (b) his or her target annual cash bonus opportunity for 2021 and the corporate objectives for 2021, and (c) his or her annual stock option award for 2021.

In the case of Dr. Kinney, the Committee recommended to the full Board his base salary, his annual cash bonus opportunity for fiscal year 2021, and the 2021 corporate objectives upon which that bonus opportunity would be based, and his annual stock option award. In an executive session without Dr. Kinney present, the Board considered, discussed, and approved the compensation recommended by the Committee with respect to Dr. Kinney.

In the case of Dr. Garren, his compensation was determined by the Committee in connection with his appointment as our Chief Medical Officer after the Committee reviewed the market data provided by Radford, as well as Dr. Kinney's recommendations following arm's length negotiations with Dr. Garren. His compensation, including his base salary, annual cash bonus opportunity, stock option award, and retention (hire-on) bonus, was approved by the Committee.

In the case of Mr. Smith, his compensation, including his base salary and annual cash bonus opportunity, was further adjusted in connection with his promotion to Chief Operating Officer. Additionally, he received a stock option award in connection with such appointment. These adjustments were made after the Committee reviewed the market data provided by Radford, as well as Dr. Kinney's recommendations, and were approved by the Committee.

After completion of fiscal year 2021, the Committee received Dr. Kinney's report on the Company's performance relative to the pre-established corporate objectives for 2021, as well as on the individual performance of each executive officer other than himself. The Company's Vice President, Human Resources (who is not an executive officer) participated in that Committee meeting, as did the Radford consultant. After receiving that report, the Committee determined the annual cash bonus to be paid to each executive officer other than Dr. Kinney for 2021.

After completion of fiscal year 2021, the Nominating and Corporate Governance Committee of the Board completed a review of Dr. Kinney's performance during 2021 (with input from all other independent members of the Board) and this review was reported to both the Compensation Commit

tee and the full Board. The Compensation Committee also met in executive session with the Radford consultant to discuss Dr. Kinney's compensation. The Committee determined and recommended to the full Board (other than Dr. Kinney) Dr. Kinney's annual cash bonus for 2021 based on attainment of pre-established corporate objectives for 2021. In an executive session without Dr. Kinney present, the Board considered, discussed, and approved the bonus amount recommended by the Committee.

Stock Option Grant Practices and Procedures. All stock options awarded to our executive officers other than the CEO are approved by the Committee, and stock options awarded to our CEO are

approved by our Board (based on recommendations from the Committee). Grants to other employees are made pursuant to specific delegations of authority from the Committee, which delegations include individual grant limits, aggregate grant limits, specification of grant terms and specification of grant dates.

Stock option awards approved (or delegated for approval) by the Committee and the Board have always been granted on a date not earlier than the date of approval by the Committee, Board, or delegated officer, and with an exercise price that is not less than the fair market value (as defined by the applicable LTIP) on the date of grant.

Executive Compensation for Fiscal Year 2021

The three key elements of our executive officer compensation programs for fiscal year 2021 were: base salaries, annual cash bonuses, and long-term incentive compensation in the form of stock option awards. In addition, the Committee (or the Board) has approved arrangements providing for certain payments and benefits in the event of certain terminations of employment.

Base Salaries. Base salaries are intended to compensate our executive officers for serving as the senior members of our executive team. Salaries are also considered an important element of compensation necessary to retain the Company's executive officers in a highly competitive marketplace. To accomplish these objectives, the Committee reviews and sets base salaries annually, taking into account many factors including but not limited to market competition for a particular position (typically evaluating the 50th percentile of the market data specific to each executive officer's position); experience and past performance inside or outside the Company; role and responsibilities with the Company; tenure with the Company and associated institutional knowledge; innovative thinking and leadership; personal performance and contributions; succession planning; and past and future performance, and any other factors which the Committee considers appropriate to accomplish the purposes of this element of executive compensation.

The base salaries approved in early 2021 for our named executive officers continuing from 2020 were as follows: Dr. Kinney - \$576,500; Mr. Nguyen - \$461,173; Ms. Karp - \$453,268; and Mr. Smith - \$414,000. Dr. Kinney's salary resulted from the Board's approval of a 3.5% increase to his base salary, after considering the market data provided by Radford

and consistent with the budgeted standard merit increase for the general employee population. Based on the same considerations, the salaries of Mr. Nguyen, Ms. Karp, and Mr. Smith reflect the Committee's approval of 3.5% increases to their base salaries. These adjustments resulted in these executive officers' base salaries being positioned between the 50th and 75th percentiles of the market data.

The Committee approved Dr. Garren's base salary of \$490,000 in connection with his appointment as our Chief Medical Officer in April 2021, following the Committee's review of market data for that position and negotiations with Dr. Garren.

The Committee approved an adjustment of Mr. Smith's base salary to \$450,000 in connection with his promotion to Chief Operating Officer in September 2021, following the Committee's review of market data for that position.

Annual Cash Bonuses. Annual cash bonus opportunities are intended principally to motivate executive officers to achieve pre-determined annual operational and financial ("corporate") objectives set by the Committee and the Board to promote achievement of our business strategies and drive increases in shareholder value. Following the end of each fiscal year, the Committee and the Board determine to what extent those corporate objectives were as a whole met, based on a review of the degree of achievement of each individual corporate objective. The annual cash bonuses for our executive officers other than the CEO depend 75% on the Company's achievement of those corporate objectives and 25% on individual performance as determined by the Committee based on assessments by and a report from the CEO on each such

executive officer's individual performance (relative to the pre-determined corporate objectives as well as more generally). Our CEO's annual cash bonus depends exclusively on the Company's achievement of the pre-established corporate objectives. The Committee believes that broader corporate objectives are appropriate to ensure all executive officers are working together toward those goals, and that individual performance is in some cases an appropriate additional consideration to motivate and reward individual contributions to the Company's overall success. These cash bonus awards are made under our Incentive Compensation Plan (the "ICP") and are shown in the *Grants of Plan-Based Awards - Fiscal Year 2021* table below.

In determining the targeted annual cash bonus opportunity for each named executive officer at the beginning of fiscal year 2021, the Committee considered Radford's market data on targeted annual cash bonus opportunity and total targeted annual cash compensation among our peers. The Committee also considered the experience, performance, and criticality of each executive officer. Based on these considerations, the Committee determined each executive officer's targeted annual cash bonus. The resulting total targeted annual cash compensation for each executive officer fell within the range of the 50th to 75th percentiles, although the Committee did not necessarily target that range.

Targeted annual cash bonuses are expressed as a percentage of base salary earned during the performance period. At the beginning of fiscal year 2021, the Committee determined not to change the target bonuses of our continuing named executive officers from their respective levels set in 2020. Specifically, the Committee recommended and the Board approved setting Dr. Kinney's targeted cash bonus at 60% of his base salary earned in 2021, the Committee set Mr. Nguyen's cash bonus at 50% of his base salary earned in 2021, and the Committee set Ms. Karp's and Mr. Smith's targeted cash bonuses at 40% of their respective base salaries earned in 2021. In the case of Dr. Garren, his targeted cash bonus was set at 50% of his annualized base salary at the time of his appointment as our Chief Medical Officer. In connection with Mr. Smith's promotion to Chief Operating Officer in September 2021, the Committee determined to increase his bonus oppor-

tunity from 40% to 50% of his base salary earned in the fourth quarter of the fiscal year 2021. The maximum cash bonus that could have been earned by the named executive officers was 150% of their respective target bonuses.

In setting these target bonus opportunities, the Committee determined that a higher target bonus opportunity for the CEO, relative to the other executive officers, was appropriate because of the position and responsibilities. The Committee similarly determined that a higher target bonus opportunity for Mr. Nguyen, relative to other named executive officers, was appropriate given his dual positions at the time of Chief Operating Officer and Chief Financial Officer. The Committee determined that the bonus opportunities for Mr. Smith and Ms. Karp should be at the same level, given that the differences in their base salaries were sufficient to distinguish between their relative positions, experience, and criticality. In connection with Dr. Garren's appointment as our Chief Medical Officer in April 2021, and Mr. Smith's promotion to Chief Operating Officer in September 2021, the Committee determined their bonus opportunities after considering Radford's market data.

Dr. Kinney's annual cash bonus for fiscal year 2021 depended 100% on the Company's performance relative to pre-established corporate objectives established by the Committee (and approved by the Board). The other named executive officers' annual cash bonuses for fiscal year 2021 depended 75% on those same corporate objectives and 25% on their respective individual performance, as determined by the Committee based on assessments by the CEO and the Committee's assessment of each executive officer's individual performance.

For fiscal year 2021, the Committee (and the Board, with respect to Dr. Kinney) established pre-determined corporate objectives that it considered critical to the near- and long-term success of the Company. No payout would be earned if achievement of these objectives in the aggregate was below 60% of target. Those objectives were as set forth below, with the weightings shown. The Committee and Board considered these objectives as constituting an appropriate balance of being realistic but challenging, and that exceeding these objectives would, as a whole, require a significant "stretch."

Objective	Weighting	Result
Progress R&D portfolio to achieve primary 2021 milestones:	90%	
For Birtamimab, achieve a study start up goal; execute on external communication plan to support AFFIRM-AL; and deliver initial commercialization plan.	40%	Largely Met
For PRX004, complete a Board-approved transaction or initiate Phase 2 study start-up	15%	Met
For PRX005, complete IND submission by third quarter; execute external preclinical data communication plan; achieve next collaboration milestone	15%	Exceeded
For Prasinezumab, achieve next collaboration milestone	10%	Met
For PRX012, determine program plan based on emerging Alzheimer's disease landscape; complete IND-enabling activities; and execute external preclinical data communication plan	5%	Exceeded
For a proprietary platform technology, execute in vivo validation study and deliver strategic plan	5%	Met
Meet cash burn guidance range and optimize shareholder base:	10%	
Meet publicly-disclosed cash burn guidance range	2.5%	Met
Optimize shareholder base by galvanizing at least one institutional investor (existing or new) to take a > 10% ownership stake; or galvanizing at least two institutional investors (existing or new) to take a > 5% ownership stake; or galvanizing at least five institutional investors (existing or new) to take a >1% ownership stake.	7.5%	Exceeded

Actual attainment of these objectives, as determined by the Committee and the Board, is shown above. Based on this assessment and the overall performance of the Company, the Committee and the Board determined that Company performance exceeded the pre-determined corporate objectives as a whole, resulting in achievement of 125% of target.

Based on Dr. Kinney's assessment and report to the Committee on each other named executive officer's individual performance, the Committee approved annual cash bonuses to the named executive officers (other than Dr. Kinney) at 118.75% of their targeted annual cash bonuses. The Committee recommended to the Board that Dr. Kinney's annual cash bonus be 125% of his targeted annual bonus opportunity - consistent with the Committee's determination described above - which recommendation was considered, discussed, and approved by the Board. The actual annual cash bonus paid to each named executive officer for fiscal year 2021 performance is set forth in the *Non-Equity Incentive Plan Compensation* column of the *Summary Compensation Table - Fiscal Year 2021* below.

In connection with the recruitment of Dr. Garren, we agreed to pay him a \$50,000 retention (hire-on) bonus. That retention bonus will be repayable by Dr. Garren on a pro-rata basis if he ceases his employment prior to the one-year anniversary of his employ

ment start date, unless his employment ends for a reason that would make him eligible for severance benefits under our Amended and Restated Severance Plan. The Committee considered this arrangement appropriate and necessary in order to induce Dr. Garren to leave his prior employer to join the Company.

Long-Term Incentive Compensation. Long-term incentives are an important element of our executive compensation that the Committee uses primarily to motivate our executive officers to increase shareholder value and secondarily to retain executive officers. The Committee believes that long-term incentive compensation also encourages our executive officers to identify, pursue, and invest in appropriate long-term strategies for increasing shareholder value. Our long-term incentives for fiscal year 2021 were solely in the form of nonqualified stock options awarded under our 2018 Long Term Incentive Plan, as amended (the "2018 LTIP"), or our 2020 Employment Inducement Incentive Plan, as amended (the "2020 EIIP").

We use stock options to link executive officer compensation directly to increases in the price of our ordinary shares, which directly reflects shareholder value. All stock options are granted with an exercise price equal to the fair market value (as defined by the 2018 LTIP and the 2020 EIIP, as applicable) of our ordinary shares on the date of grant, and they require

continued employment for four years in order to vest fully (except in the case of certain terminations of employment). Stock options therefore compensate our executive officers only if our share price increases after the date of grant and the executive officer remains employed for the periods required for the stock option to become exercisable. The Committee thus considers stock options to be a particularly effective incentive and retention tool because they motivate our executive officers to increase shareholder value and remain with the Company.

In determining the annual stock option to award to each named executive officer in February 2021, the Committee considered Radford's market data, including:

- The prevalence of other forms of equity-based incentive compensation used by the peer group companies;
- For each executive officer, the grant date Black-Scholes values of the annual stock option awarded to the executive officer in 2020 (where such grants were awarded), and as a general reference, Radford's market data for the 50th and 75th percentiles and the number of option shares that would align with those 50th and 75th percentiles (although the Committee did not necessarily target that range);
- For each executive officer (where such grants were awarded) and all executive officers as a whole, the annual stock options awarded in 2020 as a percent of the Company's outstanding shares, with comparisons to the peer group data;
- For all executive officers as a whole, the grant-date values of the annual stock options awarded in 2020, with comparisons to the peer group data for that year;
- Executive officers' individual and collective equity "ownership" through vested and unvested stock options relative to the peer group data, and the unvested value as a multiple of base salaries;
- Other market data on equity compensation practices, including with respect to "burn rate" and dilution ("overhang"); and
- Each executive officer's total targeted direct compensation relative to the peer group data.

The Committee also considered the relative position, experience, performance, and criticality of each named executive officer. The Committee con

sidered it critical to retain these executive officers to meet 2021 and longer-term objectives and decided that stock options would best serve that retention need.

The Committee considered the use of one or more performance-based option awards to Dr. Kinney and decided not to use this vehicle in 2021 because, given the current business environment, it determined that it did not have an adequate line of sight to issue performance-based option awards with a sufficiently differentiated term and focus from objectives already covered under annual corporate objectives nor with a readily measurable long-term performance period. However, the Committee will continue to evaluate the potential use of performance-based option awards for Dr. Kinney in the future.

Based on all the above considerations, in 2021, the Committee approved annual stock option awards to each of our then-serving named executive officers continuing from 2020 other than Dr. Kinney, i.e., Mr. Nguyen, Mr. Smith, and Ms. Karp, and the Board approved an annual stock option award for Dr. Kinney. The grant-date Black-Scholes values of those stock options awarded to the named executive officers were in aggregate between the 50th and 75th percentiles as indicated by Radford's market data. The grant-date Black-Scholes value of the stock options awarded to Dr. Kinney was at the 50th percentile as indicated by Radford's market data. The 2021 grant date fair values increased as compared to the 2020 grant date fair values due to the competitive position versus the Company's revised peer group, reflecting an increase in the market capitalization of the Company and the peer members, as well as the appreciation in the Company's stock price since 2020. Those stock options vest as to 25% of the shares subject to the option on the first anniversary of the grant date and as to 1/48th of the shares subject to the option on each monthly anniversary thereafter, subject to continued employment on each applicable vesting date.

The Committee approved an initial stock option award (for 250,000 shares) to Dr. Garren in connection with his appointment as our Chief Medical Officer effective in April 2021. That stock option vests as to 25% of the shares subject to the option on the first anniversary of his date of appointment and as to 1/48th of the shares subject to the option on each monthly anniversary thereafter, subject to Dr. Garren's continued employment on each applicable

vesting date. In determining the size of that stock option award, the Committee considered the market data and negotiations with Dr. Garren.

The Committee approved a stock option award (for 25,000 shares) to Mr. Smith in connection with his promotion to Chief Operating Officer in September 2021. That stock option vests as to 25% of the shares subject to the option on the first anniversary of his date of appointment and as to 1/48th of the shares subject to the option on each monthly anniversary thereafter, subject to Mr. Smith's continued employment on each applicable vesting date. In determining the size of that stock option award, the Committee considered the market data.

On May 19, 2020, our shareholders approved a "value-for-value" option exchange program. Pursuant to this approval, we offered the option exchange in an issuer tender offer closing on February 12, 2021. Under the terms of the program, eligible employees and directors could surrender outstanding options for ordinary shares granted prior to April 23, 2018, and with exercise prices equal to or greater than \$17.63, in exchange for a new option award. In order to promote retention, new options granted in the exchange were not vested on the date of grant regardless of whether the surrendered option was fully vested. Instead, the new options are scheduled to vest on the later of the first anniversary of their grant date or the date on which the corresponding option would have vested. Our executive officers were eligible to participate in the

option exchange program. An objective of our equity incentive programs has been, and continues to be, to align the interests of equity incentive plan participants with those of our shareholders, and the Board and the Compensation Committee determined that the option exchange was an important component in our efforts to achieve that goal.

The stock options granted to our named executive officers in fiscal year 2021 and the grant date fair value of those options are set forth in the *Summary Compensation Table - Fiscal Year 2021* and the *Grants of Plan-Based Awards - Fiscal Year 2021* table below.

Deferred Compensation. Our named executive officers were eligible to participate in our tax-qualified 401(k) plan on the same terms as all other U.S. employees. The Company makes non-discretionary contributions to the accounts of all participants in the 401(k) plan, equal to 3.0% of each participant's eligible earnings in 2021, and may also make discretionary matching contributions to all participants' accounts (which it did for fiscal year 2021, equal to 2.0% of each participant's eligible earnings in 2021), so long as each participant had deferred an equal number of dollars into their 401(k) plan account during 2021.

Perquisites and Other Personal Benefits. No perquisites or other personal benefits are provided to our named executive officers.

Employment and Severance Arrangements

Dr. Kinney. In connection with his appointment as our CEO in September 2016, we entered into an employment agreement with Dr. Kinney that sets forth the terms and conditions of his employment as our CEO. That employment agreement provides for an annual base salary of \$500,000, which has subsequently been increased as shown above, and a targeted annual cash bonus equal to 60% of his base salary. Dr. Kinney's employment agreement also provides for certain severance payments and benefits in the event of a qualifying termination of his employment. We have also awarded stock options to Dr. Kinney containing accelerated vesting provisions in the event of a qualifying termination of his employment. The material terms of that employment agreement and those stock options, as they relate to certain potential terminations of

Dr. Kinney's employment, are described below under the heading *Change in Control and Severance Arrangements - Gene G. Kinney*.

The Committee and the Board considered these arrangements to be necessary in order to secure Dr. Kinney's services as our CEO, as well as generally consistent with peer group data presented to the Committee by its compensation consultant. The Committee and the Board believe that these arrangements ensure that Dr. Kinney focuses solely on the best interests of our shareholders in the event of a possible, threatened, or pending change in control, despite how a change in control might affect him personally. These change in control arrangements therefore serve as an important retention tool and help retain, stabilize, and focus Dr. Kinney in the event of a change in control.

Other Named Executive Officers. Each of Mr. Nguyen, Dr. Garren, Mr. Smith, and Ms. Karp, are eligible to participate in our Amended and Restated Severance Plan (the “Severance Plan”), which provides for certain severance payments and benefits in the event of a qualifying termination of employment. In addition, they have each been awarded stock options containing certain accelerated vesting provisions in the event of a qualifying termination of employment. The material terms of the Severance Plan and these option agreements, as they

relate to certain potential terminations of employment, are described below under the heading *Change in Control and Severance Arrangements - Other Named Executive Officers*. For the same reasons described above with respect to Dr. Kinney, the Committee considered these arrangements to be necessary in order to secure the services of these named executive officers and an important retention tool that helps retain, stabilize, and focus our executive officers in the event of a change of control.

REPORT OF THE COMPENSATION COMMITTEE OF THE BOARD OF DIRECTORS

The information in this report is not “soliciting material,” is not deemed “filed” with the SEC and is not to be incorporated by reference into any filing by the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether before or after the date hereof and irrespective of any general incorporation language in any such filing.

The Compensation Committee reviewed and discussed with management the *Compensation Discussion and Analysis* included in this Proxy Statement. Based on those reviews and discussions, the Committee recommended to the Board of Directors that the *Compensation Discussion and Analysis* be included in this Proxy Statement and incorporated by reference into the Company’s Annual Report on Form 10-K.

Paula K. Cobb (Committee Chair)
Christopher S. Henney
Oleg Nodelman
Sanjiv K. Patel

EXECUTIVE COMPENSATION

The following table provides certain information on compensation earned by or awarded to the named executive officers of the Company during our fiscal year 2021, and to the extent required by applicable SEC disclosure rules, fiscal years 2020 and 2019.

Summary Compensation Table - Fiscal Year 2021

Name and Principal Position	Year	Salary (\$)	Bonus (\$)	Option Awards ⁽¹⁾ (\$)	Non-Equity Incentive Plan Compensation ⁽²⁾ (\$)	All Other Compensation ⁽³⁾ (\$)	Total (\$)
Gene G. Kinney, Ph.D. <i>President and Chief Executive Officer</i>	2021	573,250	—	3,900,675	429,938	14,500	4,918,363
	2020	554,292	—	2,526,450	332,575	14,250	3,427,567
	2019	538,125	—	2,338,354	322,875	14,000	3,213,354
Tran B. Nguyen <i>Chief Strategy Officer and Chief Financial Officer</i>	2021	458,574	—	1,310,627	272,278	14,500	2,055,979
	2020	443,415	—	884,258	221,708	14,250	1,563,631
	2019	430,500	—	906,709	215,250	14,000	1,566,459
Hideki Garren, M.D., Ph.D.⁽⁴⁾ <i>Chief Medical Officer</i>	2021	364,044	50,000 ⁽⁵⁾	4,319,200	290,938	14,500	5,038,682
Brandon S. Smith <i>Chief Operating Officer</i>	2021	420,667	—	2,113,654	213,176	14,500	2,761,997
	2020	333,333	100,000 ⁽⁶⁾	1,843,368	133,333	14,250	2,424,284
Carol D. Karp <i>Chief Regulatory Officer</i>	2021	450,713	—	873,751	214,089	14,500	1,553,053
	2020	435,814	—	589,505	174,326	14,250	1,213,895
	2019	423,120	—	477,215	169,248	14,000	1,083,583

- (1) Consists of NQSOs (nonqualified stock options) awarded under our 2018 Long Term Incentive Plan, as amended (the "2018 LTIP"), and our 2020 Employment Inducement Incentive Plan, as amended (the "2020 EIIP"). These amounts do not reflect compensation actually received. Rather, these amounts represent the grant date fair value of the options awarded, calculated in accordance with Financial Accounting Standards Board ASC Topic 718. For a discussion of the assumptions made in calculating the values reflected for fiscal year 2021, see Note 9 of the Consolidated Financial Statements included in our Form 10-K. Dr. Kinney, Mr. Nguyen, and Ms. Karp received replacement options in the "value-for-value" option exchange program described above. Based on the exchange ratio in relation to the price of the Company's ordinary shares at the time of the exchange, there was no aggregate incremental fair value associated with the "value-for-value" option exchange program and, thus, no additional amounts are reflected in this table due to the exchange.
- (2) Consists of cash bonuses paid under our Incentive Compensation Plan (the "ICP") for the fiscal year performance periods indicated (these bonuses were paid in the subsequent year, but are reported for the fiscal year for which they were earned). For more information, see the *Grants of Plan Based Awards - Fiscal Year 2021* table below.
- (3) Consists only of Company contributions to the named executive officer's account under the Company's tax-qualified 401(k) defined contribution plan.
- (4) Dr. Garren commenced employment on April 5, 2021, and was appointed as our Chief Medical Officer effective as of the commencement of his employment.
- (5) Consists of a retention bonus paid to Dr. Garren in connection with the commencement of his employment and appointment as our Chief Medical Officer.
- (6) Consists of a retention bonus paid to Mr. Smith in connection with the commencement of his employment and appointment as our Chief Business Officer.

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The following table shows all plan-based awards granted to our named executive officers during our fiscal year 2021.

Grants of Plan-Based Awards Fiscal Year 2021

Name	Grant Date	Approval Date ⁽¹⁾	Estimated Future Payouts Under Non-Equity Incentive Plan Awards ⁽²⁾			All Other Option Awards: Number of Securities Underlying Options (#)	Exercise or Base Price of Option Awards (\$/sh)	Grant Date Fair Value of Option Awards ⁽³⁾ (\$)
			Threshold (\$)	Target (\$)	Maximum (\$)			
Gene G. Kinney	2/25/2021					250,000 ⁽⁴⁾	22.60	3,900,675
	2/12/2021					344,700 ⁽⁵⁾	22.85	— ⁽⁶⁾
			207,540	345,900	518,850			
Tran B. Nguyen	2/25/2021	2/18/2021				84,000 ⁽⁴⁾	22.60	1,310,627
	2/12/2021					189,837 ⁽⁵⁾	22.85	— ⁽⁶⁾
			103,764	230,587	345,880			
Hideki Garren	4/5/2021	4/1/2021				250,000 ⁽⁴⁾	24.90	4,319,200
			110,250	245,000	367,500			
Brandon S. Smith	2/25/2021	2/18/2021				56,000 ⁽⁴⁾	22.60	873,751
	9/29/2021					25,000 ⁽⁴⁾	70.81	1,239,903
			81,203	180,450	270,675			
Carol D. Karp	2/25/2021	2/18/2021				56,000 ⁽⁴⁾	22.60	873,751
	2/12/2021					96,394 ⁽⁵⁾	22.85	— ⁽⁶⁾
			81,588	181,307	271,961			

- (1) This column shows the date that the Compensation Committee took action with respect to the award if that date is different than the grant date. If the grant date is not the meeting date, it is a fixed, future date specified at the time of the grant.
- (2) Consists of cash bonus awards under the ICP for our fiscal year 2021. Under these awards, the named executive officers were eligible to receive a cash payout depending entirely or primarily upon Company performance relative to pre-determined objectives for fiscal year 2021. In the case of Dr. Kinney, his earned cash payout depended 100% upon Company performance against those pre-determined objectives. In the case of the other named executive officers, their earned cash payouts depended 75% on Company performance against those pre-determined objectives and 25% on individual performance for fiscal year 2021. The amounts shown in the *Threshold* column are those that would have been paid if the minimum or threshold level of Company performance relative to the pre-determined objectives established by the Committee had been achieved for payouts to have been earned (which minimum performance the Committee had set at 60% of the pre-determined corporate objectives) and, in the case of the named executive officers other than Dr. Kinney, no amount was paid for the individual performance component of the bonus opportunity. The amounts shown in the *Target* column are those that would have been paid if each of the pre-determined objectives for Company performance established by the Committee had been achieved, and assume that the Committee also determined that individual performance supported a 100% payout. The amounts shown in the *Maximum* column are those that would have been paid if the each of the pre-determined objectives for Company performance established by the Committee had been achieved and the Committee determined that other Company and individual accomplishments supported a maximum payout. If Company performance relative to the pre-determined objectives for fiscal year 2021 had not at least equaled the minimum (threshold) level of 60%, no payout would have been earned. Regardless of Company and/or individual performance, the maximum payout for each named executive officer was 150% of their targeted bonus payout. In addition, regardless of actual performance relative to the pre-determined objectives, the Committee retained discretion to reduce or eliminate any amount that otherwise would be payable. The amounts reported in this table are "estimated future payouts" as they existed at the time the award was made, and assume that each named executive officer actually earned his or her target annual base salary in 2021; the actual cash payouts to each executive officer are reported in the *Non-Equity Incentive Plan* column of the *Summary Compensation Table - Fiscal Year 2021* above.
- (3) These amounts do not reflect compensation actually received. Rather, these amounts represent the grant date fair value of the option awards, calculated in accordance with Financial Accounting Standards Board ASC Topic 718. For a discussion of the assumptions made in calculating the values reflected, see Note 9 of the Consolidated Financial Statements included in our Form 10-K. The fair values reported in this table are also reported in the *Option Awards* column of the *Summary Compensation Table - Fiscal Year 2021* above.
- (4) Consists of ordinary shares that may be acquired by exercise of nonqualified stock options awarded under the 2018 LTIP or 2020 EIIP. These option awards have a four-year vesting schedule from the vesting commencement date (which varied by individual and grant), with 25% of the shares subject to the option vesting on the first anniversary of that vesting commencement date, and the remainder vesting in equal monthly installments over the next three years thereafter, subject to continued employment (except in the event of certain terminations).

of employment, as described below under the heading *Change in Control and Severance Arrangements*). The option exercise price per share for each of these option awards is the closing market price of the Company's ordinary shares on the date of grant. These option awards expire no later than ten years after the grant date. These option awards are also reported in the *Outstanding Equity Awards at Fiscal Year-End - Fiscal Year 2021* table below.

- (5) Represents replacement option awards received in the "value-for-value" option exchange program described above. Consists of ordinary shares that may be acquired by exercise of nonqualified stock options awarded under the 2018 LTIP. Pursuant to the terms of the option exchange program, these option awards are subject to a new initial one-year vesting period from the date of grant. Upon the cliff vesting date, a number of shares corresponding to the surrendered option shares that (1) were vested at the time of the exchange or (2) would have vested during the one-year period prior to the cliff vesting date will vest. Any remaining unvested portion of the new replacement option award will vest on the same monthly schedule that previously applied to the applicable surrendered option award. The applicable surrendered option awards have a four-year vesting schedule from the vesting commencement date (which varied by individual and grant), with 25% of the shares subject to the option vesting on the first anniversary of that vesting commencement date, and the remainder vesting in equal monthly installments over the next three years thereafter, subject to continued employment (except in the event of certain terminations of employment, as described below under the heading *Change in Control and Severance Arrangements*). The option exercise price per share for each of these option awards is the closing market price of the Company's ordinary shares on the date of grant. These option awards have the same expiration date as the applicable surrendered options for which they were exchanged and expire no later than ten years after the grant date of the applicable surrendered option award. These option awards are also reported in the *Outstanding Equity Awards at Fiscal Year-End - Fiscal Year 2021* table below.
- (6) Represents replacement option awards received in the "value-for-value" option exchange program described above. Based on the exchange ratio in relation to the price of the Company's ordinary shares at the time of the exchange, there was no aggregate incremental fair value associated with the "value-for-value" option exchange program and, thus, no additional amounts are reflected in this table due to the exchange.

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The following table shows all outstanding equity awards - which were only nonqualified stock options - held by our named executive officers at the end of our fiscal year 2021. Certain of the stock option awards reported in this table are also reported in the *Grants of Plan-Based Awards - Fiscal Year 2021* table above.

Outstanding Equity Awards at Fiscal Year-End Fiscal Year 2021

Name	Option Awards ⁽¹⁾			
	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price (\$)	Option Expiration Date
Gene G. Kinney	99,074	—	6.41	01/29/2023
	45,000	—	29.81	02/04/2024
	542,500	77,500 ⁽²⁾	15.04	06/21/2028
	173,541	71,459 ⁽³⁾	13.53	02/27/2029
	91,666	108,334 ⁽⁴⁾	12.15	02/25/2030
	50,000	—	12.15	02/25/2030
	—	59,090 ⁽⁵⁾	22.85	03/11/2025
	—	40,625 ⁽⁶⁾	22.85	02/24/2026
	—	25,125 ⁽⁷⁾	22.85	09/01/2026
	—	16,759 ⁽⁸⁾	22.85	11/02/2026
	—	62,500 ⁽⁹⁾	22.85	02/22/2027
	—	140,601 ⁽¹⁰⁾	22.85	02/21/2028
	—	250,000 ⁽¹¹⁾	22.60	02/25/2031
Tran B. Nguyen	150,000	—	6.73	04/01/2023
	45,000	—	29.81	02/04/2024
	218,750	31,250 ⁽²⁾	15.04	06/21/2028
	67,291	27,709 ⁽³⁾	13.53	02/27/2029
	48,125	56,875 ⁽⁴⁾	12.15	02/25/2030
	—	50,000 ⁽⁵⁾	22.85	03/11/2025
	—	40,625 ⁽⁶⁾	22.85	02/24/2026
	—	39,062 ⁽⁹⁾	22.85	02/22/2027
	—	60,150 ⁽¹⁰⁾	22.85	02/21/2028
	—	84,000 ⁽¹¹⁾	22.60	02/25/2031
Hideki Garren	—	250,000 ⁽¹²⁾	24.90	04/05/2031
Brandon S. Smith	105,000	135,000 ⁽¹³⁾	11.12	03/02/2030
	—	56,000 ⁽¹¹⁾	22.60	02/25/2031
	—	25,000 ⁽¹⁴⁾	70.81	09/29/2031

Name	Option Awards ⁽¹⁾			
	Number of Securities Underlying Exercisable Options (#)	Number of Securities Underlying Unexercised Options (#)	Option Exercise Price (\$)	Option Expiration Date
Carol D. Karp	101,250	18,750 ⁽²⁾	15.04	06/21/2028
	35,416	14,584 ⁽³⁾	13.53	02/27/2029
	32,083	37,917 ⁽⁴⁾	12.15	02/25/2030
	—	51,282 ⁽¹⁵⁾	22.85	12/14/2026
	—	45,112 ⁽¹⁰⁾	22.85	02/21/2028
	—	56,000 ⁽¹¹⁾	22.60	02/25/2031

- (1) All option awards were granted under our 2012 LTIP, our 2018 LTIP, or our 2020 EIIP, and are subject to accelerated vesting in the event of certain terminations of employment, as further described below under the heading *Potential Payments and Benefits upon Termination of Employment*.
- (2) These option awards have a four-year vesting schedule from a vesting commencement date of June 21, 2018, with 25% of the shares subject to the option vesting on the first anniversary of the vesting commencement date, and the remainder vesting in equal monthly installments over the next three years thereafter (subject to continued employment).
- (3) These option awards have a four-year vesting schedule from a vesting commencement date of February 27, 2019, with 25% of the shares subject to the option vesting on the first anniversary of the vesting commencement date, and the remainder vesting in equal monthly installments over the next three years thereafter (subject to continued employment).
- (4) These option awards have a four-year vesting schedule from a vesting commencement date of February 25, 2020, with 25% of the shares subject to the option vesting on the first anniversary of the vesting commencement date, and the remainder vesting in equal monthly installments over the next three years thereafter (subject to continued employment).
- (5) These option awards represent replacement option awards received in the "value-for-value" option exchange program described above. Pursuant to the terms of the option exchange program, these option awards are subject to a new initial one-year vesting period from the date of grant. Upon the cliff vesting date, a number of shares corresponding to the surrendered option shares that (1) were vested at the time of the exchange or (2) would have vested during the one-year period prior to the cliff vesting date will vest. Any remaining unvested portion of the new replacement option award will vest on the same monthly schedule that previously applied to the applicable surrendered option award. The surrendered option awards have a four-year vesting schedule from a vesting commencement date of March 11, 2015, with 25% of the shares subject to the option vesting on the first anniversary of the vesting commencement date, and the remainder vesting in equal monthly installments over the next three years thereafter (subject to continued employment).
- (6) These option awards represent replacement option awards received in the "value-for-value" option exchange program described above. Pursuant to the terms of the option exchange program, these option awards are subject to a new initial one-year vesting period from the date of grant. Upon the cliff vesting date, a number of shares corresponding to the surrendered option shares that (1) were vested at the time of the exchange or (2) would have vested during the one-year period prior to the cliff vesting date will vest. Any remaining unvested portion of the new replacement option award will vest on the same monthly schedule that previously applied to the applicable surrendered option award. The surrendered option awards have a four-year vesting schedule from a vesting commencement date of February 24, 2016, with 25% of the shares subject to the option vesting on the first anniversary of the vesting commencement date, and the remainder vesting in equal monthly installments over the next three years thereafter (subject to continued employment).
- (7) This option award represents a replacement option award received in the "value-for-value" option exchange program described above. Pursuant to the terms of the option exchange program, this option award is subject to a new initial one-year vesting period from the date of grant. Upon the cliff vesting date, a number of shares corresponding to the surrendered option shares that (1) were vested at the time of the exchange or (2) would have vested during the one-year period prior to the cliff vesting date will vest. Any remaining unvested portion of the new replacement option award will vest on the same monthly schedule that previously applied to the applicable surrendered option award. The surrendered option award has a four-year vesting schedule from a vesting commencement date of September 1, 2016, with 25% of the shares subject to the option vesting on the first anniversary of the vesting commencement date, and the remainder vesting in equal monthly installments over the three years thereafter (subject to continued employment).
- (8) This option award represents a replacement option award received in the "value-for-value" option exchange program described above. Pursuant to the terms of the option exchange program, this option award is subject to a new initial one-year vesting period from the date of grant. Upon the cliff vesting date, a number of shares corresponding to the surrendered option shares that (1) were vested at the time of the exchange or (2) would have vested during the one-year period prior to the cliff vesting date will vest. Any remaining unvested portion of the new replacement option award will vest on the same monthly schedule that previously applied to the applicable surrendered option award. The surrendered option award has a four-year vesting schedule from a vesting commencement date of September 30, 2016, with 25% of the shares subject to the option vesting on the first anniversary of the vesting commencement date, and the remainder vesting in equal monthly installments over the three years thereafter (subject to continued employment).
- (9) These option awards represent replacement option awards received in the "value-for-value" option exchange program described above. Pursuant to the terms of the option exchange program, these option awards are subject to a new initial one-year vesting period from the date of grant. Upon the cliff vesting date, a number of shares corresponding to the surrendered option shares that (1) were vested at the time of the exchange or (2) would have vested during the one-year period prior to the cliff vesting date will vest. Any remaining unvested portion of the new replacement option award will vest on the same monthly schedule that previously applied to the applicable

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- surrendered option award. The surrendered option awards have a four-year vesting schedule from a vesting commencement date of February 22, 2017, with 25% of the shares subject to the option vesting on the first anniversary of the vesting commencement date, and the remainder vesting in equal monthly installments over the next three years thereafter (subject to continued employment).
- (10) These option awards represent replacement option awards received in the “value-for-value” option exchange program described above. Pursuant to the terms of the option exchange program, these option awards are subject to a new initial one-year vesting period from the date of grant. Upon the cliff vesting date, a number of shares corresponding to the surrendered option shares that (1) were vested at the time of the exchange or (2) would have vested during the one-year period prior to the cliff vesting date will vest. Any remaining unvested portion of the new replacement option award will vest on the same monthly schedule that previously applied to the applicable surrendered option award. The surrendered option awards have a four-year vesting schedule from a vesting commencement date of February 21, 2018, with 25% of the shares subject to the option vesting on the first anniversary of the vesting commencement date, and the remainder vesting in equal monthly installments over the next three years thereafter (subject to continued employment).
- (11) These option awards have a four-year vesting schedule from a vesting commencement date of February 25, 2021, with 25% of the shares subject to the option vesting on the first anniversary of the vesting commencement date, and the remainder vesting in equal monthly installments over the next three years thereafter (subject to continued employment).
- (12) This option award has a four-year vesting schedule from a vesting commencement date of April 5, 2021, with 25% of the shares subject to the option vesting on the first anniversary of the vesting commencement date, and the remainder vesting in equal monthly installments over the three years thereafter (subject to continued employment).
- (13) This option award has a four-year vesting schedule from a vesting commencement date of March 2, 2020, with 25% of the shares subject to the option vesting on the first anniversary of the vesting commencement date, and the remainder vesting in equal monthly installments over the three years thereafter (subject to continued employment).
- (14) This option award has a four-year vesting schedule from a vesting commencement date of September 29, 2021, with 25% of the shares subject to the option vesting on the first anniversary of the vesting commencement date, and the remainder vesting in equal monthly installments over the three years thereafter (subject to continued employment).
- (15) This option award represents a replacement option award received in the “value-for-value” option exchange program described above. Pursuant to the terms of the option exchange program, this option award is subject to a new initial one-year vesting period from the date of grant. Upon the cliff vesting date, a number of shares corresponding to the surrendered option shares that (1) were vested at the time of the exchange or (2) would have vested during the one-year period prior to the cliff vesting date will vest. Any remaining unvested portion of the new replacement option award will vest on the same monthly schedule that previously applied to the applicable surrendered option award. The surrendered option award has a four-year vesting schedule from a vesting commencement date of December 14, 2016, with 25% of the shares subject to the option vesting on the first anniversary of the vesting commencement date, and the remainder vesting in equal monthly installments over the three years thereafter (subject to continued employment).

The following table shows options exercised by our named executive officers during fiscal year 2021.

Options Exercised and Stock Vested⁽¹⁾
Fiscal Year 2021

Name	Number of Shares Acquired on Exercise (#)	Value Realized on Exercise (\$) ⁽²⁾
Gene G. Kinney	—	—
Tran B. Nguyen	—	—
Hideki Garren	—	—
Brandon S. Smith	—	—
Carol D. Karp	30,000	1,522,801

(1) The Company has granted only stock options.

(2) The value realized on exercise of stock options as shown in this chart was calculated by subtracting the option exercise price from the market price to obtain the value realized per share, and multiplying the value realized per share by the number of shares acquired upon exercise. The market price for each transaction was determined as follows: If upon exercising, the named executive officer sold the shares acquired, the market price was determined to be the sale price. If upon exercising, the named executive officer kept the shares acquired, then the market price was determined to be the closing price of the Company’s ordinary shares on the date of the exercise.

Potential Payments and Benefits upon Termination of Employment

The following table shows the potential payments and benefits that the Company would be obligated to make or provide upon termination of employment of each of our named executive officers. Amounts shown do not include salary, any bonus earned but not paid through the date of termination, accrued but unused vacation time or amounts or benefits required to be paid or provided by law and applicable to all employees. For purposes of this table, it is assumed that each named executive officer's employment terminated at the close of business on December 31, 2021, the last day of our fiscal year 2021. Following this table, under the heading *Change in Control and Severance Arrangements*, is a narrative description of the arrangements under which these potential payments and benefits could be provided.

Name	Nature of Payment or Benefit	Termination by Company ⁽¹⁾			Termination by Executive ⁽¹⁾			Termination Following Change in Control ⁽²⁾
		For Cause	Due to a Business Condition	For Any Other Reason	Due to Voluntary Resignation	For Good Reason	Due to Death or Disability	
Gene G. Kinney	Cash Severance ⁽³⁾	—	720,625	720,625	—	720,625	720,625	1,153,000
	Cash Bonus ⁽³⁾	—	345,900	345,900	—	345,900	345,900	691,800
	Accelerated Options ⁽⁴⁾	—	21,079,994	21,079,994	—	21,079,994	25,113,361	25,113,361
	COBRA Coverage ⁽⁵⁾	—	48,662	48,662	—	48,662	48,662	48,662
	Career Assistance ⁽⁶⁾	—	15,000	15,000	—	15,000	15,000	15,000
	Total	\$—	\$22,210,181	\$22,210,181	\$—	\$22,210,181	\$26,243,548	\$27,021,823
Tran B. Nguyen	Cash Severance ⁽³⁾	—	461,173	—	—	461,173	—	691,760
	Cash Bonus ⁽³⁾	—	230,587	—	—	230,587	—	345,880
	Accelerated Options ⁽⁴⁾	—	8,975,447	—	—	8,975,447	11,477,638	11,477,638
	COBRA Coverage ⁽⁵⁾	—	20,305	—	—	20,305	—	30,458
	Career Assistance ⁽⁶⁾	—	15,000	—	—	15,000	—	15,000
	Total	\$—	\$ 9,702,512	\$ —	\$—	\$ 9,702,512	\$11,477,638	\$12,560,736
Hideki Garren	Cash Severance ⁽³⁾	—	490,000	—	—	490,000	—	735,000
	Cash Bonus ⁽³⁾	—	245,000	—	—	245,000	—	367,500
	Accelerated Options ⁽⁴⁾	—	2,552,067	—	—	2,552,067	6,125,000	6,125,000
	COBRA Coverage ⁽⁵⁾	—	32,441	—	—	32,441	—	48,662
	Career Assistance ⁽⁶⁾	—	15,000	—	—	15,000	—	15,000
	Total	\$—	\$ 3,334,508	\$ —	\$—	\$ 3,334,508	\$ 6,125,000	\$ 7,291,162
Brandon S. Smith	Cash Severance ⁽³⁾	—	450,000	—	—	450,000	—	675,000
	Cash Bonus ⁽³⁾	—	225,000	—	—	225,000	—	337,500
	Accelerated Options ⁽⁴⁾	—	2,984,649	—	—	2,984,649	6,668,600	6,668,600
	COBRA Coverage ⁽⁵⁾	—	32,441	—	—	32,441	—	48,662
	Career Assistance ⁽⁶⁾	—	15,000	—	—	15,000	—	15,000
	Total	\$—	\$ 3,707,090	\$ —	\$—	\$ 3,707,090	\$ 6,668,600	\$ 7,744,762
Carol D. Karp	Cash Severance ⁽³⁾	—	453,268	—	—	453,268	—	679,902
	Cash Bonus ⁽³⁾	—	181,307	—	—	181,307	—	271,961
	Accelerated Options ⁽⁴⁾	—	4,991,610	—	—	4,991,610	6,639,847	6,639,847
	COBRA Coverage ⁽⁵⁾	—	23,004	—	—	23,004	—	34,506
	Career Assistance ⁽⁶⁾	—	15,000	—	—	15,000	—	15,000
	Total	\$—	\$ 5,664,189	\$ —	\$—	\$ 5,664,189	\$ 6,639,847	\$ 7,641,216

(1) Occurring outside of the 24-month period commencing on the consummation of a Change in Control, as defined in the Employment Agreement (in

the case of Dr. Kinney) or the Severance Plan (in the case of the other named executive officers) and the executive officer's option award agreements. For more information, see the narrative description below under the heading *Change in Control and Severance Arrangements*.

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- (2) Due to (a) death or disability, (b) termination without Cause or resignation for Good Reason under the Employment Agreement and option agreements (in the case of Dr. Kinney) or the option agreements (in the case of the other named executive officers), or (c) a Triggering Event under the Severance Plan (in the case of the other named executive officers), in each case occurring within the 24-month period commencing on the consummation of a Change in Control, as defined in the Employment Agreement (in the case of Dr. Kinney) or the Severance Plan (in the case of the other named executive officers) and the executive officer's option award agreements. For more information, see the narrative description below under the heading *Change in Control and Severance Arrangements*.
- (3) Consists of the applicable multiple of annual base salary and targeted annual cash bonus pursuant to the Employment Agreement (in the case of Dr. Kinney) or the Severance Plan (in the case of the other named executive officers).
- (4) Consists of the in-the-money value of certain unvested nonqualified stock options as of December 31, 2021 at the closing market price per share of our ordinary shares (\$49.40) on December 31, 2021, the last trading date of fiscal year 2021. For more information, see the footnotes to the *Outstanding Equity Awards at Fiscal Year-End - Fiscal Year 2021* table above.
- (5) Amounts shown are estimates of what the Company would pay in COBRA premiums for continued medical, dental and vision coverage after a qualifying termination of employment. The reported amounts (a) include only the portion of the COBRA premiums for the executive officer and his or her covered dependents that exceeds the amount the executive officer would have paid as an employee, (b) assume that the executive officer and all covered dependents do not cease to be eligible for COBRA during the relevant period, and (c) assume that the executive officer does not become eligible to receive new healthcare coverage during the relevant period.
- (6) Amounts shown are estimates of what the Company would pay to provide career transition assistance to the executive officer. The reported amounts assume that the executive officer (a) commences this assistance within 60 days following the date his or her employment terminates, and (b) uses this benefit for the full 12 months it is available to the executive officer.

Change in Control and Severance Arrangements

Gene G. Kinney

Dr. Kinney, our President and Chief Executive Officer, is party to an Employment Agreement, dated November 2, 2016, with Prothena Biosciences Inc ("PBI"), a wholly-owned subsidiary of the Company and Dr. Kinney's employer (referred to in this *Change in Control and Severance Arrangements* section as the "Company"). That Employment Agreement was approved by our Board. The Employment Agreement provides for certain compensation to be paid and benefits to be provided to Dr. Kinney (or his estate) in the event of certain involuntary terminations of his employment. In addition, stock options awarded to Dr. Kinney are subject to terms (approved or recommended by the Compensation Committee and approved by the Board) providing for accelerated vesting and extensions of time to exercise in the event of certain involuntary terminations of employment.

The Employment Agreement and option award agreements with Dr. Kinney provide for the following compensation and benefits to be provided to Dr. Kinney in the event of certain involuntary terminations of his employment:

Accrued Payments. Upon a termination of Dr. Kinney's employment for any reason, Dr. Kinney (or his estate) will be entitled to receive (a) any portion of his annual base salary and targeted annual performance-based bonus that is earned but not paid through the date of termination; (b) any unreimbursed business expenses; (c) any accrued but unused vacation and/or floating holi

days; and (d) any amount arising from Dr. Kinney's participation in, or benefits under, any employee benefit plans, programs or arrangements.

Severance Payments and Benefits Not in Connection with a Change in Control. In the event of Dr. Kinney's termination of employment by the Company without Cause (defined below), by Dr. Kinney for Good Reason (defined below) or because of Dr. Kinney's death or Disability (as defined in the Employment Agreement), in each case that occurs outside of the 24-month period commencing on the consummation of a Change in Control (defined below), in addition to the accrued payments described above, the Company will (a) pay in a lump sum cash payment an amount equal to 125% of Dr. Kinney's annual base salary as of the date of termination; (b) pay in a lump sum cash payment an amount equal to 100% of Dr. Kinney's annual target bonus; (c) if Dr. Kinney elects to receive continued healthcare coverage pursuant to COBRA, directly pay, or reimburse him for, the portion of the COBRA premiums for Dr. Kinney and his covered dependents that exceeds the amount of such premium an active employee would be required to pay during the period commencing on his termination of employment and ending upon the earliest of (1) the 18-month anniversary of the date of termination, (2) the date that he and/or his covered dependents, as applicable, become no longer eligible for COBRA, or (3) the date that he becomes eligible to receive healthcare coverage from a subsequent employer; and (d) if Dr. Kinney commences a career transition assistance program sponsored or arranged for by

the Company within 60 days following the date of termination, pay for such program for a period of 12 months. In addition, if Dr. Kinney's termination of employment by the Company without Cause or by Dr. Kinney for Good Reason, (i) each outstanding equity award granted to Dr. Kinney on or after the date of the Employment Agreement will accelerate with respect to that number of shares that would have vested had he continued employment for the 18-month period immediately following the date of termination, and the post-termination exercise period will extend to 18 months from the date of termination (unless it expires earlier under its term), and (ii) each outstanding option award granted to Dr. Kinney before the date of the Employment Agreement will accelerate with respect to that number of shares that would have vested had he continued employment for the 12-month period immediately following the date of termination, and the post-termination exercise period will extend to 12 months from the date of termination (unless it expires earlier under its term). In the event of the termination of Dr. Kinney's employment due to his death or Total and Permanent Disability (as defined in the option award agreements), each outstanding option award held by him will accelerate with respect to 100% of the then unvested shares subject to each such option award, and the post-termination exercise period will extend to 12 months from the date of termination (unless it expires earlier under its term).

Severance Payments and Benefits in Connection with a Change in Control. In the event of Dr. Kinney's termination of employment by the Company without Cause, by Dr. Kinney for Good Reason or because of Dr. Kinney's death or Disability, in each case that occurs within the 24-month period commencing on the consummation of a Change in Control, in addition to the accrued payments described above, the Company will (a) pay in a lump sum cash payment an amount equal to 200% of Dr. Kinney's annual base salary as of the date of termination; (b) pay in a lump sum cash payment an amount equal to 200% of Dr. Kinney's annual target bonus; (c) if Dr. Kinney elects to receive continued healthcare coverage pursuant to COBRA, directly pay, or reimburse him for, the portion of the COBRA premiums for Dr. Kinney and his covered dependents that exceeds the amount of such premium an active employee would be required to pay during the period commencing on his termination of employment and ending upon the earliest of (1) the 18-month anniversary of the date of termination, (2) the date that he and/or his covered dependents, as applicable, become no longer eligible for

COBRA, or (3) the date he becomes eligible to receive healthcare coverage from a subsequent employer; and (d) if Dr. Kinney commences a career transition assistance program sponsored or arranged for by the Company within 60 days following the date of termination, pay for such program for a period of 12 months. In addition, each outstanding equity award held by Dr. Kinney will accelerate with respect to 100% of the then unvested shares subject to each such equity award, and the post-termination exercise period will extend to 18 months from the date of termination (unless it expires earlier under its term).

Dr. Kinney's employment agreement also includes a Section 280G "best pay" provision, which provides that in the event that any payments or benefits received by Dr. Kinney in connection with a Change in Control would be subject to the excise tax under Section 4999 of the U.S. Internal Revenue Code of 1986, as amended (the "Code"), Dr. Kinney will receive either a reduced portion of such payments and benefits such that no excise tax would apply or the full amount of the payments and benefits, whichever results in a greater after-tax benefit to Dr. Kinney.

"Change in Control" is defined in the Employment Agreement as (a) the consummation of a merger or consolidation of the Company with or into another entity or any other corporate reorganization, if more than 50% of the combined voting power of the continuing or surviving entity's issued shares or securities outstanding immediately after such merger, consolidation or other reorganization is owned by persons who were not shareholders of the Company immediately prior to such merger, consolidation or other reorganization; (b) the sale, transfer or other disposition of all or substantially all of the Company's assets; (c) individuals who as of the date the Board first consists of at least seven members constitute the Board (the "Original Directors") cease for any reason to constitute at least a majority of the Board; provided, however, that any individual who becomes a director of the Company subsequent to the date the Board first consists of at least seven members shall be considered an Original Director if the individual's election or nomination for election to the Board was approved by a vote of at least a majority of the Original Directors; but, provided further that any such individual whose initial assumption of office is in connection with an actual or threatened solicitation of proxies or consents by or on behalf of a person other than the Board, including by reason of agreement intended to avoid or settle any such actual or threatened contest or solicitation will not be considered an Original Direc

tor; (d) a transaction as a result of which any person or company obtains the ownership directly or indirectly of the shares in the Company carrying more than 50% of the total voting power represented by the Company's issued share capital in pursuance of a compromise or arrangement sanctioned by the court under Section 453 of the Irish Companies Act 2014, or becomes bound or entitled to acquire ordinary shares in the Company under Section 457 of the Irish Companies Act 2014; (e) any transaction as a result of which any person becomes the "beneficial owner" (as defined in Rule 13d-3 under the Exchange Act), directly or indirectly, of securities of the Company, representing at least 50% of the total voting power represented by the Company's then outstanding voting securities (e.g., issued shares); or (f) certain similar transactions taking place with respect to PBI, as set forth more fully in the Employment Agreement. The definition of "Change in Control" for purposes of the option award agreements is substantially similar to the definition in the Employment Agreement, except that similar transactions with respect to PBI are not included.

"Cause" is defined in the Employment Agreement as (a) the willful and continued failure by Dr. Kinney to substantially perform his duties with the Company (other than as a result of physical or mental disability) after a written demand for substantial performance is delivered to Dr. Kinney by the Board, which demand specifically identifies the manner in which the Board believes that Dr. Kinney has not substantially performed his duties and that has not been cured within 30 days following receipt by him of the written demand; (b) commission by Dr. Kinney of a felony (other than a traffic-related offense) that in the written determination of the Board is likely to cause or has caused material injury to our business;

(c) documented intentional misrepresentation or omission of material fact with respect to a significant matter relating to our business; or (d) material breach of any agreement by and between Dr. Kinney and the Company, which material breach has not been cured within 30 days following receipt by Dr. Kinney of written notice from the Board identifying such material breach. "Cause" is defined in the option award agreements as (i) the willful breach, habitual neglect or poor performance of job duties and responsibilities; (ii) conviction (or entry of a guilty plea or plea of nolo contendere) of any crime, excluding minor traffic offenses; (iii) commission of an act of dishonesty or breach of fiduciary duty; (iv) commission of a material violation of any of the Company's personnel policies; or (v) any act or omission which is contrary to the business interest, reputation or goodwill of the Company.

"Good Reason" is defined in the Employment Agreement as (a) a material diminution in Dr. Kinney's base compensation; (b) a material diminution in his authority, duties or responsibilities; (c) a change in the geographic location at which he must perform his services that increases his one-way commute by more than 30 miles; or (d) a material breach of the Employment Agreement by the Company. Notwithstanding the foregoing, Dr. Kinney will not have "Good Reason" unless the condition giving rise to his resignation continues more than 30 days following his written notice of the condition provided to the Company within 90 days of the first occurrence of such condition and his resignation is effective within 180 days following the first occurrence of such condition. The definition of "Good Reason" in the option award agreements is substantially similar to the definition in the Employment Agreement.

Other Named Executive Officers

The other named executive officers (*i.e.*, the named executive officers other than Dr. Kinney) are eligible to participate in PBI's Amended and Restated Severance Plan (the "Severance Plan"), which was approved by the Compensation Committee of our Board. The Severance Plan provides for certain compensation to be paid and benefits to be provided to them (or their estates) in the event of certain involuntary terminations of their employment. In addition, stock options awarded to those named executive officers are subject to terms providing for accelerated vesting and extensions of time to exercise in the event of certain involuntary terminations of employment.

The Severance Plan and option award agreements provide for the following compensation and benefits to be provided to the other named executive officers in the event of certain involuntary terminations of employment:

Severance Payments and Benefits Not in Connection with a Change in Control. Under the Severance Plan, in the event of a named executive officer's termination of employment by the Company on account of a Triggering

Event (defined below) that occurs outside of the 24-month period commencing on the consummation of a Change in Control (defined below), the

Company will (a) pay in a lump sum cash payment an amount equal to 100% of the named executive officer's annual base salary as of the date of termination; (b) pay in a lump sum cash payment an amount equal to 100% of the annual target bonus; (c) if the named executive officer elects to receive continued healthcare coverage pursuant to COBRA, directly pay, or reimburse him or her for, the portion of the COBRA premiums for the named executive officer and his or her covered dependents that exceeds the amount of such premium an active employee would be required to pay during the period commencing on his or her termination of employment and ending upon the earliest of (1) the 12-month anniversary of the date of termination, (2) the date that he or she and/or his or her covered dependents, as applicable, become no longer eligible for COBRA, or (3) the date he or she becomes eligible for new healthcare coverage (other than through his or her spouse); and (d) if the named executive officer commences a career transition assistance program sponsored or arranged for by the Company within 60 days following the date of termination, pay for such program for a period of 12 months.

Under the option award agreements, in the event of the named executive officer's termination of employment by the Company without Cause (defined below) or by the executive officer for Good Reason (defined below), in each case that occurs outside of the 24-month period commencing on the consummation of a Change in Control (defined below), each outstanding option award held by the named executive officer will accelerate with respect to that number of shares that would have vested had he or she continued employment for the 12-month period immediately following the date of termination, and the post-termination exercise period will extend to 12 months from the date of termination (unless it expires earlier under its term). In the event of a named executive officer's termination of employment because of the executive officer's death or Total and Permanent Disability (as defined in the agreements), each outstanding option award held by the named executive officer will accelerate with respect to 100% of the then unvested shares subject to each such option award, and the post-termination exercise period will extend to 12 months from the date of termination (unless it expires earlier under its term).

Severance Payments and Benefits in Connection with a Change in Control. In the event of a named executive officer's termination of employment by the Company in connection with a Triggering Event

that occurs within the 24-month period commencing on the consummation of a Change in Control, the Company will (a) pay in a lump sum cash payment an amount equal to 150% of the named executive officer's annual base salary as of the date of termination; (b) pay 150% of the annual target bonus in a lump sum cash payment; (c) if the named executive officer elects to receive continued healthcare coverage pursuant to COBRA, directly pay, or reimburse him or her for, the portion of the COBRA premiums for the named executive officer and his or her covered dependents that exceeds the amount of such premium an active employee would be required to pay during the period commencing on his or her termination of employment and ending upon the earliest of (1) the 18-month anniversary of the date of termination, (2) the date that he or she and/or his or her covered dependents, as applicable, become no longer eligible for COBRA, or (3) the date he or she becomes eligible for new healthcare coverage (other than through his or her spouse); and (d) if the named executive officer commences a career transition assistance program sponsored or arranged for by the Company within 60 days following the date of termination, pay for such program for a period of 12 months.

The Severance Plan also includes a Section 280G "best pay" provision, which provides that in the event that any payments or benefits received by the named executive officer in connection with a Change in Control would be subject to the excise tax under Section 4999 of the Code, the named executive officer will receive either a reduced portion of such payments and benefits such that no excise tax would apply or the full amount of the payments and benefits, whichever results in a greater after-tax benefit to the named executive officer.

Under the option award agreements, in the event of a named executive officer's termination of employment by the Company without Cause or by the executive officer for Good Reason, in each case that occurs within the 24-month period commencing on the consummation of a Change in Control, the Company will accelerate each outstanding option award held by the named executive officer with respect to 100% of the then unvested shares subject to each such option award, and extend the post-termination exercise period to 12 months from the date of termination (unless it expires earlier under its term).

The definitions of "Change in Control" in the Severance Plan and for purposes of the option award

EXECUTIVE COMPENSATION

agreements are substantially similar to the definition in Dr. Kinney's Employment Agreement described above, except that similar transactions with respect to PBI are not included.

"Cause" is defined in the option award agreements as (a) the willful breach, habitual neglect or poor performance of job duties and responsibilities; (b) conviction (or entry of a guilty plea or plea of nolo contendere)

of any crime, excluding minor traffic offenses; (c) commission of an act of dishonesty or breach of fiduciary duty; (d) commission of a material violation of any of the Company's personnel policies; or (e) any act or omission which is contrary to the business interest, reputation or goodwill of the Company.

The definition of "Good Reason" in the option award agreements is substantially similar to the definition in Dr. Kinney's Employment Agreement described above.

"Triggering Event" is defined in the Severance Plan as (a) an Involuntary Termination, (b) a Relocation, or (c) a Significant Reduction in Scope or Base Compensation, which are defined as follows: "Involuntary Termination" is defined as a termination by the Company of the named executive officer due to a business condition; "Relocation" is defined as a material change in the geographic location at which the named executive officer is required to perform services, which is defined as including a relocation that increases his or her one-way commute by at least 30 miles or relocation that requires moving his or her home to a new location more than 30 miles from his or her current home; and "Significant Reduction in Scope or Base Compensation" is defined as material diminution in the named executive officer's authority, duties or responsibilities or a material diminution in his or her base compensation.

Compensation Risk Assessment

Consistent with the SEC's disclosure requirements, we have assessed our compensation programs for all employees. We have concluded that our compensation policies and practices do not create risks that are reasonably likely to have a material adverse effect on us. Management has evaluated our executive and employee compensation and benefits programs to determine if these programs' provisions and operations create undesired or unintentional risk of a material nature. The risk assessment process includes a review of program policies and practices; analysis to identify risks and risk controls related to our compensation programs; and determinations as to the sufficiency of risk identification, the balance of potential risk to potential reward, the effectiveness of our risk controls, and the impacts of

our compensation programs and their risks to our strategy. Although we periodically review all compensation programs, we focus on the programs with variability of payout, with the ability of a participant to directly affect payout and the controls on participant action and payout. In relation to this, we believe that our incentive compensation arrangements provide incentives that do not encourage risk taking beyond our ability to effectively identify and manage significant risks and are compatible with effective internal controls and our risk management practices. The Compensation Committee monitors our compensation programs on an annual basis and expects to make modifications as necessary to address any changes in our business or risk profile.

Pay Ratio of CEO to Median Employee

The total compensation in 2021 of Dr. Kinney, our President and Chief Executive Officer, was approximately 9 times the median total compensation in 2021 of all of our other employees. The total compensation in 2021 of Dr. Kinney was \$4,918,363. The median of the total compensation in 2021 of all other employees was \$521,645.

We calculated this median employee's total compensation for 2021 using the same methodology used to calculate our CEO's total compensation for 2021, as set forth in the *Summary Compensation Table - Fiscal Year 2021* above. The median employee's total compensation for 2021 included salary, an annual cash bonus paid in 2022 for 2021, stock option awards in 2021, and Company contributions in 2021 to that employee's account under our tax-qualified 401(k) defined contribution plan, each cal

culated for purposes of this pay ratio on the same basis as those same compensation elements of our CEO as explained in footnotes 1, 2 and 3 of the *Summary Compensation Table - Fiscal Year 2021*.

The same median employee was used for 2021 as was used in 2020 and 2019 as the changes to our employee population and compensation arrangements have not significantly impacted the pay ratio disclosure.

We believe that our CEO-to-median employee pay ratio is a reasonable estimate and was calculated in accordance with SEC regulations. In order to identify the Company's median employee in 2019, we used the base salary or wages (based on our payroll records) earned from January 1 through September 30, 2019, for each employee who was employed as of October 1, 2019. We included all of our full-time, part-time, temporary and seasonal employees, globally, but excluded our CEO. For

permanent full- and part-time employees who were hired after January 1, 2019, or who were on an unpaid leave of absence during a part of 2019, we adjusted their salaries or wages to reflect what they would have earned had they worked the entire nine-month period through September 30, 2019.

We believe that this use of salary or wages earned through the first nine months of 2019 is an appropriate and consistently applied compensation measure for purposes of identifying the "median employee" from a compensation standpoint because all employees were eligible for annual cash bonuses and received stock option awards in 2019 and the distribution of cash bonuses and option awards were generally consistent with annual base pay. Earnings of our employees outside the U.S. were converted to U.S. dollars using an average currency exchange rate over the nine-month measurement period. We did not make any cost-of-living adjustments.

EQUITY COMPENSATION PLAN INFORMATION

The following table provides certain information as of December 31, 2021, regarding securities of the Company that may be issued under our equity compensation plans.

Plan Category	(a) Number of securities to be issued upon exercise of outstanding options, warrants and rights	(b) Weighted-average exercise price of outstanding options, warrants and rights	(c) Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a)) ⁽¹⁾
Equity Compensation Plans Approved by Shareholders ⁽²⁾	7,356,384	\$18.06	3,131,355
Equity Compensation Plans Not Approved by Shareholders ⁽³⁾	1,327,938	25.54	0
Total	8,684,322	\$19.20	3,131,355

(1) Represents ordinary shares available for issuance under our 2018 Long Term Incentive Plan, as amended (the "2018 LTIP") and our 2020 Employment Inducement Incentive Plan, as amended (the "2020 EIIP"), that may be granted in the form of stock options, stock appreciation rights, restricted shares, restricted share units, performance share units and other share-based awards. This number of shares will be reduced by 1.5 shares for each share that may be issued under an award other than an option or stock appreciation right.

(2) Column (a) represents the sum of nonqualified stock options outstanding under our Amended and Restated 2012 Long Term Incentive Plan and the 2018 LTIP, and column (c) represents ordinary shares available for future issuance under the 2018 LTIP.

(3) Column (a) represents nonqualified stock options outstanding under the 2020 EIIP, and column (c) represents ordinary shares available for future issuance under the 2020 EIIP.

TRANSACTIONS WITH RELATED PERSONS AND INDEMNIFICATION

Policies and Procedures on Transactions with Related Persons

The Company has adopted written policies and procedures for the review and approval or ratification of any transaction constituting a transaction with a related person as defined under Item 404(a) of Regulation S-K under the Securities Act (a “Related Person Transaction”). Subject to certain exceptions, Item 404(a) defines a Related Person Transaction as a transaction, arrangement or relationship, or series of similar transactions, arrangements or relationships, in which the Company was, is or will be a participant, where the amount involved exceeds \$120,000 and a related person had, has or will have a direct or indirect material interest. A related person is (a) any director (or nominee for director) or executive officer of the Company, (b) any beneficial owner of more than 5% of the Company's ordinary shares, or (c) certain “immediate family members” of such director (or nominee for director), executive officer or beneficial owner.

Under our written policies and procedures for Related Person Transactions, which were approved by our Board, all proposed Related Person Transac

tions (which includes a proposed material modifications to previously approved Related Person Transactions) must be reviewed and approved or ratified by the Audit Committee of our Board, although (a) the chair of the Audit Committee may approve a Related Person Transaction if it is not practical for the Committee to do so, subject to subsequent ratification by the Audit Committee, (b) if the Related Person Transaction relates to compensation of a director or executive officer, it must be reviewed and approved or ratified by the Compensation Committee of our Board, and (c) the Board may approve or ratify a Related Person Transaction by an affirmative vote of a majority of directors who do not have a direct or indirect material interest in the Related Person Transaction. Prior to approval or ratification of a proposed Related Person Transaction, the Audit Committee considers all relevant facts and circumstances including, but not limited to, the financial and other terms and whether such terms, taken as a whole, are no less favorable to the Company than could be obtained in an arms-length transaction with an unrelated third party.

Transactions with Related Persons

We have no Related Person Transactions to report.

Director and Executive Officer Indemnification Arrangements

Our Constitution contains provisions requiring that we indemnify our directors, officers, and executives against all costs, charges, losses, expenses, and liabilities incurred by them the execution of their duties or in relation thereto, and to advance expenses (including attorneys' fees) incurred in defending any action, suit or proceeding for which indemnification would be allowed, all to the extent permissible under Irish law. In addition, the Company has entered into a deed of indemnification agreement with each of

our directors and executive officers that provides for indemnification of that director and/or executive officer against certain claims that arise by reason of their status or service as a director or executive officer. The Company purchases directors and officers liability insurance to cover its indemnification obligations to our directors and executive officers as well as to cover directly certain claims made against our directors and executive officers.

HOUSEHOLDING OF PROXY MATERIALS

The SEC has adopted rules that permit companies and intermediaries (e.g., brokers) to satisfy the delivery requirements for Notices of Internet Availability of Proxy Materials or other Annual Meeting materials with respect to two or more shareholders sharing the same address by delivering a single Notice of Internet Availability of Proxy Materials or other Annual Meeting materials addressed to those shareholders. This process, which is commonly referred to as “householding,” potentially means extra convenience for shareholders and cost savings for companies.

Brokers with account holders who are Prothena shareholders may be “householding” our proxy materials. A single Notice of Internet Availability of Proxy Materials or other Annual Meeting materials may be delivered to multiple shareholders sharing an address unless contrary instructions have been received from the affected shareholders. Once you have received notice from your broker that it will be “householding” communications to your address, “householding” will continue until you are notified otherwise or until you notify your broker or the Company that you no longer wish to participate in “householding.”

If, at any time, you no longer wish to participate in “householding” and would prefer to receive a separate Notice of Internet Availability of Proxy Materials or other Annual Meeting materials, you may (a) notify your broker, (b) direct your written request to our Company Secretary at Prothena Corporation plc, 77 Sir John Rogerson’s Quay, Block C, Grand Canal Docklands, Dublin 2, D02 VK60, Ireland, or (c) contact Prothena Investor Relations by telephone at (650) 837-8535 (a U.S. telephone number). Shareholders who currently receive multiple copies of the Notice of Internet Availability of Proxy Materials or other Annual Meeting materials at their address and would like to request “householding” of their communications should contact their broker. In addition, the Company will promptly deliver, upon written or oral request to the address or telephone number above, a separate copy of the Notice of Internet Availability of Proxy Materials or other Annual Meeting materials to a shareholder at a shared address to which a single copy of the documents was delivered.

ANNUAL REPORT

Our Annual Report on Form 10-K for fiscal year 2021 is being mailed with this Proxy Statement to those shareholders that receive this Proxy Statement in the mail. Shareholders that receive the Notice of Internet Availability of Proxy Materials can access our Annual Report on Form 10-K for 2021 at www.proxyvote.com (which does not have “cookies” that identify visitors to the site).

Our Annual Report on Form 10-K for our fiscal year 2021 has also been filed with the SEC. It is available free of charge at the SEC’s website at www.sec.gov. Upon written request by a shareholder, we will mail without charge a copy of our Annual Report on Form 10-K, including the financial statements and financial statement schedules, but excluding exhibits. Exhibits to our Annual Report on Form 10-K are available upon payment of a reasonable fee, which is limited to our expenses in furnishing the requested exhibit. All requests should be directed to our Company Secretary at Prothena Corporation plc, 77 Sir John Rogerson’s Quay, Block C, Grand Canal Docklands, Dublin 2, D02 VK60, Ireland.

By Order of the Board of Directors



Yvonne M. Tchrahan
Company Secretary
Dublin, Ireland
March 31, 2022

APPENDIX A

NASDAQ BOARD DIVERSITY MATRIX

Board Diversity Matrix (As of March 31, 2022)				
Total Number of Directors	10			
	Female	Male	Non-Binary	Did Not Disclose Gender
Part 1: Gender Identity				
Directors	1	9	0	0
Part II: Demographic Background				
African American or Black	0	0	0	0
Alaskan Native or Native American	0	0	0	0
Asian	0	1	0	0
Hispanic or Latinx	0	0	0	0
Native Hawaiian or Pacific Islander	0	0	0	0
White	1	8	0	0
Two or More Races or Ethnicities	0	0	0	0
LGBTQ+	1			
Did Not Disclose Demographic Background	0			

APPENDIX B

AMENDMENT TO

THE PROTHENA CORPORATION PLC 2018

LONG TERM INCENTIVE PLAN

Section 2.28 of the Prothena Corporation plc 2018 Long Term Incentive Plan is proposed to be amended as indicated below:

2.28 **“Overall Share Limit”** means the sum of (i) 7,100,000~~5,100,000~~ Shares; (ii) the aggregate number of Shares that remain available for future awards under the Prior Plan as of immediately prior to the Effective Date; and (iii) any Shares that are subject to Prior Plan Awards that become available for issuance under the Plan pursuant to Article V.





PROTHENA CORPORATION PLC
77 SIR JOHN ROGERSON'S QUAY, BLOCK C
GRAND CANAL DOCKLANDS
DUBLIN 2, D02 VK60, IRELAND



SCAN TO
VIEW MATERIALS & VOTE



VOTE BY INTERNET - www.proxyvote.com or scan the QR Barcode above
Use the Internet to transmit your voting instructions and for electronic delivery of information up until 11:59 P.M. Eastern Time on May 16, 2022. Have your proxy card in hand when you access the web site and follow the instructions to obtain your records and to create an electronic voting instruction form.

ELECTRONIC DELIVERY OF FUTURE PROXY MATERIALS

If you would like to reduce the costs incurred by our company in mailing proxy materials, you can consent to receiving all future proxy statements, proxy cards and annual reports electronically via e-mail or the Internet. To sign up for electronic delivery, please follow the instructions above to vote using the Internet and, when prompted, indicate that you agree to receive or access proxy materials electronically in future years.

VOTE BY PHONE - 1-800-690-6903

Use any touch-tone telephone to transmit your voting instructions up until 11:59 P.M. Eastern Time on May 16, 2022. Have your proxy card in hand when you call and then follow the instructions.

VOTE BY MAIL

Mark, sign and date your proxy card and return it in the postage-paid envelope we have provided or return it to Vote Processing, c/o Broadridge, 51 Mercedes Way, Edgewood, NY 11717.

TO VOTE, MARK BLOCKS BELOW IN BLUE OR BLACK INK AS FOLLOWS:

D67536-P68468

KEEP THIS PORTION FOR YOUR RECORDS

THIS PROXY CARD IS VALID ONLY WHEN SIGNED AND DATED.

DETACH AND RETURN THIS PORTION ONLY

PROTHENA CORPORATION PLC (the "Company")

The Board of Directors recommends you vote FOR each of the following director nominees:

- To elect, by separate resolutions, three directors to hold office until no later than the Annual General Meeting of the Company's Shareholders in 2025, unless they resign, are removed from office, or are otherwise disqualified from serving as directors of the Company.

Nominees

1a. Paula K. Cobb

For Against Abstain

☐ ☐ ☐

1b. Lars G. Ekman

☐ ☐ ☐

1c. Sanjiv K. Patel

☐ ☐ ☐

The Board of Directors recommends you vote FOR the following proposals:

For Against Abstain

- To ratify, in a non-binding vote, the appointment of KPMG LLP as the Company's independent registered public accounting firm for its fiscal year 2022 and to authorise, in a binding vote, the Company's Board of Directors, acting through its Audit Committee, to approve the remuneration of that auditor.
- To approve, in a non-binding advisory vote, the compensation of the executive officers named in the Company's Proxy Statement for the Annual General Meeting.

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The Board of Directors recommends you vote 1 YEAR on the following proposal:

1 Year 2 Years 3 Years Abstain

- To approve, in a non-binding advisory vote, the frequency of future advisory votes by shareholders on the compensation of the Company's named executive officers.

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The Board of Directors recommends you vote FOR the following proposals:

For Against Abstain

- To approve an amendment to the Company's 2018 Long Term Incentive Plan to increase the number of ordinary shares available for issuance under that Plan by 2,000,000 ordinary shares.
- To renew the Board of Directors' existing authority under Irish law to allot and issue ordinary shares.
- To renew the Board of Directors' existing authority under Irish law to allot and issue ordinary shares for cash without first offering those shares to existing shareholders pursuant to the statutory pre-emption right that would otherwise apply.
- To approve any motion to adjourn the Annual General Meeting, or any adjournment thereof, to another time and place in order to solicit additional proxies if there are insufficient votes at the time of the Annual General Meeting to approve Proposal No. 7.

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NOTE: To transact such other business as may properly come before the Annual General Meeting.

Please sign exactly as your name(s) appear(s) hereon. When signing as attorney, executor, administrator, or other fiduciary, please give full title as such. Joint owners should each sign personally. All holders must sign. If a corporation or partnership, please sign in full corporate or partnership name by authorized officer.

Signature [PLEASE SIGN WITHIN BOX] Date

Signature (Joint Owners) Date

Any shareholder entitled to attend and vote at the Annual General Meeting may appoint one or more proxies, who need not be shareholder(s) of Prothena Corporation plc (the "**Company**"). If you wish to appoint a person other than the individuals designated herein, please contact the Secretary of the Company and also note that your nominated proxy must attend the Annual General Meeting in person in order for your votes to be voted. A proxy is required to vote in accordance with any instructions given to him or her. Completion of a form of proxy will not preclude a shareholder from attending and voting at the Annual General Meeting in person.

Important Notice Regarding the Availability of Proxy Materials for the Annual General Meeting:

The Combined Notice and Proxy Statement and Annual Report on Form 10-K are available at www.proxyvote.com.

D67537-P68468

**PROTHENA CORPORATION PLC
Annual General Meeting of Shareholders
May 17, 2022, 4:00 P.M. Local Time
This proxy is solicited by the Board of Directors**

The undersigned, having received the Notice of the 2022 Annual General Meeting of Shareholders of Prothena Corporation plc (the "**Company**"), to be held on May 17, 2022, at 4:00 P.M. Local Time, at The Merrion Hotel, Upper Merrion Street, Dublin 2, D02 KF79, Ireland, and the Proxy Statement, appoints Dr. Lars G. Ekman and Ms. Yvonne M. Tchrakian, and each of them acting individually, as the undersigned's proxies with full power of substitution, for and in the name, place and stead of the undersigned, to vote and act with respect to all of the ordinary shares of the Company standing in the name of the undersigned or with respect to which the undersigned is entitled to vote and act, at the Annual General Meeting and at any adjournment or postponement thereof, and the undersigned directs that this proxy be voted as specified herein.

THIS PROXY, WHEN PROPERLY EXECUTED, WILL BE VOTED IN THE MANNER DIRECTED HEREIN. IF NO DIRECTION IS MADE FOR A PROPOSAL, THE PROXY WILL BE VOTED "FOR" PROPOSALS 1, 2, 3, 5, 6, 7 AND 8 AND 1 YEAR FOR PROPOSAL NO. 4 AND IN THE DISCRETION OF THE PROXIES UPON SUCH OTHER MATTERS AS MAY PROPERLY COME BEFORE THE ANNUAL GENERAL MEETING. THE UNDERSIGNED HEREBY REVOKES ANY PROXY OR PROXIES HERETOFORE GIVEN TO VOTE UPON OR ACT WITH RESPECT TO SUCH SHARES.

Continued and to be signed on reverse side