PROTHENA CORPORATION PLC

Registered in Ireland - No. 518146
77 Sir John Rogerson's Quay, Block C, Grand Canal Docklands, Dublin 2, D02 VK60, Ireland

NOTICE OF ANNUAL GENERAL MEETING OF SHAREHOLDERS TO BE HELD ON MAY 13, 2025

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 13, 2025, 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 elect, by separate resolutions, Paula K. Cobb, Lars G. Ekman, and Gene G. Kinney, as directors, to hold office until no later than the annual general meeting of shareholders in 2028;

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, 2025, 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 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; and

5. 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 2024, 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, and 4 are deemed to be ordinary resolutions requiring the approval of a simple majority of the votes cast at the Annual Meeting.

Only shareholders who owned our ordinary shares at the close of business on March 3, 2025, 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 election of Paula K. Cobb, Lars G. Ekman, and Gene G. Kinney, 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 2025, 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; and

4. **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. 4.

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 2024; 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.

By Order of the Board of Directors

Yvonne M. Tchrakian
Company Secretary
Dublin, Ireland
March 28, 2025

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PROTHENA CORPORATION PLC

Registered in Ireland - No. 518146
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PROXY STATEMENT FOR THE ANNUAL GENERAL MEETING OF SHAREHOLDERS TO BE HELD ON MAY 13, 2025

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 13, 2025, 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 28, 2025, 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 2024 available on the internet and mailing a Notice of Internet Availability of Proxy Materials to shareholders of record as of close of business on March 3, 2025 (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 our ordinary shares, $0.01 par value per share ("ordinary shares"). There were 53,826,982 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. As of the Record Date, there were 53,826,982 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:**

- Election, by separate resolutions, of Ms. Cobb, Dr. Ekman, and Dr. Kinney as directors, to hold office until no later than our annual general meeting of shareholders in 2028;
- Ratification, in a non-binding vote, of the appointment of KPMG LLP as our independent registered public accounting firm for our fiscal year 2025, 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; and
- 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.

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, and 4, you may vote "FOR" or "AGAINST" 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, and 4, an affirmative vote of a simple majority of the votes cast in person or by proxy at the Annual Meeting is required for approval.

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 register 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 12, 2025. 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 election, by separate resolutions, of Ms. Cobb, Dr. Ekman, and Dr. Kinney, as directors, to hold office until no later than our annual general meeting of shareholders in 2028;
- 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 2025 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; and
- 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.

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 $24,000, 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 12, 2025.
- 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 12, 2025.
- 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 November 28, 2025, 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 13, 2026, 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 2026 annual general meeting of shareholders, the shareholder must provide notice to the Company not earlier than October 29, 2025, and not later than December 28, 2025, 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, 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 14, 2026.

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 53,826,982 ordinary shares issued and outstanding and entitled to vote. Accordingly, 26,913,491 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 Corporation 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 2024, 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 Companies 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/investors/financials-filings/Irish-Statutory-Financial-Statements/*. 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

Summary

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 election at each annual general meeting of shareholders, and that directors must stand for 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 nine directors serving on our Board. Our Board currently is divided into the following groups:

- Paula K. Cobb and Lars G. Ekman, whose current terms will expire at the Annual Meeting;
- Helen S. Kim, Gene G. Kinney, and Dennis J. Selkoe, whose current terms will expire no later than the annual general meeting of shareholders to be held in 2026; and
- Richard T. Collier, Shane M. Cooke, William H. Dunn, Jr., and Daniel G. Welch, whose current terms will expire no later than the annual general meeting of shareholders to be held in 2027.

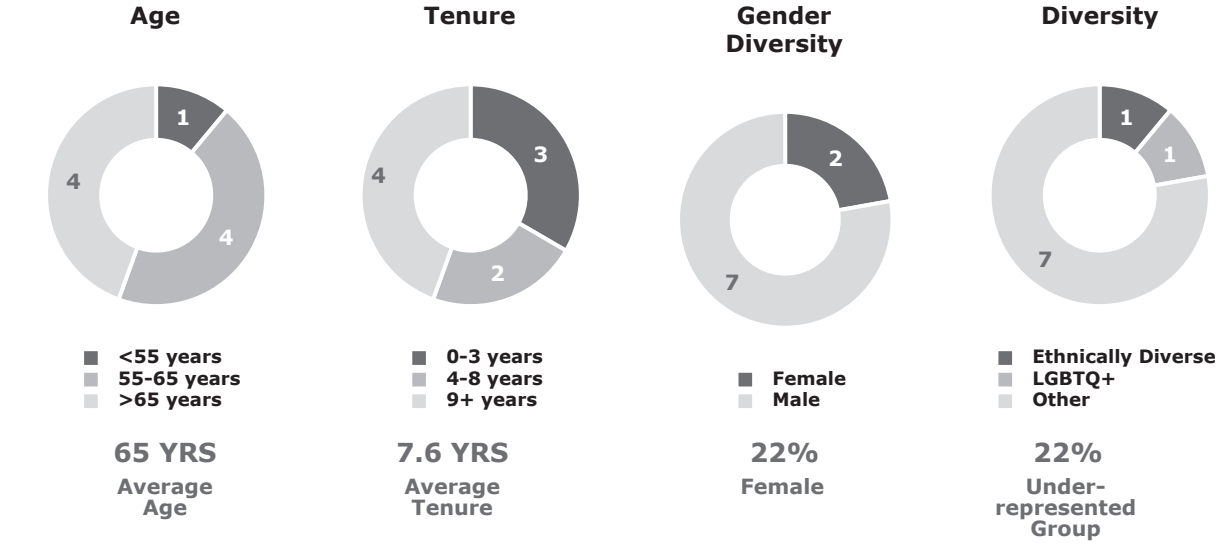
Ms. Cobb, Dr. Ekman, and Dr. Kinney have been nominated by the Board to stand for election. Each of Ms. Cobb, Dr. Ekman, and Dr. Kinney were previously elected to the Board by our shareholders. The Board nominated Dr. Kinney to stand for election even though his three-year term does not expire until 2026 because the Company's Constitution requires that 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) 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. If elected by our shareholders at the Annual Meeting, Ms. Cobb, Dr. Ekman, and Dr. Kinney 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 2028), 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 the 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. Following the table below 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	Paula K. Cobb	Richard T. Collier	Shane M. Cooke	William H. Dunn, Jr.	Lars G. Ekman	Helen S. Kim	Gene G. Kinney	Dennis J. Selkoe	Daniel G. Welch
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 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 3/28/2025)	Paula K. Cobb	Richard T. Collier	Shane M. Cooke	William H. Dunn, Jr.	Lars G. Ekman	Helen S. Kim	Gene G. Kinney	Dennis J. Selkoe	Daniel G. Welch
Independent	●	●	●	●	●	●		●	●
Age	52	71	62	55	75	62	56	81	67
Tenure (Years)	5.7	12.3	12.3	1.9	12.3	2.6	8.5	11.7	1.1



Nominees for Election to Terms Expiring No Later than the Annual General Meeting of Shareholders in 2028; Recommendation of the Board

Paula K. Cobb was most recently Chief Business Officer at Affinia Therapeutics, Inc., a biotechnology company developing gene therapies, a position she held from 2020 through 2023. 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: 52

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 an executive partner at Sofinnova Ventures, Inc. (a venture capital firm), a position he has held since 2008. Dr. Ekman served as a director of Ultragenyx Pharmaceutical Inc. (from 2016 to June 2023), as a director and then chair of the board of Amarin Corporation plc (from 2008 to 2022), as a director of Intermune Inc. (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 Sophiris 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 and served as Chair of our Board from 2012 until May 2024. Age: 75

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.

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 held various positions with Elan Pharmaceuticals, Inc.: Vice President, Pharmacology (from 2011 to 2012) and Senior Vice President of Pharmacological Sciences (from 2009 to 2011); and 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: 56

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.

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

Directors Continuing in Office Until No Later than the Annual General Meeting of Shareholders in 2026

Helen S. Kim is a Senior Managing Director at Vida Ventures, LLC (a venture capital firm), a position she has held since April 2019. Prior to her current role, Ms. Kim was a Partner at The Column Group (a venture capital firm) from 2018 to 2019 and the Executive Vice President, Business Development, at Kite Pharma, Inc. (a biotechnology company specializing in cancer immunotherapy) from 2014 to 2018 (through its acquisition by Gilead Sciences, Inc.). Previously, Ms. Kim held positions as Chief Business Officer (2009-2012) and then Strategic Advisor (2012-2014) of NGM Biopharmaceuticals, Inc. Prior to NGM, she was the Chief Executive Officer and President of Kosan Biosciences (a pharmaceutical company) where she restructured and repositioned the company prior to a successful transaction with Bristol Myers Squibb in 2008. Ms. Kim's additional industry experience includes executive and leadership positions at Affymax, Inc., Onyx Pharmaceuticals, Inc., Protein Design Labs, Inc. (a technology company), and Chiron Corporation. Ms. Kim also currently serves as a director of several private companies: ReCode Therapeutics, Inc., IconOVir Bio, Inc., Aktis Oncology, Protego Therapeutics, Souffle, Alterome, Scorpion Therapeutics, and AffiniT Therapeutics. Ms. Kim received a B.S. in Chemical Engineering from Northwestern University and an M.B.A. from the University of Chicago. She has served on our Board since 2022. Age: 62

The Board concluded that Ms. Kim should continue to serve as a director given her experience in venture capital investment in the life science industry. The Board also considered her experience serving on the boards of directors of public and private companies in the pharmaceutical/biotechnology industry, as well as her roles in executive management at several publicly-traded companies in the pharmaceutical/ biotechnology industry.

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 Solowey 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: 81

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 2027

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: 71

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 chair of the board (from 2020 until its acquisition by Clayton, Dubilier & Rice, LLC in 2021) of UDG Healthcare plc (a pharmaceutical services 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: 62

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.

William H. Dunn, Jr., M.D., was the founding director of the Office of Neuroscience, Center for Drug Evaluation and Research, at the U.S. Food and Drug Administration, a position he held since the founding of the office in 2019 through February 2023. He was responsible for the regulatory oversight of all research conducted to support neuroscience drug development, including the regulation and review of investigational new drug applications and marketing applications for drug and biologic products. From 2005 to 2019, he held positions of increasing seniority in the Division of Neurology Products, Center for Drug Evaluation and Research, including his role as director of that division. Dr. Dunn is a trained neurologist and vascular neurologist with experience in basic research, clinical research, and clinical care. He earned his B.A. from the University of Virginia and his M.D. from the F. Edward Hébert School of Medicine in Bethesda, Maryland. He has served on our Board since 2023. Age: 55

The Board concluded that Dr. Dunn should serve as a director given his significant regulatory experience with the U.S. FDA and experience in the design and implementation of clinical studies in support of drug development. The Board also considered his scientific and medical expertise in the neurodegenerative field, and operational experience in a large organization.

Daniel G. Welch serves as the chair of the boards of Structure Therapeutics Inc. (since January 2022) and Ultragenyx Pharmaceuticals Inc. (since 2015). He previously served as chair of the board of Nuvation Bio Inc. (from 2020 to September 2024), as a director of SeaGen Inc. (from 2007 until its acquisition by Pfizer in 2023), as chair of the board of AveXis Inc (from 2016 until its acquisition by Novartis in 2018), as a director of Intercept Pharmaceuticals, Inc. (from 2015 to 2020), and as a director of Hyperion Therapeutics (from 2012 until its acquisition by Horizon Pharma in 2015). Prior to these roles he served as an executive partner at Sofinnova Ventures (from 2015 to 2018), as Chief Executive Officer and President of InterMune, Inc. (from 2003 until its acquisition by Roche Holdings in 2014), as chair of the board of InterMune (from 2008 to 2014), as chair of the board and Chief Executive Officer of Triangle Pharmaceuticals, Inc. (from 2002 until its acquisition by Gilead Sciences in 2003), and as President of the pharmaceutical division of Elan Corporation, plc (from 2000 to 2002). Mr. Welch earned his B.A. from the University of Miami and his M.B.A. from the University of North Carolina. He has served on our Board since February 2024 and as Chair of our Board since May 2024. Age: 67

The Board concluded that Mr. Welch should serve as a director given his significant experience serving on the boards of public companies in the pharmaceutical/ biotechnology industry. The Board also considered his experience in executive management at several publicly-traded companies in the pharmaceutical/ biotechnology industry.

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 *https://ir.prothena.com/corporate-governance*, including in our Corporate Governance Guidelines; the charters for our Audit, Compensation, Nominating and Corporate Governance, and Research and Development 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 (including K. Anders O. Härfstrand and Oleg Nodelman, who each served on our Board during 2024) qualify as "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 as described in more detail below and in the respective charters of each committee. 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. Mr. Welch serves as Chair of the Board, and Dr. Kinney serves as our President and Chief Executive Officer. In his role as Chair, Mr. Welch 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. Since Mr. Welch's appointment as Chair of the Board in May 2024, Dr. Ekman, who had served as Chair of our Board since 2012, has served as Chair Emeritus. Our Board has concluded that the proposed 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, the Nominating and Corporate Governance Committee, and the Research and Development Committee. Each of these committees operates under a written charter which sets forth the functions and responsibilities of

the committee, a copy of which is available on our website at *https://ir.prothena.com/corporate-governance*. 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	Research and Development Committee
Paula K. Cobb	X	Chair	—	—
Richard T. Collier	X	—	Chair	—
Shane M. Cooke	Chair	X	—	—
William H. Dunn, Jr.	—	—	X	X
Lars G. Ekman	—	—	—	Chair
Helen S. Kim	—	—	X	—
Gene G. Kinney	—	—	—	—
Dennis J. Selkoe	—	—	—	X
Daniel G. Welch	—	X	—	—

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. The Audit Committee also reviews the Company's major risk exposures — including cybersecurity risks — and steps to control them, and reviews 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 Ms. Cobb, Mr. Collier, and Mr. Cooke. 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 is 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 *https://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 and consider and recommend to the Board all compensation of our Chief Executive Officer; 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, Mr. Cooke, and Mr. Welch. 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 *https://ir.prothena.com/corporate-governance*.

Our Chief Executive Officer 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

assessment 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 Pay Governance LLC ("Pay Governance") 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 2024. The Committee assessed Pay Governance's independence prior to that engagement and the Committee concluded that the work performed by Pay Governance for the Committee did not raise any conflict of interest.

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 Chief Executive Officer; develop a succession plan for our Chief Executive Officer; and develop corporate governance guidelines applicable to the Company. The Nominating and Corporate Governance Committee also oversees the Company's policies with regard to human capital management and environmental, social, and corporate responsibility.

The current members of our Nominating and Corporate Governance Committee are Mr. Collier, Dr. Dunn, and Ms. Kim. 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 *https://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.

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 their 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?"

Research and Development Committee

Our Research and Development Committee's primary purpose is to review and advise management and the Board on the strategic direction for the Company's pipeline and investment in research and development. In connection with such purpose the Research and Development Committee may evaluate and advise on the Company's key R&D activities, early pipeline development goals and strategy, and maintaining product flow for the Company's program pipeline; evaluate and provide input with respect to the strategic direction of the science being conducted and overall program execution; and confer with the Company's research and development and management teams regarding significant emerging regulatory, research, scientific, and medical trends and developments relevant to the Company's research and development activities and strategy, including their potential impact on the Company's programs or plans.

The current members of our Research and Development Committee are Dr. Dunn, Dr. Ekman, and Dr. Selkoe. Dr. Ekman 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 *https://ir.prothena.com/corporate-governance*.

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

During our fiscal year 2024, our Board met four times, our Audit Committee met seven times, our Compensation Committee met five times, our Nominating and Corporate Governance Committee met four times, and our Research and Development Committee met three times.

During our fiscal year 2024, each of our current 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 2024, ten of our eleven directors then serving on our Board attended our annual general meeting of shareholders 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 *https://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 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 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 (Prothena Corporation plc, 77 Sir John Rogerson's Quay, Block C, Grand Canal Docklands, Dublin 2, D02 VK60, Ireland) 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 *https://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 *https://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 2024

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 fiscal year 2024 compensation program as described below.

For fiscal year 2024, our Chair and Chair Designate each received an annual cash retainer fee of $90,000, and all other non-employee directors received an annual cash retainer fee of $60,000. In addition, all of our non-employee directors who served on or chaired a Board committee received the following annual committee fees:

Committee	Chair	Other Member
Audit Committee	$20,000	$10,000
Compensation Committee	$15,000	$7,500
Nominating and Corporate Governance Committee	$10,000	$5,000
Research and Development Committee	$20,000	$10,000

For fiscal year 2024, the annual committee fees for non-chair members of the Audit Committee were increased to $10,000 (from $9,000 with respect to fiscal year 2023) and for non-chair members of the Compensation Committee were increased to $7,500 (from $6,000 with respect to fiscal year 2023). The Board also approved payment of an annual committee fee to members of the newly-formed Research and Development Committee of $20,000 for chair members and $10,000 for non-chair members. Director and committee fees are paid in quarterly installments and pro-rated as necessary for partial year service.

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. After considering input from the independent consultant engaged by the Compensation Committee, the number of shares subject to the annual option awards was set at 15,000 shares (consistent with the annual director stock option grants for fiscal year 2023). 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.

In connection with Mr. Welch's initial appointment as Chair Designate to the Board in February 2024, after considering input from the Compensation Committee's independent consultant, he was granted a nonqualified stock option to acquire 132,000 of the Company's ordinary shares. This option vests in equal annual installments over five years following the grant date (subject to Mr. Welch's 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. This option was a one-time grant to induce Mr. Welch, who has significant experience serving on the boards of public companies in the pharmaceutical/biotechnology industry, to join as Chair Designate to the Board.

All of the options granted to our non-employee directors were 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, 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 2024* for a summary of the compensation received by Dr. Kinney with respect to fiscal year 2024.

The following table sets forth the compensation paid to our non-employee directors in our fiscal year 2024.

Name	Fees Earned or Paid in Cash[1] ($)	Option Awards[2] ($)	All Other Compensation[3] ($)	Total ($)
Paula K. Cobb	81,339	223,007	—	304,346
Richard T. Collier	79,634	223,007	—	302,641
Shane M. Cooke	86,951	223,007	—	309,958
William H. Dunn, Jr.	65,430	223,007	—	288,437
Lars G. Ekman	81,844	223,007	—	304,851
K. Anders O. Härfstrand[4]	27,295	—	—	27,295
Helen S. Kim	65,000	223,007	—	288,007
Oleg Nodelman[5]	—	—	—	—
Dennis J. Selkoe	65,430	223,007	9,500	297,937
Daniel G. Welch[6]	77,459	2,590,229		2,667,688

(1) Consists of Board retainer, committee chair, and committee service fees, pro-rated as necessary for partial year service, 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 fiscal year 2024, 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 2024, filed with the SEC on February 27, 2025 (our "Form 10-K"). Except in the case of Mr. Welch, the amounts reported represent the grant date fair value of options granted on May 15, 2024, to acquire 15,000 shares, which options have an exercise price of $22.39 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 Mr. Welch, the amount reported represents the following: (a) the grant date fair value of options granted on February 21, 2024, to acquire 132,000 shares, which options have an exercise price of $27.05 per share (the fair market value per share on the date of grant), vest in equal annual installments over five years following the grant date (subject to continuous service as a director until each such vesting date), and have a ten-year term; and (b) the grant date fair value of options granted on May 15, 2024, to acquire 15,000 shares, which options have an exercise price of $22.39 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.

(3) Consists of consulting fees paid pursuant to a consulting arrangement with the Company’s wholly-owned subsidiary, Prothena Biosciences Inc, under which Dr. Selkoe provides consulting services in connection with matters related to the Company’s partnered collaboration programs.

(4) Dr. Härfstrand’s term expired on May 14, 2024, and his cash compensation was pro-rated for his service as a director in fiscal year 2024.

(5) Mr. Nodelman has declined to receive any cash or equity compensation for his service as a director.

(6) Mr. Welch was appointed to the Board on February 21, 2024, and his cash compensation was pro-rated for his service as a director in fiscal year 2024.

As of the end of our fiscal year 2024, the total number of shares subject to outstanding option awards held by each non-employee director serving during fiscal year 2024 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 2024.

Name	Outstanding Option Awards (Shares)
Paula K. Cobb	112,500
Richard T. Collier	131,554
Shane M. Cooke	131,554
William H. Dunn, Jr.	45,000
Lars G. Ekman	131,544
K. Anders O. Härfstrand	122,614
Helen S. Kim	60,000
Oleg Nodelman	—
Dennis J. Selkoe	100,044
Daniel G. Welch	147,000

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 2025 AND AUTHORIZATION, IN A BINDING VOTE, OF OUR BOARD OF DIRECTORS, ACTING THROUGH ITS AUDIT COMMITTEE, TO APPROVE THE REMUNERATION OF THAT AUDITOR

Summary

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, 2025, 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 2025. 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 Audit 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, 2024, and 2023.

	Year Ended December 31,	
	2024	2023
Audit Fees[(1)]	$1,436,701	$1,366,000
Audit-Related Fees	—	—
Tax Fees[(2)]	$172,872	$97,215
All Other Fees	—	—
Total Fees	$1,609,573	$1,463,215

(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; Recommendation of the Board

The Audit Committee has adopted policies and procedures requiring that the Company obtain the Audit 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 Audit Committee (although certain services may be pre-approved by the chair of the Audit Committee followed by Audit Committee ratification at the next Audit Committee meeting). Before pre-approving services, the Audit 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 2024 and 2023.

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 2025 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 *https://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, 2024.

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 applicable requirements of the PCAOB regarding KPMG LLP's communications with the Audit Committee concerning independence. 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 fiscal year ended December 31, 2024, for filing with the U.S. Securities and Exchange Commission.

Shane M. Cooke (Committee Chair)
Paula K. Cobb
Richard T. Collier

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 for fiscal year 2024. 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 program as described 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 2024 was aligned with the Company's performance during 2024 and its go-forward strategy. As is described in the *Compensation Discussion and Analysis*:

2024 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 2024 was aligned with the Company's performance during 2024 and its go-forward strategy. Highlights of that performance include:

- ***We Made Significant Advances in our Neurodegenerative Diseases Portfolio.***
  - PRX012, a wholly-owned potential best-in-class, next-generation subcutaneous antibody for the treatment of Alzheimer's disease (AD) that targets a key epitope at the N-terminus of amyloid beta (Aβ) with high binding potency. In 2024, Prothena continued enrollment in our ongoing ASCENT clinical trials (reaching approximately 260 patients) and presented posters at the Alzheimer's Association International Conference (AAIC) and the Clinical Trials on Alzheimer's Disease conference (CTAD) highlighting the clinical trial design of the Phase 1 ASCENT clinical trials.
  - BMS-986446 (formerly PRX005), a potential best-in-class antibody for the treatment of AD that specifically targets a key epitope within the microtubule binding region (MTBR) of tau, a protein implicated in the causal pathophysiology of AD. BMS-986446 is part of the global neuroscience research and development collaboration with Bristol Myers Squibb (BMS). In 2024, BMS continued to enroll the ongoing Phase 2 TargetTau-1 clinical trial in approximately 475 patients with early Alzheimer's disease and presented the design of the ongoing Phase 2 TargetTau-1 clinical trial in a poster presentation at AAIC and an oral encore presentation at CTAD.
  - Prasinezumab, a potential first-in-class antibody, for the treatment for Parkinson's disease (PD), that is designed to target key epitopes within the C-terminus of alpha-synuclein and is the focus of the worldwide collaboration with Roche. In 2024, Roche reported results from the Phase 2b PADOVA clinical trial in patients with early-stage Parkinson's disease missed the primary endpoint but showed a numerical delay in motor progression and positive trends on multiple secondary and exploratory endpoints suggesting possible clinical benefit. Roche announced that they will continue to evaluate the data and work together with health authorities to determine next steps.
  - PRX019, a potential treatment of neurodegenerative diseases with an undisclosed target, is part of the global neuroscience research and development collaboration with BMS. In 2024, Bristol Myers Squibb obtained the exclusive global license for PRX019 for $80 million; and Prothena initiated a Phase 1 first-in-human clinical trial to evaluate the safety, tolerability, immunogenicity, and pharmaco-kinetics of single ascending and multiple doses in healthy adults.
- ***We Made Significant Advances in our Rare Peripheral Amyloid Diseases Portfolio.***
  - Birtamimab, a wholly-owned potential best-in-class amyloid depleter antibody for the treatment of AL amyloidosis designed to directly neutralize soluble toxic light chain aggregates and promote clearance of amyloid that causes organ dysfunction and failure. In 2024, Prothena published Birtamimab's mechanism of action and pharmacological characteristics in Leukemia & Lymphoma and presented Longitudinal Health-Related Quality of Life data (SF-36v2) across

domains from the VITAL Phase 3 clinical trial at the International Society of Amyloidosis. We continued the confirmatory Phase 3 AFFIRM-AL clinical trial (NCT04973137) in patients with Mayo Stage IV AL amyloidosis under a Special Protocol Assessment (SPA) agreement with the FDA with a primary endpoint of all cause mortality (time-to-event) at a significance level of 0.10.

- Coramitug (formerly PRX004), a potential first-in-class amyloid depleter antibody for the treatment of ATTR cardiomyopathy designed to deplete the pathogenic, non-native forms of the transthyretin (TTR) protein and is being developed by Novo Nordisk as part of their up to $1.2 billion acquisition of our ATTR amyloidosis business and pipeline. In 2024, Phase 1 clinical trial results for coramitug in patients with ATTR amyloidosis was published in Amyloid, the official journal of the International Society of Amyloidosis, and Novo Nordisk continued the ongoing Phase 2 signal-detection clinical trial in patients with ATTR-CM.

- ***We Carefully Managed our Cash Balance***.
  - During fiscal year 2024, we carefully managed our capital. While progressing all of our development programs described above, our cash used in operating and investing activities was $150.3 million, which was in-line with our guidance range of $148 to $160 million. We finished fiscal year 2024 with $472.2 million in cash, cash equivalents, and restricted cash, including cash used in operating and financing activities, which exceeded our guidance of $468.0 million, providing a solid financial foundation for continuing to advance the Company's discovery and clinical programs.

Recommendation of the Board

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 further 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 2024. 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 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 26, 2025, 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 ordinary 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 has been subsequently amended by our Board and approved by our shareholders on five occasions. 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) 11,100,000 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, in the form of 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 commonly 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 1,333,333.
- ***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 3, 2025, under the 2018 LTIP and the 2012 LTIP:

- 10,424,163 of our ordinary shares were subject to outstanding option awards, with a weighted average exercise price of $28.32 and a weighted average remaining term of 6.00 years;
- 6,000 ordinary shares were subject to unvested restricted share unit awards;
- No ordinary shares were subject to any other types of outstanding awards; and
- 3,857,181 ordinary shares remained available for future grant under the 2018 LTIP.

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 under such plan (as amended, the "2020 EIIP"). Since adoption through the Record Date, we have used the 2020 EIIP to induce our Chief Business Officer (now our Chief Operating Officer) and 24 other employees at the director level and above to join the Company. As of March 3, 2025, under the 2020 EIIP:

- 703,246 of our ordinary shares were subject to new-hire option awards, with a weighted average exercise price of $33.06, and a weighted average remaining term of 6.17 years;
- No ordinary shares were subject to any other types of outstanding awards; and
- 341,584 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 3, 2025, under the 2018 LTIP, the 2012 LTIP, and the 2020 EIIP:

- 11,127,409 of our ordinary shares were subject to outstanding option awards, with a weighted average exercise price of $28.62 and a weighted average remaining term of 6.01 years;
- 6,000 ordinary shares were subject to unvested restricted share unit awards;
- No ordinary shares were subject to any other types of outstanding awards; and
- 4,198,765 ordinary shares remained available for future grant under the 2018 LTIP and the 2020 EIIP.

The closing price of our ordinary shares on March 3, 2025, was $14.33 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 the compensation consultant engaged by the Compensation Committee, 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 ordinary 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 2026).

- In determining the reasonableness of the Amendment, our Board considered our historical 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 2024, 2023, and 2022, we awarded options and restricted share units representing a total of 2,288,450 ordinary shares, 1,802,621 ordinary shares, and 2,343,936 ordinary shares, respectively, under the 2018 LTIP and the 2020 EIIP. This level of option awards represents a three-year average burn rate of approximately 4.20% of weighted average ordinary shares outstanding.
- We do not have an evergreen provision in our 2018 LTIP.
- Our Compensation Committee considers equity awards to be a particularly effective incentive and retention tool because they motivate our employees to increase shareholder value and remain with the Company. Equity awards link compensation directly to increases in the price of our ordinary shares, which directly reflects increased shareholder value; and our equity awards 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 equity 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 A 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; and the First through Fifth Amendments to the Prothena Corporation plc 2018 Long Term Incentive Plan, which are available as Exhibit 10.11(b) of the Company's Annual Report on Form 10-K filed with the SEC on February 27, 2025.

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 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 delegated. 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 3, 2025, was comprised of eight non-employee directors, and as of the same date approximately 164 employees (including nine executive officers) and approximately 58 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) 13,100,000 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) 5,520,433 shares, which is the number of shares that were subject to issued and outstanding awards under the 2012 LTIP that as of March 3, 2025, 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 3, 2025; 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 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 vest.

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 outstanding 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 (or the applicable employer) 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 participants in the Amended 2018 LTIP. Information regarding awards granted in fiscal year 2024 under the Amended 2018 LTIP to the named executive officers is provided in the *Summary Compensation Table – Fiscal Year 2024* and the *Grants of Plan-Based Awards – Fiscal Year 2024* table. Information regarding awards granted in fiscal year 2024 under the Amended 2018 LTIP to non-employee directors is provided in the *Director Compensation – Fiscal Year 2024* table.

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

The following table provides summary information concerning the number of our ordinary shares subject to awards granted under the 2018 LTIP and the 2020 EIIP to our named executive officers, directors, and employees since the 2018 LTIP's effective date through March 3, 2025.

Name and Position	Number of Shares Underlying RSU Awards (#)	Number of Shares Underlying Option Grants (#)	Weighted Average Exercise Price of Options ($)
Gene G. Kinney, Ph.D., President and Chief Executive Officer, Director and director nominee	—	2,471,700	22.43
Tran B. Nguyen, Chief Strategy Officer and Chief Financial Officer	—	941,837	21.70
Brandon S. Smith, Chief Operating Officer	—	539,000	25.20
Carol D. Karp, Chief Regulatory Officer	—	640,394	23.62
Wagner M. Zago, Chief Scientific Officer	—	544,000	23.76
All current executive officers as a group	—	6,384,386	23.25
All current directors who are not executive officers as a group	—	890,676	28.00
Paula K. Cobb, Director and director nominee	—	112,500	24.61
Lars G. Ekman, Director and director nominee	—	131,544	25.37
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	31,000	8,778,707	28.10

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.

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 3, 2025, (except as noted) 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 2024* 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 of Beneficial Owner	Amount and Nature of Beneficial Ownership[1]			
5% Shareholders:	Shares	Shares Acquirable Within 60 Days[2]	Total Shares Deemed Beneficially Owned	Percent of Outstanding Shares[3]
Entities Associated with EcoR1 Capital, LLC[4]	11,584,280	—	11,584,280	21.5%
Entities Associated with Fidelity Investments[5]	8,049,796	—	8,049,796	15.0%
William P. Scully[6]	5,558,290	—	5,558,290	10.3%
Wellington Management Company LLP[7]	5,130,876	—	5,130,876	9.5%
Todd W. Fennell[8]	4,645,147	—	4,645,147	8.6%
T. Rowe Price Associates, Inc.[9]	3,822,434	—	3,822,434	7.1%
BlackRock, Inc.[10]	3,770,650	—	3,770,650	7.0%
Directors and Named Executive Officers:				
Paula K. Cobb	—	97,500	97,500	*
Richard T. Collier	1,219	116,544	117,763	*
Shane M. Cooke	—	116,544	116,544	*
William H. Dunn, Jr.	—	10,000	10,000	*
Lars G. Ekman	243	116,544	116,787	*
Helen S. Kim	—	35,000	35,000	*
Dennis J. Selkoe[11]	4,208	85,044	89,252	*
Daniel G. Welch	—	26,400	26,400	*
Gene G. Kinney	12,793	2,081,115	2,093,908	3.7%
Tran B. Nguyen	2,205	791,919	794,124	1.5%
Brandon S. Smith	—	415,144	415,144	*
Carol D. Karp	—	470,476	470,476	*
Wagner M. Zago	—	453,082	453,082	*
All 17 directors and executive officers as a group	20,668	5,451,661	5,472,329	9.2%

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

(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 3, 2025. 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 53,826,982 ordinary shares issued and outstanding on March 3, 2025. 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 3, 2025, 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 (i) Amendment No. 4 to Schedule 13D filed with the SEC on January 3, 2025, by EcoR1 Capital, LLC ("EcoR1"), EcoR1 Capital Fund Qualified, L.P. ("Qualified Fund") and Oleg Nodelman, reporting beneficial ownership as of December 31, 2024. 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 10,847,852 ordinary shares. Mr. Nodelman is the manager and control person of EcoR1. EcoR1 is an investment advisor to Qualified Fund and EcoR1 Capital Fund, L.P. 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. The address of the beneficial owner is 357 Tehama Street, #3, San Francisco, California 94103, USA.

(5) As reported on Amendment No. 3 to Schedule 13G filed with the SEC on February 9, 2024, by FMR LLC ("FMR") and Abigail P. Johnson, reporting beneficial ownership as of December 29, 2023. FMR has sole voting power over 8,049,190 ordinary shares and sole dispositive power over 8,049,796 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. According to FMR's most recent Form 13F filed with the SEC on February 13, 2025, reporting the securities it held as of December 31, 2024, FMR reported ownership of 8,071,309 ordinary shares (or 15.0% of our outstanding shares as of March 3, 2025). The address of the beneficial owner is 245 Summer Street, Boston, Massachusetts 02210, USA.

(6) As reported on Amendment No. 2 to Schedule 13G filed with the SEC on February 21, 2025, by William P. Scully, reporting beneficial ownership as of December 31, 2024. Mr. Scully has sole voting power over 708,143 ordinary shares and sole dispositive voting power over 708,143 ordinary shares, consisting of (i) 49,193 ordinary shares owned directly by Mr. Scully over which he has sole voting and dispositive power, (ii) 75,950 ordinary shares owned by Manatee Equity Fund LLC, of which Mr. Scully is the sole manager with sole voting and dispositive power, and (iii) 583,000 ordinary shares owned by the Mr. Scully's individual retirement account, over which he has sole voting and dispositive power. Mr. Scully has shared voting power over 4,850,147 ordinary shares and shared dispositive power over 4,850,147 ordinary shares, consisting of (i) 42,000 ordinary shares owned by Mr. Scully's spouse's individual retirement account, over which Mr. Scully has shared voting and dispositive power, (ii) 17,000 ordinary shares owned by Mr. Scully's spouse, over which Mr. Scully has shared voting and dispositive power, (iii) 18,000 ordinary shares owned by an individual retirement account subject to an investment management agreement over which Mr. Scully may be deemed to have shared voting and dispositive power by reason of his right to terminate such agreement, (iv) 128,000 ordinary shares owned in the aggregate by various trusts over which Mr. Scully may be deemed to have shared voting and dispositive power by virtue of being a co-trustee, (v) 4,092,346 ordinary shares owned in the aggregate by various grantor retained annuity trusts, which have an independent trustee, but over which Mr. Scully may be deemed to have shared voting and dispositive power by reason of his retained right to substitute assets in such trusts, and (vi) 552,801 ordinary shares owned in the aggregate by various irrevocable gift trusts, which have an independent trustee, but over which Mr. Scully may be deemed to have shared voting and dispositive power by reason of his retained right to substitute assets in such trusts. The address of the beneficial owner is 771 Manatee Cove, Vero Beach, Florida 32963, USA.

(7) As reported on Amendment No. 2 to Schedule 13G filed with the SEC on February 10, 2025, by Wellington Management Group LLP ("Wellington Management"), Wellington Group Holdings LLP ("Wellington Holdings"), Wellington Investment Advisors Holdings LLP ("Wellington Advisors"), and Wellington Management Company LLP ("Wellington Company") reporting beneficial ownership of December 31, 2024. These shares are owned of record by clients of Wellington Company, Wellington Management Canada LLC, Wellington Management Singapore Pte Ltd, Wellington Management Hong Kong Ltd, Wellington Management International Ltd, Wellington Management Japan Pte Ltd, and Wellington Management Australia Pty Ltd (collectively, the "Wellington Investment Advisors"). Wellington Advisors controls directly, or indirectly through Wellington Management Global Holdings Ltd., the Wellington Investment Advisors. Wellington Advisors is owned by Wellington Holdings. Wellington Holdings is owned by Wellington Management. The clients of the Wellington Investment Advisors have the right to receive, or the power to direct the receipt of, dividends from, or the proceeds from the sale of, such securities. No such client is known to have such right or power with respect to more than five percent of this class of securities, except Vanguard Health Care Fund. Each of Wellington Management, Wellington Holdings, and Wellington Advisors has shared voting power over 5,094,682 ordinary shares and shared dispositive power over 5,130,876 ordinary shares. Wellington Company has shared voting power over 5,090,828 ordinary shares and shared dispositive power over 5,090,828 ordinary shares. The address of the beneficial owner is c/o Wellington Management Company LLP, 280 Congress Street, Boston, Massachusetts 02210, USA

(8) As reported on Amendment No. 2 to Schedule 13G filed with the SEC on February 14, 2025, by Todd W. Fennell, reporting beneficial ownership as of December 31, 2024. Todd W. Fennell has shared voting and dispositive power over 4,645,147 ordinary shares, consisting of (i) 552,801 ordinary shares owned in the aggregate by various irrevocable gift trusts, for which Mr. Fennell serves as an independent trustee, and (ii) 4,092,346 ordinary shares owned in the aggregate by various grantor retained annuity trusts, for which Mr. Fennell serves as an independent trustee. The address of the beneficial owner is 979 Beachland Boulevard, Vero Beach, Florida 32963, USA.

(9) As reported on Amendment No. 5 to Schedule 13G filed with the SEC on November 14, 2024, by T. Rowe Price Associates, Inc., reporting beneficial ownership of September 30, 2024. T. Rowe Price has sole voting power over 3,741,201 ordinary shares and sole dispositive power over 3,822,434 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 address of the beneficial owner is 100 E Pratt Street, Baltimore, Maryland, 21202, USA.

(10) As reported on Amendment No. 9 to Schedule 13G filed with the SEC on February 2, 2024, by BlackRock, Inc. ("BlackRock"), reporting beneficial ownership of December 31, 2023. BlackRock, Inc. is a parent holding company/control person that has sole voting power over 3,684,648 ordinary shares and sole dispositive power over 3,770,650 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 Japan Co., Ltd; BlackRock Asset Management Schweiz AG; BlackRock Investment Management, LLC; BlackRock Investment Management (UK) Limited; BlackRock Asset Management Canada Limited; BlackRock Investment Management (Australia) Limited; BlackRock Fund Advisors; and BlackRock Fund Managers Ltd. According to BlackRock's most recent Form 13F filed with the SEC on February 7, 2025, reporting the securities it held as of December 31, 2024, BlackRock reported ownership of 4,122,376 ordinary shares (or 7.7% of our outstanding shares as of March 3, 2025). The address for the beneficial owner is 55 East 52nd Street, New York, New York 10055, USA.

(11) Includes 2,845 ordinary shares held by Dr. Selkoe and 1,363 ordinary shares held by Dr. Selkoe's spouse.

Delinquent Section 16(a) Reports

Section 16(a) of the Securities Exchange Act of 1934, as amended, requires our executive officers and directors, and persons who own more than 10% of our ordinary shares, to file reports of ownership and changes in ownership electronically with the SEC. Based on a review of such forms filed electronically with the SEC and our officers' and directors' written representations, we believe that each person who, at any time during fiscal year 2024, was an executive officer, director, or beneficial owner of more than 10% of our ordinary shares, complied with all filing requirements in a timely fashion, except for one Form 4 for Tran B. Nguyen reporting one transaction on April 8, 2020, which was filed on February 14, 2025.

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 2024 (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;
- Brandon S. Smith, our Chief Operating Officer;
- Carol D. Karp, our Chief Regulatory Officer; and
- Wagner M. Zago, Ph.D., our Chief Scientific Officer.

Executive Summary: Fiscal Year 2024 Company Performance and Key Pay Decisions

2024 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 2024 was aligned with the Company's performance during 2024 and its go-forward strategy. Highlights of that performance include:

- ***We Made Significant Advances in our Neurodegenerative Diseases Portfolio.***
  - PRX012, a wholly-owned potential best-in-class, next-generation subcutaneous antibody for the treatment of Alzheimer's disease (AD) that targets a key epitope at the N-terminus of amyloid beta (Aβ) with high binding potency. In 2024, Prothena continued enrollment in our ongoing ASCENT clinical trials (reaching approximately 260 patients) and presented posters at the Alzheimer's Association International Conference (AAIC) and the Clinical Trials on Alzheimer's Disease conference (CTAD) highlighting the clinical trial design of the Phase 1 ASCENT clinical trials.
  - BMS-986446 (formerly PRX005), a potential best-in-class antibody for the treatment of AD that specifically targets a key epitope within the microtubule binding region (MTBR) of tau, a protein implicated in the causal pathophysiology of AD. BMS-986446 is part of the global neuroscience research and development collaboration with Bristol Myers Squibb (BMS). In 2024, BMS continued to enroll the ongoing Phase 2 TargetTau-1 clinical trial in approximately 475 patients with early Alzheimer's disease and presented the design of the ongoing Phase 2 TargetTau-1 clinical trial in a poster presentation at AAIC and an oral encore presentation at CTAD.
  - Prasinezumab, a potential first-in-class antibody, for the treatment for Parkinson's disease (PD), that is designed to target key epitopes within the C-terminus of alpha-synuclein and is the focus of the worldwide collaboration with Roche. In 2024, Roche reported results from the Phase 2b PADOVA clinical trial in patients with early-stage Parkinson's disease missed the primary endpoint but showed a numerical delay in motor progression and positive trends on multiple secondary and exploratory endpoints suggesting possible clinical benefit. Roche announced that they will continue to evaluate the data and work together with health authorities to determine next steps.
  - PRX019, a potential treatment of neurodegenerative diseases with an undisclosed target, is part of the global neuroscience research and development collaboration with BMS. In 2024, Bristol Myers Squibb obtained the exclusive global license for PRX019 for $80 million; and Prothena initiated a Phase 1 first-in-human clinical trial to evaluate the safety, tolerability, immunogenicity, and pharmaco-kinetics of single ascending and multiple doses in healthy adults.
- ***We Made Significant Advances in our Rare Peripheral Amyloid Diseases Portfolio.***
  - Birtamimab, a wholly-owned potential best-in-class amyloid depleter antibody for the treatment of AL amyloidosis designed to directly neutralize soluble toxic light chain aggregates and promote clearance of amyloid that causes organ dysfunction and failure. In 2024, Prothena published Birtamimab's mechanism of action and pharmacological characteristics in Leukemia & Lymphoma and presented Longitudinal Health-Related Quality of Life data (SF-36v2) across domains from the VITAL Phase 3 clinical trial at the International Society of Amyloidosis. We continued the confirmatory Phase 3 AFFIRM-AL clinical trial (NCT04973137) in patients with Mayo Stage IV AL amyloidosis under a Special Protocol Assessment (SPA) agreement with the

FDA with a primary endpoint of all cause mortality (time-to-event) at a significance level of 0.10.

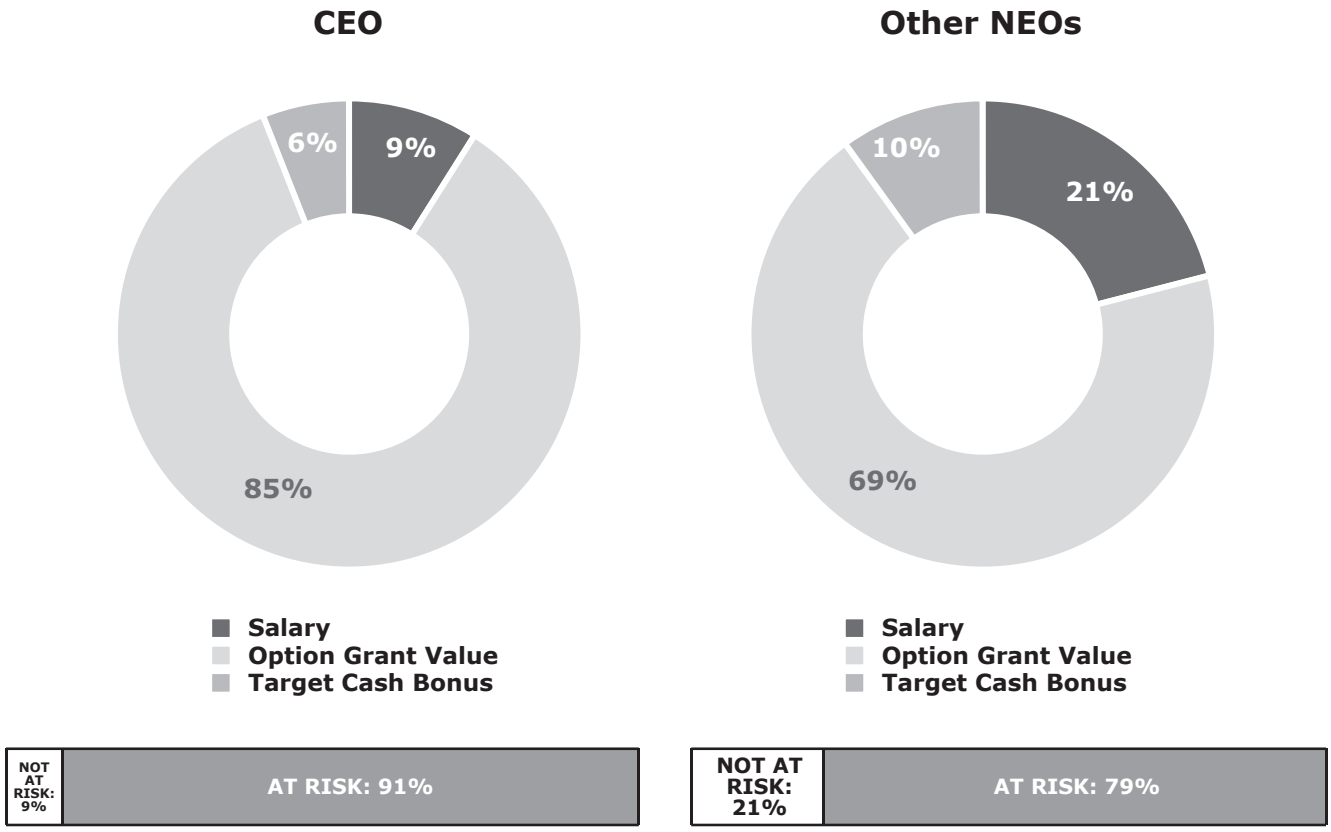
- Coramitug (formerly PRX004), a potential first-in-class amyloid depleter antibody for the treatment of ATTR cardiomyopathy designed to deplete the pathogenic, non-native forms of the transthyretin (TTR) protein and is being developed by Novo Nordisk as part of their up to $1.2 billion acquisition of our ATTR amyloidosis business and pipeline. In 2024, Phase 1 clinical trial results for coramitug in patients with ATTR amyloidosis was published in Amyloid, the official journal of the International Society of Amyloidosis, and Novo Nordisk continued the ongoing Phase 2 signal-detection clinical trial in patients with ATTR-CM.

- ***We Carefully Managed our Cash Balance***.
  - During fiscal year 2024, we carefully managed our capital. While progressing all of our development programs described above, our cash used in operating and investing activities was $150.3 million, which was in-line with our guidance range of $148 to $160 million. We finished fiscal year 2024 with $472.2 million in cash, cash equivalents, and restricted cash, including cash used in operating and financing activities, which exceeded our guidance of $468 million, providing a solid financial foundation for continuing to advance the Company's discovery and clinical programs.

2024 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. We believe that our 2024 executive compensation program reflected this philosophy as highlighted by the following features:

- ***Modest Base Salary Adjustments.*** In 2024, our Chief Executive Officer, Dr. Kinney, and each of our other named executive officers other than Dr. Zago, all received 3.5% increases in their base salaries. Dr. Zago received a 4.2% increase in his base salary to align his base compensation with market data for his position.
- ***Annual Bonuses Reflected 2024 Company Performance.*** At the beginning of fiscal year 2024, the Committee determined not to change the target bonus opportunities of our named executive officers from their respective levels in 2023. For fiscal year 2024, the Committee and Board established pre-determined corporate objectives that they considered critical to the near- and long-term success of the Company. Following 2024, the Committee and the Board determined that Company performance relative to the corporate objectives was 100%. Based on that corporate performance (weighted at 75% of total bonus opportunity) and the individual performance (weighted at 25% of total bonus opportunity) of each named executive officer other than Dr. Kinney, the Committee approved payouts at 100% of the target bonuses as to the corporate portion of the bonus for those named executive officers. Dr. Kinney's bonus was based solely on corporate performance, and the Board therefore approved his payout at 100% of his target bonus for 2024.
- ***Equity as a Key Component of Compensation.*** We use stock options in our executive compensation program 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 named executive officers early in 2024.
- ***Commitment to Pay for Performance.*** Our executive compensation programs are designed to deliver pay that is tied to our corporate and individual performance. Accordingly, 90.9% of our Chief Executive Officer's and on average 78.6% of each of our other named executive officers' total targeted compensation for fiscal year 2024 (based on annual base salary, target annual cash bonus, and grant date fair value of stock option award granted in 2024) was provided in the form of (a) cash incentives tied to actual performance against pre-determined strategic, operational, and financial objectives; and (b) stock options, which further 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 2024 for our Chief Executive Officer 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 Don't Do
✓ **Pay for performance.** A significant percentage of total target compensation is pay at-risk that is connected to performance.	X **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.	X **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.	X **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 composition of our comparator peer group at least annually.	X **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 for both cash and equity have double triggers requiring a change-in-control and a qualifying termination.	X **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.
✓ **Annual say-on-pay vote.** The Company seeks annual input from our shareholders regarding our named executive officer compensation.	X **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 2024 annual general meeting of our shareholders, our shareholders voted to approve the 2023 compensation of our named executive officers, with 99% 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, based on this strong favorable shareholder response to our existing executive compensation programs, 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 Chief Executive Officer. In the case of our Chief Executive Officer, the Committee makes recommendations to the Board regarding his compensation, and the Board (excluding the Chief Executive Officer) makes all final decisions on his compensation. Information on the Committee and its responsibilities is provided in this Proxy Statement under the heading *Corporate Governance and Board Matters - Board Committees - Compensation Committee*.

The Committee Utilizes an Independent Compensation Consultant. The Committee annually retains an independent executive compensation consultant to assist the Committee in making informed decisions on executive officer compensation. For fiscal year 2024 compensation decisions, the Committee retained Pay Governance as its independent executive compensation consultant. Pay Governance was engaged directly by the Committee, after the Committee assessed Pay Governance's independence from the Company and its management. This process is repeated annually before the Committee selects its executive compensation consultant for that year.

For fiscal year 2024, Pay Governance 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. Pay Governance was also asked to provide to the Committee specific recommendations on our executive compensation programs generally.

The Committee Reviews Competitive Market Data. For fiscal year 2024, the Committee approved a "peer group" of companies to assist the Committee in its annual compensation assessments and decision-making. At the Committee's instruction, Pay Governance 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 $1.0 billion and $10.0 billion (based on the Company's then-market capitalization of approximately $3.0 billion), and (c) number of employees (generally under 500 employees). These criteria were used to develop a recommended list of peer companies, with respect to fiscal year 2024, which Pay Governance presented to the Committee. As a result of this analysis, ACADIA Pharmaceuticals, Axsome, Biohaven Ltd., Cerevel Therapeutics, Intra-Cellular, Sage Therapeutics, and Xenon Pharmaceuticals were added to our peer group; AnaptsysBio, ImmunoGen, Iovance Biotherapeutics, Kodiak Sciences, Krystal Biotech, Kura Oncology, Mersana Therapeutics, NGM Biopharmaceuticals, and Sangamo Therapeutics were removed from our peer group. The peer group companies identified by Pay Governance and considered, discussed, and approved by the Committee to assist the Committee in its evaluation of 2024 compensation decisions were:

ACADIA Pharm.	Crinetics Pharm.
Alector	Cytokinetics
Anavex Life Sciences	Denali Therapeutics
Arcus Biosciences	Intra-Cellular
Arrowhead Pharm.	Karuna Therapeutics
Axsome	Replimune Group
Biohaven Ltd.	Sage Therapeutics
Celldex Therapeutics	Xenon Pharm.
Cerevel Therapeutics	

For competitive assessment purposes, Pay Governance used executive compensation data publicly reported by these peer group companies (*i.e.*, proxy statement data), as well as survey data from other publicly-traded pre-commercial biotechnology companies with characteristics (*e.g.*, market capitalization, stage of development, and number of

employees) deemed comparable to these peer group companies and the Company.

Pay Governance'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. Pay Governance's reports also provided recommendations on changes that might be made to our executive compensation programs generally and to each executive officer's compensation. Pay Governance provided its written report in advance of Committee meetings, at which the Pay Governance consultant presented and responded to questions from the Committee.

The Committee believes that compensation decisions are complex and require a deliberate review of Company performance, peer compensation levels, experience and impact of individual executive officers, and individual performance. In determining executive compensation, the Committee considers all forms of compensation and the value delivered by each component of compensation. When evaluating total target compensation, the Committee generally strives to set executive officer compensation around the 50th percentile of the market data. The Committee may, however, determine that it is appropriate for total target compensation or any particular element of compensation to exceed or fall below the 50th percentile of the market data for an executive officer. The factors that might influence the amount of compensation awarded include market competition for a particular position, the strategic importance of the position, requirements of the position relative to benchmark norms, retention considerations, an individual's performance, possession of a unique skill or knowledge set, proven leadership capabilities, and internal pay equity.

The Chief Executive Officer and Management Make Recommendations. For fiscal year 2024, Dr. Kinney and a senior member of management presented to the Committee their recommendations on compensation for the executive officers, provided that Dr. Kinney did not make recommendations as to his own compensation. Prior to completion of fiscal year 2024, Dr. Kinney and other executive officers and members of management presented their assessments and recommendations to the Committee and the Board regarding the Company's performance relative to the pre-established corporate objectives for 2024. After completion of fiscal year 2024, Dr. Kinney and other executive officers and members of management presented additional assessments and recommendations to the Committee as described below. The Committee and the Board may consider any such recommendations but are not required to follow any recommendations and may adjust compensation up or down at their discretion.

The Committee or Board Makes Compensation Decisions. At the beginning of 2024, the Committee determined the structure of our executive officer compensation programs for that year, after receiving Pay Governance'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 their base salary, (b) their target annual cash bonus opportunity for 2024 and the corporate objectives for 2024, and (c) their annual stock option award for 2024.

In the case of Dr. Kinney, after discussion with a senior member of management and Pay Governance, the Committee recommended to the Board his base salary, his annual cash bonus opportunity for fiscal year 2024 and the 2024 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.

After completion of fiscal year 2024, the Committee received management's report on the Company's performance relative to the pre-established corporate objectives for 2024, and Dr. Kinney, and our Chief People Officer, Chief Legal Officer, and another senior member of management discussed such report and presented their assessments and recommendations with the Committee. Dr. Kinney presented on and discussed the individual performance of each executive officer, provided that Dr. Kinney did not make recommendations as to his own compensation nor participate in discussion with the Committee regarding his own compensation. Pay Governance participated in discussions with the Committee. After receiving that report, and assessment and recommendations from management, the Committee determined the annual cash bonus to be paid to each executive officer other than Dr. Kinney for 2024.

After completion of fiscal year 2024, the Nominating and Corporate Governance Committee of the Board completed a review of Dr. Kinney's performance during 2024 (with input from all other independent members of the Board) and this review was reported to both the Compensation Committee and the Board. The Compensation Committee also met in executive session with Pay Governance to discuss Dr. Kinney's compensation. The Committee determined and recommended to the Board (other than Dr. Kinney) Dr. Kinney's annual cash bonus for 2024 based on attainment of pre-established corporate objectives for 2024. In an executive session without Dr. Kinney present, the Board considered, discussed, and approved the bonus amount recommended by the Committee.

Equity Grant Practices and Procedures. All stock options awarded to our executive officers other than the Chief Executive Officer are approved by the Committee, and stock options awarded to our Chief Executive Officer are approved by our Board (based

on recommendations from the Committee). Equity grants to other employees are made pursuant to specific delegations of authority from the Committee, which delegations include individual grant limits, aggregate grant limits, and specification of grant terms. Please see the section entitled "Policies and Practices Related to the Timing of Grants of Certain Awards" for further information regarding our equity grant practices.

Executive Compensation for Fiscal Year 2024

The three key elements of our executive officer compensation programs for fiscal year 2024 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 2024 for our named executive officers were as follows: Dr. Kinney - $657,837; Mr. Nguyen - $583,374; Mr. Smith - $523,270; Ms. Karp - $517,218, and Dr. Zago - 495,327. 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 Pay Governance and consistent with the budgeted standard merit increase for the general employee population. Based on the same considerations, the salaries of Mr. Nguyen, Mr. Smith and Ms. Karp reflect the Committee's approval of 3.5% increases to their base salaries. Dr. Zago's increase of 4.2% to his base salary reflects an adjustment following the Committee's review of market data for his 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 support shareholder value creation. Following the end of each fiscal year, the Committee and the Board determine to what extent those corporate objectives were 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 Chief Executive Officer are based 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 Chief Executive Officer on each such executive officer's individual performance (relative to the pre-determined corporate objectives as well as more generally). Our Chief Executive Officer's annual cash bonus depends exclusively on the Company's achievement of the pre-established corporate objectives. The Committee believes that corporate objectives are appropriate to ensure all executive officers are working together toward those goals, and that individual performance is an appropriate additional consideration to 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 2024* table below.

In determining the targeted annual cash bonus opportunity for each named executive officer at the beginning of fiscal year 2024, the Committee considered Pay Governance'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.

Targeted annual cash bonuses are expressed as a percentage of base salary earned during the performance period. At the beginning of fiscal year 2024, the Committee determined not to change the target bonuses of our named executive officers from their respective levels set in 2023. Specifically, the Committee recommended and the Board approved setting Dr. Kinney's targeted cash bonus at 60% of his base salary earned in 2024, the Committee set Mr. Nguyen's and Mr. Smith's cash bonuses at 50% of their respective base salaries earned in 2024, and the Committee set Ms. Karp's and Dr. Zago's targeted cash bonus at 40% of their respective base salaries earned in 2024. 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 Chief Executive Officer, relative to the other executive officers, was appropriate because of the position and responsibilities that our Chief Executive Officer holds. The Committee further determined that the target bonus opportunities for Mr. Nguyen and Mr. Smith (both at 50%) and Ms. Karp and Dr. Zago (both at 40%) continued to be appropriate based on a review of market factors, as well as, the corporate duties and responsibilities of each such officer.

For fiscal year 2024, 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 significant "stretch" performance.

Objective	Weighting	Result
Progress R&D portfolio to achieve primary 2024 milestones:	**95%**	
For Birtamimab, reach decision re expansion of total enrollment in the AFFIRM-AL clinical trial; achieve an enrollment goal for the AFFIRM-AL clinical trial; execute engagement plan to support enrollment.	40%	Met
For PRX012, complete Phase 1 clinical trial through a specified cohort; execute communication plan to support positioning.	45%	Met
For PRX019, obtain BMS option exercise and initiate Phase 1 clinical trial.	5%	Met
For novel platform, reach development decision based on *in vivo* results; initiate additional activities based on such results.	5%	Met
Meet cash burn guidance range and optimize shareholder base:	**5%**	
Meet publicly-disclosed cash burn guidance range.	2.5%	Met
Optimize shareholder base by: retaining four of top six institutional investors; galvanizing at least one institutional investor (existing or new) to take a $\geq$5% ownership stake; or galvanizing at least five institutional investors (existing or new) to take a $\geq$1% ownership stake.	2.5%	Met

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 achieved the pre-determined corporate objectives resulting in achievement of 100% 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 100% of their targeted annual cash bonuses, based on aggregated performance against both corporate and individual performance objectives. The Committee recommended to the Board that Dr. Kinney's annual cash bonus be 100% 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 2024 performance is set forth in the *Non-Equity Incentive Plan Compensation* column of the *Summary Compensation Table - Fiscal Year 2024* below.

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 by encouraging them to identify, pursue, and invest in appropriate long-term strategies and secondarily to retain executive officers. The long-term incentives granted to our named executive officers for fiscal year 2024 were solely in the form of nonqualified stock options awarded under the 2018 LTIP.

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) 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 value and form of long-term incentive compensation to be provided to each named

executive officer in February 2024, the Committee considered Pay Governance'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 value of the annual stock option awarded to the executive officer in 2023;
- For each executive officer and all executive officers as a whole, the annual stock options awarded in 2023 as a percent of the Company's outstanding shares, with comparisons to the peer group data for that year;
- For all executive officers as a whole, the grant-date values of the annual stock options awarded in 2023, 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 the estimated value of a new hire award which would be required to replace each named executive officer;
- 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 considered it critical to retain these executive officers to meet 2024 and longer-term objectives and decided that time-vested stock options continued to be the best vehicle to serve that retention need.

Based on all the above considerations, in 2024, the Committee approved annual stock option awards to each of our named executive officers other than Dr. Kinney, i.e., Mr. Nguyen, Mr. Smith, Ms. Karp, and Dr. Zago, and the Board approved an annual stock option award for Dr. Kinney. 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 (except in the event of certain terminations of employment, as described below under the heading *Change in Control and Severance Arrangements*).

The stock options granted to our named executive officers in fiscal year 2024 and the grant date fair value of those options are set forth in the *Summary Compensation Table - Fiscal Year 2024* and the *Grants of Plan-Based Awards - Fiscal Year 2024* table below.

Retirement Plan. 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 2024, and may also make discretionary matching contributions to all participants' accounts (which it did for fiscal year 2024, equal to 1.5% of each participant's eligible earnings in 2024), so long as each participant had deferred an equal number of dollars into their 401(k) plan account during 2024. We do not maintain a non-qualified deferred compensation plan.

Perquisites and Other Personal Benefits. Our named executive officers participate in the same broad-based plans as our employees and 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 Chief Executive Officer in September 2016, we entered into an employment agreement with Dr. Kinney that sets forth the terms and conditions of his employment as our Chief Executive Officer. That employment agreement provides for an annual base salary of $500,000, which has subsequently been increased as described above, as well as a targeted annual cash bonus equal to 60% of his base salary earned in each performance year. 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 President and Chief Executive Officer, as well as generally consistent with peer group data presented to the Committee by its independent 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. We believe 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 our other named executive officers 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.

Policy on Recoupment of Incentive Compensation

We have a Policy on Recoupment of Incentive Compensation to comply with SEC and Nasdaq listing rules. Under that policy, the Company is required in certain situations to recoup incentive compensation paid or payable to certain current or former executive officers of the Company, including the named executive officers, in the event of an accounting restatement.

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)
Shane M. Cooke
Daniel G. Welch

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 years 2024, 2023, and 2022.

Summary Compensation Table - Fiscal Year 2024

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.	2024	654,129	—	6,168,827	392,478	15,525	7,230,959
President and Chief Executive Officer	2023	630,547	—	6,039,017	359,412	14,850	7,043,826
	2022	600,521	—	5,705,925	414,359	15,250	6,736,055
Tran B. Nguyen	2024	580,086	—	1,707,982	290,043	15,525	2,593,636
Chief Strategy Officer and Chief Financial Officer	2023	550,410	—	1,870,147	264,885	14,850	2,700,292
	2022	480,389	—	1,940,015	267,216	15,250	2,702,870
Brandon S. Smith	2024	520,321	—	1,707,982	260,160	15,525	2,503,988
Chief Operating Officer	2023	501,563	—	1,870,147	241,377	14,850	2,627,937
	2022	476,250	—	1,940,015	264,914	15,250	2,696,429
Carol D. Karp	2024	514,303	—	1,707,982	205,721	15,525	2,443,531
Chief Regulatory Officer	2023	495,762	—	1,870,147	190,868	14,850	2,571,627
	2022	472,154	—	1,940,015	210,108	15,250	2,637,527
Wagner M. Zago, Ph.D.	2024	492,000	—	1,707,982	196,800	15,525	2,412,307
Chief Scientific Officer							

(1) For 2024, consists of NQSOs (nonqualified stock options) awarded under our 2018 LTIP. 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 2024, see Note 9 of the Consolidated Financial Statements included in our Form 10-K.

(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 regarding fiscal year 2024 cash bonuses, see the *Grants of Plan Based Awards - Fiscal Year 2024* 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.

The following table shows all plan-based awards granted to our named executive officers during our fiscal year 2024.

Grants of Plan-Based Awards - Fiscal Year 2024

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[3]	Exercise or Base Price of Option Awards	Grant Date Fair Value of Option Awards[4]
			Threshold ($)	Target ($)	Maximum ($)	(#)	($/sh)	($)
Gene G. Kinney	2/27/2024	2/21/2024				307,000	30.30	6,168,827
			236,821	394,702	592,053			
Tran B. Nguyen	2/27/2024	2/15/2024				85,000	30.30	1,707,982
			131,259	291,687	437,531			
Brandon S. Smith	2/27/2024	2/15/2024				85,000	30.30	1,707,982
			117,736	261,635	392,453			
Carol D. Karp	2/27/2024	2/15/2024				85,000	30.30	1,707,982
			93,099	206,887	310,331			
Wagner M. Zago	2/27/2024	2/15/2024				85,000	30.30	1,707,982
			89,159	198,131	297,196			

(1) This column shows the date that the Board or Compensation Committee, as applicable, 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 approval of the award.

(2) Consists of cash bonus awards under the ICP for our fiscal year 2024. 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 2024. 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 2024. 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 had been 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 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 2024 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 would have been 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 2024; the actual cash payouts to each executive officer are reported in the *Non-Equity Incentive Plan* column of the Summary Compensation Table - Fiscal Year 2024 above.

(3) Consists of ordinary shares that may be acquired by exercise of nonqualified stock options awarded under our 2018 LTIP. These option awards have a four-year vesting schedule from the vesting commencement date, with 25% of the shares subject to the option vesting on the first anniversary of that grant 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 2024* table below.

(4) 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 2024* above.

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 2024. Certain of the stock option awards reported in this table are also reported in the *Grants of Plan-Based Awards - Fiscal Year 2024* table above.

Outstanding Equity Awards at Fiscal Year-End - Fiscal Year 2024

	Option Awards[1]			
Name	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($)	Option Expiration Date
Gene G. Kinney	620,000	—	15.04	06/21/2028
	245,000	—	13.53	02/27/2029
	200,000	—	12.15	02/25/2030
	50,000	—	12.15	02/25/2030
	59,090	—	22.85	03/11/2025
	40,625	—	22.85	02/24/2026
	25,125	—	22.85	09/01/2026
	16,759	—	22.85	11/02/2026
	62,500	—	22.85	02/22/2027
	140,601	—	22.85	02/21/2028
	239,583	10,417 [2]	22.60	02/25/2031
	177,083	72,917 [3]	32.45	02/23/2032
	67,812	87,188 [4]	52.97	03/02/2033
	—	307,000 [5]	30.30	02/27/2034
Tran B. Nguyen	250,000	—	15.04	06/21/2028
	95,000	—	13.53	02/27/2029
	105,000	—	12.15	02/25/2030
	40,625	—	22.85	02/24/2026
	39,062	—	22.85	02/22/2027
	60,150	—	22.85	02/21/2028
	80,500	3,500 [2]	22.60	02/25/2031
	60,208	24,792 [3]	32.45	02/23/2032
	21,000	27,000 [4]	52.97	03/02/2033
	—	85,000 [5]	30.30	02/27/2034
Brandon S. Smith	218,667	—	11.12	03/02/2030
	53,666	2,334 [2]	22.60	02/25/2031
	20,312	4,688 [6]	70.81	09/29/2031
	60,208	24,792 [3]	32.45	02/23/2032
	21,000	27,000 [4]	52.97	03/02/2033
	—	85,000 [5]	30.30	02/27/2034

Name	Option Awards[1]			
	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($)	Option Expiration Date
Carol D. Karp	120,000	—	15.04	06/21/2028
	35,000	—	13.53	02/27/2029
	45,000	—	12.15	02/25/2030
	51,282	—	22.85	12/14/2026
	45,112	—	22.85	02/21/2028
	53,666	2,334 [2]	22.60	02/25/2031
	60,208	24,792 [3]	32.45	02/23/2032
	21,000	27,000 [4]	52.97	03/02/2033
	—	85,000 [5]	30.30	02/27/2034
Wagner M. Zago	21,000	—	34.61	02/24/2026
	20,000	—	55.00	02/22/2027
	20,000	—	51.32	06/09/2027
	60,000	—	33.10	02/21/2028
	68,750	—	15.04	06/21/2028
	31,250	—	13.53	02/27/2029
	58,000	—	12.15	02/25/2030
	53,666	2,334 [2]	22.60	02/25/2031
	60,208	24,792 [3]	32.45	02/23/2032
	21,000	27,000 [4]	52.97	03/02/2033
	—	85,000 [5]	30.30	02/27/2034

(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 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).

(3) These option awards have a four-year vesting schedule from a vesting commencement date of February 23, 2022, 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 March 2, 2023, 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 have a four-year vesting schedule from a vesting commencement date of February 27, 2024, 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) 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).

The following table shows option exercises by our named executive officers during fiscal year 2024.

Option Exercises and Stock Vested[1] - Fiscal Year 2024

Name	Number of Shares Acquired on Exercise (#)	Value Realized on Exercise ($)[2]
Gene G. Kinney	—	—
Tran B. Nguyen	—	—
Brandon S. Smith	—	—
Carol D. Karp	—	—
Wagner M. Zago	—	—

(1) The Company has granted only stock options to our named executive officers.

(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 subject to the portion of the option exercised. 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, 2024, the last day of our fiscal year 2024. 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.

		Termination by Company[1]			Termination by Executive[1]			
Name	Nature of Payment or Benefit	For Cause	Due to a Business Condition	For Any Other Reason	Due to Voluntary Resignation	For Good Reason	Due to Death or Disability	Termination Following Change in Control[2]
Gene G. Kinney	Cash Severance[3]	—	822,296	822,296	—	822,296	822,296	1,315,674
	Cash Bonus[3]	—	394,702	394,702	—	394,702	394,702	789,404
	Accelerated Options[4]	—	—	—	—	—	—	—
	COBRA Coverage[5]	—	41,190	41,190	—	41,190	41,190	41,190
	Career Assistance[6]	—	25,000	25,000	—	25,000	25,000	25,000
	Total	**$—**	**$1,283,188**	**$1,283,188**	**$—**	**$1,283,188**	**$1,283,188**	**$2,171,268**
Tran B. Nguyen	Cash Severance[3]	—	583,374	—	—	583,374	—	875,061
	Cash Bonus[3]	—	291,687	—	—	291,687	—	437,531
	Accelerated Options[4]	—	—	—	—	—	—	—
	COBRA Coverage[5]	—	38,616	—	—	38,616	—	57,924
	Career Assistance[6]	—	25,000	—	—	25,000	—	25,000
	Total	**$—**	**$938,677**	**$—**	**$—**	**$938,677**	**$—**	**$1,395,516**
Brandon S. Smith	Cash Severance[3]	—	523,270	—	—	523,270	—	784,905
	Cash Bonus[3]	—	261,635	—	—	261,635	—	392,453
	Accelerated Options[4]	—	—	—	—	—	—	—
	COBRA Coverage[5]	—	38,683	—	—	38,683	—	58,025
	Career Assistance[6]	—	25,000	—	—	25,000	—	25,000
	Total	**$—**	**$848,588**	**$—**	**$—**	**$848,588**	**$—**	**$1,260,383**
Carol D. Karp	Cash Severance[3]	—	517,218	—	—	517,218	—	775,827
	Cash Bonus[3]	—	206,887	—	—	206,887	—	310,331
	Accelerated Options[4]	—	—	—	—	—	—	—
	COBRA Coverage[5]	—	33,713	—	—	33,713	—	50,570
	Career Assistance[6]	—	25,000	—	—	25,000	—	25,000
	Total	**$—**	**$782,818**	**$—**	**$—**	**$782,818**	**$—**	**$1,161,728**
Wagner M. Zago	Cash Severance[3]	—	495,327	—	—	495,327	—	742,991
	Cash Bonus[3]	—	198,131	—	—	198,131	—	297,196
	Accelerated Options[4]	—	—	—	—	—	—	—
	COBRA Coverage[5]	—	2,600	—	—	2,600	—	3,900
	Career Assistance[6]	—	25,000	—	—	25,000	—	25,000
	Total	**$—**	**$721,058**	**$—**	**$—**	**$721,058**	**$—**	**$1,069,087**

(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*.

(2) Due to (a) death or disability (under the Employment Agreement and the option award agreements), (b) termination without Cause or resignation for Good Reason under the Employment Agreement and option award agreements (in the case of Dr. Kinney) or the option award 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, 2024 at the closing market price per share of our ordinary shares ($13.85) on December 31, 2024, the last trading date of fiscal year 2024, which would vest in connection with the relevant termination of employment. Because no unvested stock options were in-the-money as of December 31, 2024, no value has been included here. For more information, see the footnotes to the *Outstanding Equity Awards at Fiscal Year-End - Fiscal Year 2024* 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 (the "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"). The 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 holidays; 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, subject in part to Dr. Kinney's timely execution of a release of claims, (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, subject in part to Dr. Kinney's timely execution of a release of claims, (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). The Employment Agreement provides that in the event Dr. Kinney is terminated by the Company without Cause or resigns for Good Reason and the event giving rise to such termination or resignation occurs at the direction of a person or entity that has entered into an agreement with the Company that contemplates a Change in Control, then for purposes of the Employment Agreement, the termination will be deemed to have occurred during the 24-month period commencing on the Change in Control.

The 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 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 Director; (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 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, subject in the case of the Severance Plan to the named executive officer's timely execution of a release of claims:

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 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 Chief Executive Officer to Median Employee

The total compensation in 2024 of Dr. Kinney, our President and Chief Executive Officer, was approximately 20 times the median total compensation in 2024 of all of our other employees. The total compensation in 2024 of Dr. Kinney was $7,230,959. The median of the total compensation in 2024 of all other employees was $369,174.

We calculated this median employee's total compensation for 2024 using the same methodology used to calculate our Chief Executive Officer's total compensation for 2024, as set forth in the *Summary Compensation Table - Fiscal Year 2024* above. The median employee's total compensation for 2024 included salary, an annual cash bonus paid in 2025 for 2024, stock option awards in 2024, and Company contributions in 2024 to that employee's account under our tax-qualified 401(k) defined contribution plan, each calculated for purposes of this pay ratio on the same basis as those same compensation elements of our Chief Executive Officer as explained in footnotes 1, 2, and 3 of the *Summary Compensation Table - Fiscal Year 2024*. We believe that our Chief Executive Officer-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, we used the base salary or wages (based on our payroll records) earned from January 1 through September 30, 2024, for each employee who was employed as of October 1, 2024. We included all of our full-time, part-time, temporary, and seasonal employees, globally, but excluded our Chief Executive Officer. For permanent full- and part-time employees who were hired after January 1, 2024, or who were on an unpaid leave of absence during a part of 2024, we adjusted their salaries or wages to reflect what they would have earned had they worked the entire nine-month period through September 30, 2024.

We believe that this use of salary or wages earned through the first nine months of 2024 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 2024 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.

Pay Versus Performance

The following table sets forth information regarding the Company's performance and the "compensation actually paid" to our named executive officers, as calculated in accordance with SEC disclosure rules:

Year [1]	Summary Compensation Table Total for PEO[2] ($)	Compensation Actually Paid to PEO[3] ($)	Average Summary Compensation Table Total for Non-PEO Named Executive Officers[2] ($)	Average Compensation Actually Paid to Non-PEO Named Executive Officers[4] ($)	Value of Initial Fixed $100 Investment Based on:[5]		Net Income (Loss) ($ in thousands)	Company Selected Measure[7]
					Total Shareholder Return ($)	Peer Group Total Shareholder Return[6] ($)		
2024	7,230,959	(1,707,034)	2,488,366	(204,492)	87.49	113.84	(122,310)	
2023	7,043,826	(3,218,100)	2,644,678	(1,225,533)	229.56	115.42	(147,028)	
2022	6,736,055	7,400,610	2,696,607	4,104,503	380.61	111.27	(116,949)	
2021[8]	4,918,363	41,144,072	2,852,428	12,625,320	312.07	124.89	66,975	
2020	3,427,567	62,288	1,594,891	866,852	75.87	125.69	(111,144)	

(1) Gene G. Kinney served as the Company's principal executive officer for the entirety of 2020, 2021, 2022, 2023, and 2024 and the Company's other named executive officers for the applicable years were as follows:

- 2024: Carol D. Karp, Tran B. Nguyen, Brandon S. Smith, Wagner M. Zago.
- 2021-2023: Hideki Garren, Carol D. Karp, Tran B. Nguyen, Brandon S. Smith.
- 2020: Carol D. Karp, Michael J. Malecek, Tran B. Nguyen, Brandon S. Smith.

(2) Amounts reported in this column represent (i) the total compensation reported in the Summary Compensation Table for the applicable year in the case of Dr. Kinney and (ii) the average of the total compensation reported in the Summary Compensation Table for the applicable year for the Company's named executive officers for the applicable year other than Dr. Kinney.

(3) Amounts reported in this column represent the compensation actually paid to Dr. Kinney as the Company's President and Chief Executive Officer in the indicated fiscal years, based on his total compensation reported in the Summary Compensation Table for the indicated fiscal years and adjusted as shown in the table below:

		PEO				
		2024 ($)	2023 ($)	2022 ($)	2021 ($)	2020 ($)
	Summary Compensation Table - Total Compensation[a]	7,230,959	7,043,826	6,736,055	4,918,363	3,427,567
-	Grant Date Fair Value of Option Awards and Stock Awards Granted in Fiscal Year[b]	(6,168,827)	(6,039,017)	(5,705,925)	(3,900,675)	(2,526,450)
+	Fair Value at Fiscal Year-End of Outstanding and Unvested Option Awards and Stock Awards Granted in Fiscal Year[c]	2,251,121	3,269,118	12,228,032	23,225,521	1,963,344
+	Change in Fair Value of Outstanding and Unvested Option Awards and Stock Awards Granted in Prior Fiscal Years[d]	(2,865,913)	(5,418,699)	2,227,286	8,810,891	(1,525,370)
+	Fair Value at Vesting of Option Awards and Stock Awards Granted in Fiscal Year That Vested During Fiscal Year[e]	—	—	—	—	—
+	Change in Fair Value as of Vesting Date of Option Awards and Stock Awards Granted in Prior Fiscal Years For Which Applicable Vesting Conditions Were Satisfied During Fiscal Year[f]	(2,154,374)	(2,073,328)	(8,084,838)	8,342,873	(1,276,803)
-	Fair Value as of Prior Fiscal Year-End of Option Awards and Stock Awards Granted in Prior Fiscal Years That Failed to Meet Applicable Vesting Conditions During Fiscal Year[g]	—	—	—	(252,901)	—
=	**Compensation Actually Paid**	**(1,707,034)**	**(3,218,100)**	**7,400,610**	**41,144,072**	**62,288**

(a) Represents Total Compensation as reported in the Summary Compensation Table for the indicated fiscal year.

(b) Represents the aggregate grant date fair value of the option awards granted to Dr. Kinney during the indicated fiscal year, computed in accordance with the methodology used for financial reporting purposes.

(c) Represents the aggregate fair value as of the indicated fiscal year-end of Dr. Kinney's outstanding and unvested option awards granted during such fiscal year, computed in accordance with the methodology used for financial reporting purposes.

(d) Represents the aggregate change in fair value during the indicated fiscal year of the outstanding and unvested option awards held by Dr. Kinney as of the last day of the indicated fiscal year, computed in accordance with the methodology used for financial reporting purposes and, for awards subject to performance-based vesting conditions, based on the probable outcome of such performance-based vesting conditions as of the last day of the fiscal year.

(e) Represents the aggregate fair value at vesting of the option awards that were granted to Dr. Kinney and vested during the indicated fiscal year, computed in accordance with the methodology used for financial reporting purposes.

(f) Represents the aggregate change in fair value, measured from the prior fiscal year-end to the vesting date, of each option award held by Dr. Kinney that was granted in a prior fiscal year and which vested during the indicated fiscal year, computed in accordance with the methodology used for financial reporting purposes.

(g) Represents the aggregate fair value as of the last day of the prior fiscal year of Dr. Kinney's option awards that were granted in a prior fiscal year and which failed to meet the applicable vesting conditions in the indicated fiscal year, computed in accordance with the methodology used for financial reporting purposes.

(4) Amounts reported in this column represent the compensation actually paid to the Company's named executive officers other than Dr. Kinney in the indicated fiscal year, based on the average total compensation for such named executive officers reported in the Summary Compensation Table for the indicated fiscal year and adjusted as shown in the table below:

		Average Other Named Executive Officers[a]				
		2024 ($)	2023 ($)	2022 ($)	2021 ($)	2020 ($)
	Summary Compensation Table - Total Compensation[b]	2,488,366	2,644,678	2,696,607	2,852,428	1,594,891
-	Grant Date Fair Value of Option Awards and Stock Awards Granted in Fiscal Year[c]	(1,707,982)	(1,870,147)	(1,940,015)	(2,154,308)	(976,659)
+	Fair Value at Fiscal Year-End of Outstanding and Unvested Option Awards and Stock Awards Granted in Fiscal Year[d]	623,274	1,012,372	4,157,531	7,328,264	963,292
+	Change in Fair Value of Outstanding and Unvested Option Awards and Stock Awards Granted in Prior Fiscal Years[e]	(931,629)	(2,233,022)	1,099,351	2,776,040	(398,568)
+	Fair Value at Vesting of Option Awards and Stock Awards Granted in Fiscal Year That Vested During Fiscal Year[f]	—	—	—	—	—
+	Change in Fair Value as of Vesting Date of Option Awards and Stock Awards Granted in Prior Fiscal Years For Which Applicable Vesting Conditions Were Satisfied During Fiscal Year[g]	(676,521)	(779,414)	(1,908,971)	1,869,973	(316,104)
-	Fair Value as of Prior Fiscal Year-End of Option Awards and Stock Awards Granted in Prior Fiscal Years That Failed to Meet Applicable Vesting Conditions During Fiscal Year[h]	—	—	—	(47,077)	—
=	**Compensation Actually Paid**	**(204,492)**	**(1,225,533)**	**4,104,503**	**12,625,320**	**866,852**

(a) Please see footnote 1 for the named executive officers included in the average for each indicated fiscal year.

(b) Represents the average Total Compensation as reported in the Summary Compensation Table for the reported named executive officers in the indicated fiscal year.

(c) Represents the average aggregate grant date fair value of the option awards granted to the reported named executive officers during the indicated fiscal year, computed in accordance with the methodology used for financial reporting purposes.

(d) Represents the average aggregate fair value as of the indicated fiscal year-end of the reported named executive officers' outstanding and unvested option awards granted during such fiscal year, computed in accordance with the methodology used for financial reporting purposes.

(e) Represents the average aggregate change in fair value during the indicated fiscal year of the outstanding and unvested option awards held by the reported named executive officers as of the last day of the indicated fiscal year, computed in accordance with the methodology used for financial reporting purposes.

(f) Represents the average aggregate fair value at vesting of the option awards that were granted to the reported named executive officers and vested during the indicated fiscal year, computed in accordance with the methodology used for financial reporting purposes.

(g) Represents the average aggregate change in fair value, measured from the prior fiscal year-end to the vesting date, of each option award held by the reported named executive officers that was granted in a prior fiscal year and which vested during the indicated fiscal year, computed in accordance with the methodology used for financial reporting purposes.

(h) Represents the average aggregate fair value as of the last day of the prior fiscal year of the reported named executive officers' option awards that were granted in a prior fiscal year and which failed to meet the applicable vesting conditions in the indicated fiscal year, computed in accordance with the methodology used for financial reporting purposes.

(5) Pursuant to rules of the SEC, the comparison assumes $100 was invested on December 31, 2019, in our ordinary shares. Historic share price performance is not necessarily indicative of future share price performance.

(6) The TSR Peer Group consists of the Nasdaq Biotechnology Index, an independently prepared index that includes companies in the biotechnology industry and which is the same industry index disclosed in our Annual Report on Form 10-K.

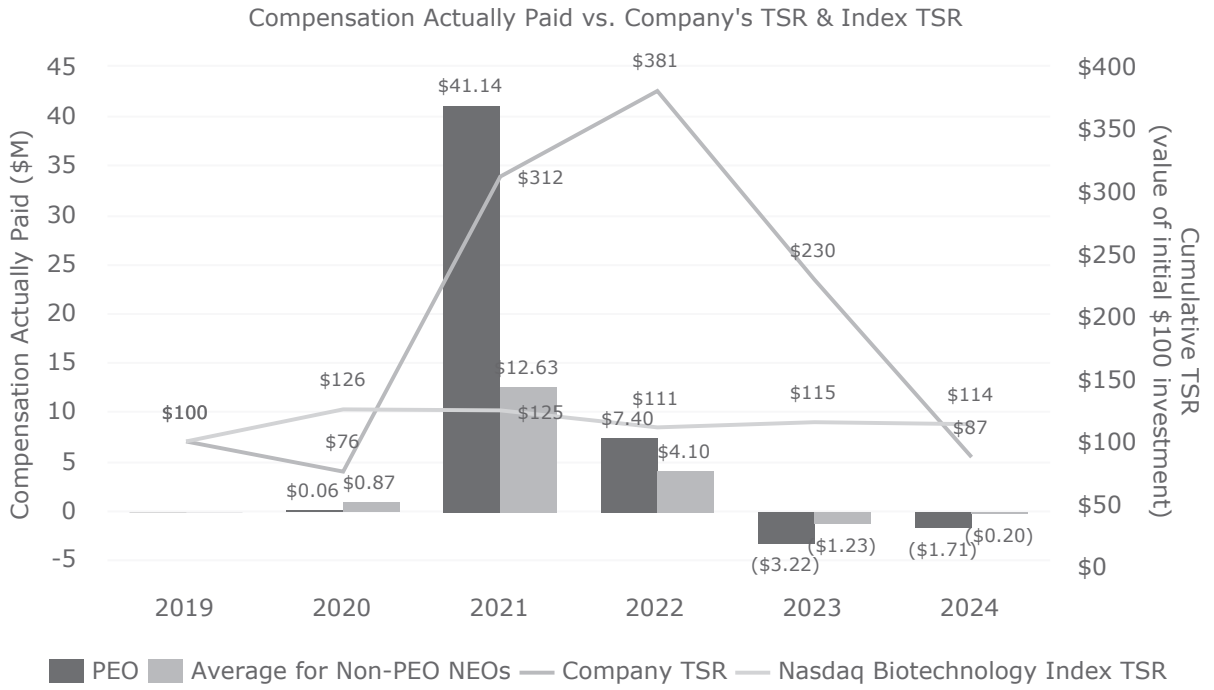
(7) As noted in the Compensation Discussion and Analysis for 2024, the principal incentive elements in the Company's executive compensation program were delivered in the form of annual cash bonuses and equity awards in the form of options. As is the case with many companies in the biotechnology industry, the Company's annual incentive objectives are generally tied to the Company's strategic and operational goals rather than financial goals. In addition, the option awards are structured as time-based awards and are not tied to the achievement of underlying performance goals. Accordingly, the Company does not have a financial metric in its program that it would have as the most important financial measure linking compensation to the Company's financial performance, particularly as the pay versus performance table includes our TSR performance which is linked to the value of the stock options held by our named executive officers.

(8) On May 19, 2020, our shareholders approved a "value-for-value" option exchange program. Pursuant to this program, we offered the option exchange in an issuer tender offer closing on February 12, 2021. Dr. Kinney, Mr. Nguyen, and Ms. Karp received replacement options in the "value-for-value" option exchange program. If those replacement options are excluded from the calculations, the compensation actually paid to Dr. Kinney in 2021 would be $29.4M (a reduction of $11.8M), and the average compensation actually paid to the Non-PEO Named Executive Officers would be $10.1M (a reduction of $2.5M).

Relationship Between Pay and Performance

We believe the compensation actually paid in each of the years reported above and over the five-year cumulative period are reflective of the Compensation Committee's emphasis on "pay-for-performance" as the compensation actually paid fluctuated year-over-year, primarily due to the result of our share performance and our varying levels of achievement against pre-established performance goals under our annual cash bonus opportunities and long-term incentive compensation.

The following graphic illustrates the relationship between the compensation actually paid to the named executive officers and the Company's TSR, as well as the relationship between the Company's TSR and the TSR of the Nasdaq Biotechnology Index, an independently prepared index that includes companies in the biotechnology industry. In addition, as noted above, as is the case with many companies in the biotechnology industry, the Company's annual incentive objectives are generally tied to the Company's strategic and operational goals rather than financial goals. Accordingly, the Company's compensation program is less influenced by metrics such as net income. In fiscal year 2020, our net income was $(111,144,000) as compared to the compensation actually paid of $62,288 for Dr. Kinney and $866,852 for the average of our other named executive officers. In fiscal year 2021, our net income increased to $66,975,000 while the compensation actually paid to Dr. Kinney and the other named executive officers increased to $41,144,072 and $12,625,320, respectively, with the increase in compensation actually paid primarily driven by an increase in our share price and the impact of the option exchange program described above. In fiscal year 2022, our net income decreased to $(116,949,000), while the compensation actually paid for Dr. Kinney and for the other named executive officers decreased to $7,400,610 and $4,104,503, respectively, primarily due to a smaller increase in our share price year-over-year as compared to the increase in our share price from 2020 to 2021. In fiscal year 2023, our net income decreased to $(147,028,000), while the compensation actually paid for Dr. Kinney and for the other named executive officers decreased to $(3,218,100) and $(1,225,533), respectively, primarily due to a decrease in our share price year-over-year. In fiscal year 2024, our net income increased to $(122,310,000), while the compensation actually paid for Dr. Kinney and for the other named executive officers increased to $(1,707,034) and $(204,492), respectively, primarily due to a smaller decrease in our share price year-over-year.



Performance Measures Used to Link Company Performance and Compensation Actually Paid to the Named Executive Officers

As noted above, as is the case with many companies in the biotechnology industry, the Company relies less on financial performance goals as compared to non-financial strategic and operational goals. Below is a list of performance measures, which in the Company's assessment represent the most important performance measures used by the Company to link compensation actually paid to the named executive officers for 2024. Please see the Compensation Discussion and Analysis for further information regarding how each of these measures is used in the Company's executive compensation program.

- Share Price
- Progress R&D Portfolio to Achieve Primary 2024 Milestones
  - For Birtamimab, reach decision re expansion of total enrollment in the AFFIRM-AL clinical trial; achieve an enrollment goal for the AFFIRM-AL clinical trial; execute engagement plan to support enrollment.
  - For PRX012, complete Phase 1 clinical trial through a specified cohort; execute communication plan to support positioning.
  - For PRX019, obtain BMS option exercise and initiate Phase 1 clinical trial.
  - For novel platform, reach development decision based on *in vivo* results; initiate additional activities based on such results.
- Meet Cash Burn Guidance Range and Optimize Shareholder Base
  - Meet publicly-disclosed cash burn guidance range.
  - Optimize shareholder base by: retaining four of top six institutional investors; galvanizing at least one institutional investor (existing or new) to take a $\geq$5% ownership stake; or galvanizing at least five institutional investors (existing or new) to take a $\geq$1% ownership stake.

Policies and Practices Related to the Grant of Certain Equity Awards

It is the Compensation Committee's (or, in the case of Dr. Kinney, the Board's) general practice to approve ordinary course annual equity awards at its regularly scheduled meeting held in February of each year. Following approval by the Compensation Committee or Board, as applicable, all annual equity awards for the fiscal year are made at a fixed, future date specified at the time of approval of the award. As in prior years, the Committee approved annual equity awards to our named executive officers in February

2024 and the Committee (or, in the case of Dr. Kinney, the Board) had the opportunity to consider our expectations and projections for fiscal year 2024. In addition, while we generally grant broad-based equity awards at approximately the same time each year following our release of full-year financial results, we may choose to grant equity awards outside of the annual broad-based awards (e.g., as a new hire, retention, or promotion award). Pursuant to the terms of the 2018 LTIP and the 2020 EIIP, stock options may be granted only with an exercise price at or above the closing market price of an ordinary share on the date of grant.

The Company does not schedule its equity awards in anticipation of the release of material, non-public information ("MNPI"), nor does the Company time the release of MNPI based on equity award grant dates.

In the event MNPI becomes known to the Committee or the Board prior to granting an equity award, the Committee or Board will take the existence of such information into consideration and use its business judgement to determine whether to delay the grant of such equity award. Since 2023, it has been both the Committee's and the Board's practice not to grant stock option awards during any period beginning four business days before the filing or furnishing of a periodic report or current report disclosing MNPI and ending one business day after the filing or furnishing of such a report with the SEC, and no stock options were granted to any of our named executive officers during such period during fiscal year 2024.

EQUITY COMPENSATION PLAN INFORMATION

The following table provides certain information as of December 31, 2024, 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[1]	(c) Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))[2]
Equity Compensation Plans Approved by Shareholders[3]	10,410,127	$28.40	3,877,217
Equity Compensation Plans Not Approved by Shareholders[4]	703,246	$33.06	341,584
Total	11,113,373	$28.70	4,218,801

(1) The weighted-average exercise price does not consider awards that have no exercise price, such as restricted share units.

(2) Represents ordinary shares available for issuance under our 2018 LTIP and our 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.

(3) Column (a) represents the sum of nonqualified stock options and restricted share units outstanding under our 2012 LTIP and our 2018 LTIP, and column (c) represents ordinary shares available for future issuance under our 2018 LTIP.

(4) Column (a) represents nonqualified stock options outstanding under our 2020 EIIP, and column (c) represents ordinary shares available for future issuance under our 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 Transactions (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

There have been no Related Person Transactions to report since January 1, 2024.

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 2024 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 2024 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 2024 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. Tchrakian
Company Secretary
Dublin, Ireland
March 28, 2025

APPENDIX A
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) 13,100,000~~11,100,000~~ 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.

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the year ended December 31, 2024

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from_____to_____

Commission file number: 001-35676

PROTHENA CORPORATION PUBLIC LIMITED COMPANY

(Exact name of registrant as specified in its charter)

Ireland	**98-1111119**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

77 Sir John Rogerson's Quay, Block C
Grand Canal Docklands
Dublin 2, D02 VK60, Ireland
(Address of principal executive offices including Zip Code)

Registrant's telephone number, including area code: 011-353-1-236-2500

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Trading Symbol	Name of Each Exchange on Which Registered
Ordinary Shares, par value $0.01 per share	**PRTA**	**The Nasdaq Global Select Market**

Securities registered pursuant to Section 12(g) of the Act: None

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Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.

Yes ☒ No ☐

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act.

Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files).

Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☐
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

As of June 30, 2024, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the voting shares held by non-affiliates of the registrant was approximately $870.3 million based on the last reported sale of the registrant's ordinary shares on the Nasdaq Global Market on such date.

53,826,982 of the Registrant's ordinary shares, par value $0.01 per share, were outstanding as of February 20, 2025.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's Proxy Statement to be delivered to shareholders in connection with the registrant's Annual General Meeting of Shareholders to be held on May 13, 2025, are incorporated by reference into Part III of this Form 10-K. The registrant intends to file its Proxy Statement within 120 days after its fiscal year ended December 31, 2024.

PROTHENA CORPORATION PLC
Annual Report on Form 10-K
For the Year Ended December 31, 2023

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Unless the context requires otherwise, references in this Form 10-K to "Prothena," the "Company," "we," "our," or "us" refer to Prothena Corporation plc and its subsidiaries.

Note Regarding Forward-Looking Statements

In addition to historical information, this Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements may include words such as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "due," "estimate," "expect," "goal," "intend," "may," "objective" "plan," "predict," "potential," "positioned," "seek," "should," "target," "will," "would," and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. In addition, any statements that refer to expectations, projections, or other characterizations of future events or circumstances are forward-looking statements.

These forward-looking statements, which reflect our beliefs, assumptions, expectations, estimates, forecasts, and projections about our business and the industry in which we operated as of the date hereof, are estimates based on our best judgment. These statements relate to, among other things, our goal to continue building a biology-directed discovery engine targeting protein dysregulation; the treatment potential, designs, proposed mechanisms of action, and potential administration of our drug candidates; potential indications and attributes of epitopes and antibodies we have identified in our programs; plans for ongoing and future clinical trials of our drug candidates; our potential to advance, initiate, and complete investigational new drug ("IND") enabling studies for our discovery and preclinical programs; the expected timing of reporting data from clinical trials of our drug candidates, including topline study results for our Phase 3 AFFIRM-AL clinical trial in the second quarter of 2025 and multiple clinical readouts starting in mid-2025 and continuing throughout the year from our Phase 1 clinical trial evaluating PRX012; our collaborations with F. Hoffman-La Roche Ltd and Hoffmann-La Roche Inc. (together "Roche"), Bristol Myers Squibb Company ("BMS"), and Novo Nordisk, and amounts we may receive under such collaborations; the sufficiency of our cash position to fund advancement of a broad pipeline and completion of our ongoing clinical trials; and our anticipated need for additional capital.

These forward-looking statements are not guarantees of future performance or development and involve known and unknown risks, uncertainties, and other factors that are in some cases beyond our control. As a result, any or all of our forward-looking statements in this Annual Report on Form 10-K may turn out to be inaccurate. Factors that could cause our actual results to differ materially include, but are not limited to, the risks and uncertainties set forth below, those discussed under Item 1A "Risk Factors" of this Annual Report on Form 10-K, and in our other filings with the U.S. Securities and Exchange Commission.

Except as required by law or by the rules and regulations of the U.S. Securities and Exchange Commission, we undertake no obligation to revise or update any forward-looking statements to reflect any event or circumstance that arises after the date of this Annual Report on Form 10-K, including without limitation:

- our ability to obtain additional financing in future offerings and/or obtain funding from future collaborations;
- our operating losses;
- our ability to successfully complete research and development of our drug candidates;
- our ability to develop, manufacture and commercialize products;
- our collaborations and other agreements with third parties, including Roche, BMS, and Novo Nordisk;
- our ability to protect our patents and other intellectual property;
- our ability to hire and retain key employees;
- our ability to maintain financial flexibility and sufficient cash, cash equivalents and investments and other assets capable of being monetized to meet our liquidity requirements;
- the timing, receipt, and amount of any capital investments, cost-sharing contributions or reimbursements, milestone payments, or royalties that we might receive under current or potential future collaborations, including any milestone payments pursuant to our agreement with Novo Nordisk;
- potential disruptions in the U.S. and global capital and credit markets, including by geopolitical conflicts and pandemics;
- government regulation of our industry;
- the volatility of the market price of our ordinary shares; and
- business disruptions.

Summary of Risks Affecting Our Business

Our business is subject to numerous risks and uncertainties. The following summary highlights some of the risks you should consider with respect to our business and prospects. These risks are described more fully in Item 1A "Risk Factors" of this Annual Report on Form 10-K which includes a more complete discussion of the risks summarized below as well as a discussion of other risks related to our business, our prospects, and your investment.

- We anticipate that we will incur losses for the foreseeable future and we may never sustain profitability.
- We will require additional capital to fund our operations, and if we are unable to obtain such capital, we will be unable to successfully develop and commercialize drug candidates.
- Our success is largely dependent on the success of our research and development programs; our drug candidates are in various stages of development and we may not be able to successfully discover, develop, obtain regulatory approval for, or commercialize any drug candidates.
- We have entered into agreements to develop and bring to market drug candidates with Roche, BMS, and Novo Nordisk and may enter into additional agreements in the future, and we might not realize the anticipated benefits of such agreements including receiving anticipated milestone payments pursuant to these agreements.
- If clinical trials of our drug candidates are prolonged, delayed, suspended, or terminated, we may be unable to commercialize our drug candidates on a timely basis, which would require us to incur additional costs and delay our receipt of any revenue from potential product sales.
- Even if any of our drug candidates receives regulatory approval, if such approved product does not achieve broad market acceptance, the revenues that we generate from sales of the product will be limited.
- If we are unable to adequately protect or enforce the intellectual property relating to our drug candidates our ability to successfully commercialize our drug candidates will be harmed.
- Our future success depends on our ability to retain key personnel and to attract, retain, and motivate qualified personnel.

PART I

ITEM 1. BUSINESS

Overview

Prothena Corporation plc ("Prothena" or the "Company") is 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 neurodegenerative and rare peripheral amyloid diseases.

Fueled by our deep scientific expertise built over decades of research, we are advancing a pipeline of therapeutic candidates for a number of indications and novel targets for which our ability to integrate scientific insights around neurological dysfunction and the biology of misfolded proteins can be leveraged. Our wholly-owned programs include birtamimab for the potential treatment of AL amyloidosis, and a portfolio of programs for the potential treatment of Alzheimer's disease including PRX012, which targets amyloid beta (Aβ), and PRX123, a novel dual Aβ-tau vaccine. Our partnered programs include prasinezumab for the potential treatment of Parkinson's disease and other related synucleinopathies that targets alpha-synuclein in collaboration with Roche. In addition, we have partnered BMS-986446 (formerly PRX005) for the potential treatment of Alzheimer's disease that targets tau and PRX019 for the potential treatment of neurodegenerative diseases with an undisclosed target in two separate license agreements with Bristol Myers Squibb (BMS). We are also entitled to certain potential milestone payments pursuant to the Company's share purchase agreement with Novo Nordisk pertaining to the Company's ATTR amyloidosis business (inclusive of coramitug, formerly PRX004).

We were formed on September 26, 2012, under the laws of Ireland and re-registered as an Irish public limited company on October 25, 2012. Our ordinary shares began trading on The Nasdaq Global Market under the symbol "PRTA" on December 21, 2012, and currently trade on The Nasdaq Global Select Market.

Our Strategy

Our goal is to be a leading biotechnology company focused on the discovery and development of novel therapies to treat diseases caused by protein dysregulation.

Under certain pathological conditions, the process by which proteins fold into specific conformations to carry out their intended biological activities becomes dysregulated. When this happens, proteins misfold and propagate many diseases that are not adequately addressed by current therapies. Proteins that misfold and aggregate to form amyloid are associated with a multitude of common and rare human diseases that can gravely damage vital organs. Amyloid can affect any organ in the body. Our pipeline reflects our deep understanding of the contribution of these toxic proteins to the cause and progression of disease. For example, the misfolding and aggregation of the amyloid beta (Aβ) protein leads to a build-up of amyloid in the brain, which scientists believe is the primary cause of Alzheimer's disease. Parkinson's disease is characterized by neuronal dysfunction and loss caused by the cell-to-cell spreading of toxic forms of aggregated alpha-synuclein protein. Transthyretin amyloidosis (ATTR amyloidosis), and AL amyloidosis are rare, progressive and fatal diseases, characterized by deposition of aggregated misfolded transthyretin and light chain proteins, respectively, in vital organs such as the heart.

We leverage pioneering protein dysregulation science to develop novel therapeutic solutions that directly target pathogenic proteins in order to change the course of devastating neurodegenerative and rare peripheral amyloid diseases. We are advancing a broad pipeline of therapies with novel mechanisms of action that are uniquely suited to address unmet medical needs in targeted patient populations.

Our plan is to become a fully integrated research, development, and commercial biotechnology company. We are currently conducting the registration-enabling confirmatory Phase 3 AFFIRM-AL clinical trial evaluating birtamimab in Mayo Stage IV patients with AL amyloidosis being conducted under a Special Protocol Assessment (SPA) agreement with FDA with significance level of $p \leq 0.10$., In December 2024, our partner Roche announced topline results from the Phase 2b PADOVA clinical trial of prasinezumab in patients with early Parkinson's disease. Roche is further evaluating the data and will work together with health authorities to determine next steps. In addition, there is an early Phase 2 clinical trial ongoing evaluating coramitug (formerly PRX004) in patients with ATTR cardiomyopathy being conducted by Novo Nordisk. In addition, we are advancing a robust portfolio of Alzheimer's disease programs designed to target the underlying disease pathology. These programs include PRX012, an anti-Aβ antibody designed to be best-in-class and dosed single-injection once-monthly subcutaneously currently in the ongoing Phase 1 ASCENT clinical trials; BMS-986446 (formerly PRX005), an investigational antibody that specifically targets a key epitope within the microtubule binding region (MTBR) of tau, and a potential best-in-class treatment, currently in an ongoing Phase 2 clinical trial being conducted by our partner BMS; and PRX123, a dual Aβ-tau

vaccine for the treatment and prevention of Alzheimer's disease. We also recently initiated a Phase 1 clinical trial for PRX-019, a potential treatment of neurodegenerative diseases in development in collaboration with BMS.

Key elements of our strategy to achieve our goal are to:

- ***Concentrate our discovery and development efforts in areas where we have decades of scientific expertise and experience.***

We leverage our core scientific expertise and proven protein dysregulation platform to develop novel therapeutics for the potential treatment of neurodegenerative and rare peripheral amyloid diseases.

Our pipeline is advanced by a team with scientific expertise and a track record of discovering and developing innovative, and often first-in-class programs. Our legacy includes fundamental discoveries in the understanding of Alzheimer's disease biology including identifying and elucidating the role Aβ plays in Alzheimer's disease pathology and discovering the biological cause of amyloid related imaging abnormalities ("ARIA"). These findings led to the development of a drug discovery and development organization that generated first-in-class clinical candidates in Alzheimer's disease, Parkinson's disease, and AL and ATTR amyloidosis.

Key elements of our biology-directed discovery engine include:

- A focus on pathophysiology-directed targeting focused on targeting proteins with the greatest effect on disease;
- Expert epitope mapping with deep expertise in determining optimal epitopes to be targeted for maximal efficacy; and
- Disease driven antibody engineering for therapeutics engineered to optimally eliminate pathogenic proteins while preserving normal biology.

Once we formulate a novel hypothesis or approach, we determine how to optimally intervene against a known target. We employ a combination of our understanding of normal protein structure, computational antibody design technologies, and an empirical and unbiased screening process to determine the optimal epitope to target on a pathogenic protein. Through our detailed screening process, we attempt to define critical regions of the protein involved in the pathological progression of a particular disease to elucidate key epitopes that are hidden when a protein is normally folded but exposed when a protein misfolds and remains exposed in all of its pathogenic aggregation states, inclusive of deposited amyloid. We engineer our molecules to interact with that epitope in a way that is most likely to intercept or halt the underlying disease process. We do this by designing molecules with a bias toward the pathogenic forms of the protein. We then develop a multitude of antibodies against the target, characterize specific and selective antibodies in vitro, and then use them to test the initial hypothesis in vivo using animal models of disease, assuming such models exist or can be successfully developed. We often rely on the use of preclinical models that have been extensively developed to establish early proof of concept for our programs. We leverage our insight of disease pathology and, when possible, employ biomarker endpoints as a way to detect signals of biological activity. We may elect to start clinical testing in indications that have well-established endpoints in order to demonstrate proof of concept as a basis for further investment in clinical trials, either by us or by potential partners.

Our biology-directed engine aims to produce molecules that specifically and selectively target the toxic, or pathogenic, protein species in order to alleviate their detrimental effects, while - to the furthest extent possible - leaving the native, or healthy, form of the protein unaffected.

We have employed our discovery engine to optimally target key epitopes on misfolded proteins including Aβ, tau, alpha-synuclein, light chain, and transthyretin to relevantly influence biology and achieve clinical benefit across a number of indications.

As a result of decades of our own investigation augmented by the work of others have elucidated that targeting the appropriate epitope, with the optimal binding strength (affinity) in the context of the right clinical design with appropriate endpoints in the right patient population, can result in meaningful clinical benefit. Our track record of combining these elements to discover and develop novel therapeutic candidates has resulted in a robust pipeline advancing multiple late-stage programs.

Today, one of the elements that distinguishes Prothena is that our pipeline has matured beyond demonstrating target engagement via downstream biomarkers. Instead, our internally discovered pipeline has generated multiple proof points that our molecules have successfully influenced biology in a manner that translates into clinical benefit. We've most recently

demonstrated this in AL amyloidosis, ATTR amyloidosis, and Parkinson's disease where preclinical findings in our programs have translated to positive clinical data.

- ***Focus on diseases that lack effective therapies.***

We focus on the development of therapies for serious and/or life-threatening diseases that currently lack effective therapies or in areas where current therapies have known limitations. Our efforts in AL amyloidosis, ATTR amyloidosis, Parkinson's disease, Alzheimer's disease, and other neurological or peripheral amyloid diseases are examples of this.

In Parkinson's disease, currently approved therapies focus on the alleviation of early motor symptoms without addressing the underlying cause of the disease. We are focusing our efforts to develop a therapeutic with the potential to slow the progression of Parkinson's disease by targeting α-synuclein protein. Synucleins are a family of proteins, of which there are three known members: α-synuclein, β-synuclein, and γ-synuclein. The α- and β-synuclein proteins are found primarily in brain tissue. There is genetic evidence that α-synuclein plays a fundamental role in Parkinson's disease, and an increasing body of evidence demonstrates that pathogenic forms of α-synuclein can be propagated and transmitted from cell to cell. Our scientists have developed prasinezumab, an investigational monoclonal antibody targeting the pathogenic aggregated form of α-synuclein, that is designed to slow or reduce the neurodegeneration associated with α-synuclein misfolding and/or its transmission. We are developing prasinezumab, in collaboration with Roche, for the potential treatment of Parkinson's disease and other related synucleinopathies.

AL amyloidosis and ATTR amyloidosis are diseases caused by misfolded, pathogenic forms of light chain (AL) or transthyretin (ATTR) protein that deposit as amyloid in vital organs such as the heart. Current therapeutic approaches seek to reduce the production of new pathogenic AL or ATTR protein in order to slow the formation of new amyloid deposits. However, simply reducing new pathogenic protein production may not be adequate for patients who are at high risk of early mortality due to the substantial existing amyloid deposition in their vital organs. The therapeutic approaches we are developing with birtamimab for AL amyloidosis and coramitug (formerly PRX004) for ATTR amyloidosis, are investigational monoclonal antibodies designed to clear the pathogenic amyloid deposits. Birtamimab and coramitug are designed to target and clear amyloid deposited in organs in order to improve organ function. Current therapies do not adequately address the needs of patients with AL and ATTR amyloidosis who have advanced stages of cardiac disease due to amyloid deposition. Improving survival for these patients is an area of urgent need which directly aligns with birtamimab and coramitug's differentiated depleter mechanism that targets the amyloid that causes organ dysfunction and failure and puts patients at risk for early mortality.

Moving forward, we intend to advance new discovery-stage therapeutics for other diseases of protein dysregulation with unmet medical needs.

- ***Pursue strategic business development opportunities and collaborations and leverage external resources.***

We capitalize on a foundation of internal discovery efforts augmented by collaborations with academic and industry partners and business development activities to build upon our internally generated pipeline.

Our robust discovery engine generates new targets and compounds that have the potential to treat unmet medical needs. For investigational therapeutic programs targeting broad patient populations that may require large clinical trials and development investment, we may seek to collaborate or license these programs to pharmaceutical or biotechnology companies for development and/or commercialization. Our collaboration with Roche to develop prasinezumab for the potential treatment of Parkinson's disease and other related synucleinopathies and our global neuroscience R&D collaboration with BMS focused on three proteins implicated in the pathogenesis of several neurodegenerative diseases are examples of this, as is the acquisition of our ATTR amyloidosis business by Novo Nordisk. Within these types of collaborations, we will evaluate several strategic options for designing and operationalizing early to late-stage development programs. This includes evaluating the option of designing and operationalizing clinical programs ourselves or with a partner.

We also consider opportunities to acquire or license rights or invest in differentiated product candidates or technologies to complement our existing R&D pipeline.

We rely on, and will expand as appropriate, strong internal talent with expertise in our core areas of focus. We also rely on external resources, as needed, to execute efficiently on our clinical development and other business objectives. We engage and collaborate with consultants and advisors with certain scientific, clinical or other functional and/or disease area expertise to

help us execute specific activities related to our programs. This may include activities such as testing and characterizing our potential therapeutic candidates and gaining feedback and guidance on our programs through advisory boards.

- ***Pursue commercialization strategies to maximize the value of our product candidates or future potential products.***

As we move our drug candidates through development toward regulatory approval, we will evaluate several strategic options for commercialization. These options include building our own internal sales force; forging partnerships with other pharmaceutical or biotechnology companies, to jointly sell and market the product; pursuing regional licensing agreements in markets where we do not have expertise or infrastructure; and out-licensing or selling the product, whereby another pharmaceutical or biotechnology company sells and markets the product and pays us a royalty on sales. We evaluate options for each product based on a number of factors including commercial synergies and expertise, capital necessary to execute on each option, size of the market to be addressed, and the expertise and terms of potential offers from other pharmaceutical and biotechnology companies. Our collaboration with Roche for the potential commercialization of prasinezumab is an example of this strategy, as is the acquisition of our ATTR amyloidosis business by Novo Nordisk.

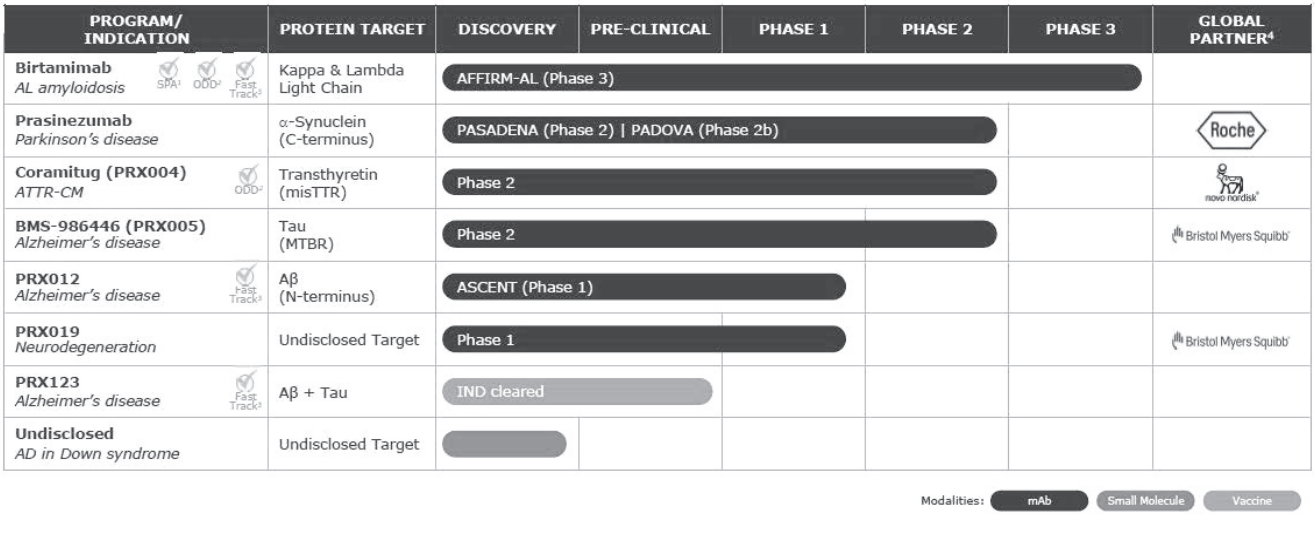
Our Research and Development Pipeline

Our clinical research and development pipeline includes six therapeutic antibody programs currently in clinical development: birtamimab for the potential treatment of AL amyloidosis; prasinezumab, in collaboration with Roche, for the potential treatment of Parkinson's disease and other related synucleinopathies; coramitug, which is being developed by Novo Nordisk, for the potential treatment of ATTR amyloidosis; PRX012 for the potential treatment of Alzheimer's disease; and BMS-986446 and PRX019, in collaboration with BMS, for the potential treatment of Alzheimer's disease and neurodegenerative diseases respectively.

In addition to our clinical development pipeline, we have recently received clearance by the FDA for an investigational new drug (IND) application for PRX123. PRX123 is our Alzheimer's disease vaccine program and was also granted Fast Track designation from the FDA. We also have a number of discovery- and late-preclinical-stage programs targeting proteins implicated in neurological diseases.

While we are modality agnostic, we have deep expertise in antibody targeting and have developed a diverse pipeline that includes antibody as well as small molecule and vaccine approaches. We believe a diverse portfolio positions us to make an impact on a broad spectrum of diseases and we may also pursue opportunities in other modalities such as gene and cell therapies.

The following table summarizes the status of our research and development pipeline:



Aβ, Abeta; AD, Alzheimer's disease; mAb, monoclonal antibody.
[1] Primary endpoint of all-cause mortality at p≤0.10 under the Special Protocol Assessment (SPA) agreement with FDA; [2] Orphan Drug Designation granted by FDA & EMA; [3] FDA Fast Track designation;
[4] In July 2021 Novo Nordisk acquired coramitug (formerly PRX004) and broader ATTR amyloidosis program and gained full worldwide rights. Prothena is eligible to receive up to $1.23 billion in total consideration

Birtamimab for the Potential Treatment of AL Amyloidosis

About Birtamimab and AL Amyloidosis

Birtamimab is an investigational humanized antibody that targets toxic misfolded light chain that causes organ dysfunction and failure in patients with AL amyloidosis. AL amyloidosis is a rare, progressive, and typically fatal disease where immunoglobulin light chain proteins produced by clonal plasma cells misfold, aggregate, and deposit as amyloid in vital organs. These toxic aggregates and amyloid deposits cause progressive damage and failure of vital organs, including the heart.

Birtamimab binds to both soluble and insoluble amyloid aggregates in multiple organs and promotes the clearance of amyloid deposits via phagocytosis. This anti-amyloid mechanism of action broadly targets misfolded kappa and lambda light chain to clear deposited amyloid that causes organ dysfunction and failure in patients with AL amyloidosis. Birtamimab is the only investigational therapeutic that has demonstrated a significant survival benefit in a randomized clinical trial in patients with Mayo Stage IV AL amyloidosis. Birtamimab has been granted Fast Track Designation by the U.S. Food and Drug Administration (FDA) for the treatment of Mayo Stage IV patients with AL amyloidosis to reduce the risk of mortality and has been granted Orphan Drug Designation by both the FDA and European Medicines Agency (EMA).

It is estimated that 200,000 to 400,000 patients globally suffer from this rare disease, with approximately 60,000 to 120,000 (or 30%) of those patients being categorized as Mayo Stage IV. Patients categorized at diagnosis as Mayo Stage IV have poor outcomes with current standard-of-care that aims to reduce the production of new protein but does not directly target and clear the toxic amyloid that deposits in organs. There are currently no approved treatments for AL amyloidosis that have demonstrated a survival benefit in a randomized clinical trial, and there is an urgent unmet medical need for therapies that improve survival in patients at risk for early mortality due to amyloid deposition.

Clinical Development Program for Birtamimab

Birtamimab reacts with a “cryptic” epitope that is exposed on misfolded kappa and lambda light chains that misfold and form amyloid. The epitope is well defined and highly conserved in light chains and exposed from early stages of aggregation throughout amyloid. Preclinical research has demonstrated that birtamimab binds to both soluble and insoluble aggregated kappa and lambda immunoglobulin light chain by recognizing this epitope that is exposed at the earliest stages of abnormal light chain misfolding and through aggregation of deposited amyloid. Our extensive preclinical findings and publications describe two proposed mechanisms of action for birtamimab: binding and neutralization of soluble toxic light chain aggregates, and clearance of amyloid deposits by phagocytosis.

In multiple clinical trials, birtamimab has been shown to be generally safe and well tolerated and has been evaluated in 302 patients receiving monthly intravenous infusions (including 294 patients who received the recommended 24 mg/kg dose), for an average of approximately 15 months.

Confirmatory Phase 3 AFFIRM-AL Clinical Trial Design under SPA Agreement with FDA

Based on further analyses of data from the VITAL clinical trial and multiple in-depth discussions with the FDA, Prothena announced plans in February 2021, to advance birtamimab into the confirmatory Phase 3 AFFIRM-AL clinical trial in patients with Mayo Stage IV AL amyloidosis. AFFIRM-AL is a registration-enabling Phase 3 clinical trial that is being conducted with a primary endpoint of time to all-cause mortality at $p \leq 0.10$ under a Special Protocol Assessment (SPA) agreement with the FDA. Patient enrollment is on track in the AFFIRM-AL trial and topline trial results are expected in the second quarter of 2025.

AFFIRM-AL is an ongoing global, multi-center, double-blind, placebo-controlled, 2:1 randomized, time-to-event trial expected to enroll up to 220 newly diagnosed, treatment naïve patients with AL amyloidosis categorized as Mayo Stage IV. Patients receive 24 mg/kg of birtamimab or placebo by intravenous infusion every 28 days, with all patients receiving concurrent standard of care chemotherapy in accordance with the institutional standard of care which includes a bortezomib-containing chemotherapy regimen such as cyclophosphamide, bortezomib, and dexamethasone (CyBorD). The initiation of daratumumab treatment at randomization is allowed at the discretion of the investigator. The trial has been designed to evaluate the primary endpoint of time to all-cause mortality with a significance level of $p \leq 0.10$. Secondary endpoints will assess change from baseline to month 9 in functional capacity as measured by 6MWT distance and quality of life as measured by SF-36v2 PCS.

Phase 3 VITAL Clinical Trial Results

In June 2023, we announced that results from the Phase 3 VITAL clinical trial were published in *Blood*, a journal of the American Society of Hematology ("ASH"). The published data demonstrate that in a post hoc analysis of patients with Mayo Stage IV AL amyloidosis, a statistically significant survival benefit of 74 percent was observed for those treated with birtamimab plus standard of care ("SOC") versus 49 percent in patients on placebo plus SOC at 9 months (HR 0.413, p=0.021).

The article, entitled "Birtamimab plus standard of care in light chain amyloidosis: the phase 3 randomized placebo-controlled VITAL clinical trial", also demonstrated that patients with Mayo Stage IV AL amyloidosis treated with birtamimab had statistically significant improvements over placebo in a post hoc assessment of two key secondary endpoints, quality of life (assessed with the Short Form-36 version 2 physical component score, SF-36v2 PCS) and cardiac function (assessed with the 6-minute walk test). Patients treated with birtamimab showed a slower decline in quality of life with a mean decrease of 0.75 in the SF-36v2 PCS at 9 months compared to a mean decrease of 5.40 in the SF-36v2 PCS for patients on placebo at 9 months (a mean difference of 4.65 favoring birtamimab; p=0.046). Patients treated with birtamimab after 9 months demonstrated an increase in mean distance of 15.22 meters in the 6-minute walk test, compared to a decrease in mean distance of 21.15 meters for patients on placebo (a mean difference of 36.37 meters favoring birtamimab; p=0.022).

Prasinezumab for the Potential Treatment of Parkinson's Disease and Other Synucleinopathies

Prasinezumab is an investigational humanized monoclonal antibody that targets alpha-synuclein, a protein found in neurons that can aggregate and spread from cell to cell, resulting in the neuronal dysfunction and loss that causes Parkinson's disease and other synucleinopathies. Prasinezumab is the focus of our worldwide collaboration with Roche.

The protein α-synuclein is found extensively in neurons and is a major component of pathological inclusions that characterize several neurodegenerative disorders, including Parkinson's disease, dementia with Lewy bodies, and multiple system atrophy, which collectively are termed synucleinopathies. While the normal function of α-synuclein is not well understood, the protein normally occurs in a soluble form. In synucleinopathies, the α-synuclein protein can misfold and aggregate to form soluble aggregates and insoluble fibrils that contribute to the pathology of the disease.

There is genetic evidence for a causal role of α-synuclein in Parkinson's disease. In rare cases of familial forms of Parkinson's disease, there are mutations in the synuclein protein sequence, or duplication and triplications of the relevant gene leading to overproduction of α-synuclein, which may cause α-synuclein protein to aggregate and form amyloid-like fibrils that contribute to the disease. There is also increasing evidence that this disease-causing α-synuclein can be propagated and transmitted from neuron to neuron, resulting in a spreading of neuronal death. Recent studies in cellular and animal models suggest that the spread of α-synuclein-associated neurodegeneration can be disrupted by targeting aberrant forms of α-synuclein.

Parkinson's disease is a progressive degenerative disorder of the central nervous system ("CNS") that affects approximately one in 100 people over the age of 60, with incidence increasing based on an aging population. With an estimated 10 million people living with Parkinson's disease worldwide today, it is the most common neurodegenerative movement disorder and fastest growing neurological disorder. The disease is characterized by the neuronal accumulation of aggregated α-synuclein in the CNS and peripheral nervous system that results in a wide spectrum of worsening progressive motor and non-motor symptoms. While diagnosis currently relies on motor symptoms classically associated with Parkinson's disease, non-motor symptoms may present many years earlier. Current treatments for Parkinson's disease are symptomatic and only address a subset of symptoms such as motor impairment, dementia or psychosis. Symptomatic therapies do not target the underlying cause of the disease and as the disease progresses and dopaminergic neurons continue to be lost, these drugs lose effectiveness, often leading to debilitating side effects as the disease progresses. There are currently no treatments available that target the underlying cause of the disease. Prasinezumab is designed to block the cell-to-cell transmission of the aggregated, pathogenic forms of alpha-synuclein in Parkinson's disease, thereby slowing clinical decline. The goal of our approach is to slow the progressive neurodegenerative consequences of disease, a current unmet need.

Clinical Development Program for Prasinezumab

Phase 2b PADOVA Clinical Trial

In December 2024, topline results were announced from the Phase 2b clinical trial (PADOVA) conducted by partner Roche investigating prasinezumab in 586 people with early-stage Parkinson's disease, treated for a minimum of 18 months while on stable symptomatic treatment. Prasinezumab showed potential clinical effect in the primary endpoint of time to confirmed motor progression, as assessed by ≥5 point increase in Movement Disorder Society – Unified Parkinson's Disease

Rating Scale ("MDS-UPDRS") Part III score from baseline, with a HR=0.84 [0.69-1.01] and p=0.0657. The effect of prasinezumab was more pronounced in a pre-specified analysis in the population treated with levodopa (75% of participants), HR=0.79 [0.63-0.99] and nominal p=0.0431. Pre-specified supplementary covariate-adjusted analyses of these endpoints demonstrated nominally significant effects on the primary endpoint (HR=0.81 [0.67-0.98]; nominal p=0.0334) and in the levodopa subgroup (HR=0.76 [0.61-0.95]; nominal p=0.0175). Covariates used for adjustment: medication at baseline, H&Y stage, DaT-SPECT, age, sex, baseline dependent parameter. Consistent positive trends across multiple secondary and exploratory endpoints were also observed. Prasinezumab continues to be well tolerated and no new safety signals were observed in the study.

Prasinezumab is the first anti-alpha synuclein antibody to advance into late-stage development. In March 2022, results from the analysis of part 2 of the Phase 2 PASADENA trial of prasinezumab were presented in an oral presentation by Roche at the International Conference on Alzheimer's and Parkinson's Diseases ("AD/PD 2022"). Results showed that participants with Parkinson's disease who were treated with prasinezumab for two years (early-start group) showed slower decline of MDS-UPDRS Part III scores relative to participants treated with placebo in the first year and prasinezumab in the second year (delayed-start group), further supporting a potential effect on delaying motor progression in patients. In October 2024, Roche published results in *Nature Medicine* from the long term open-label extension of the PASADENA trial, which compared the prasinezumab population with a propensity score-balanced cohort of real-world data ("RWD") Parkinson's Progression Markers Initiative ("PPMI"). The data suggests that prasinezumab continued to show reduced motor and functional progression in prazinezumab-treated individuals with early-stage Parkinson's disease compared to a real-world data arm on MDS-UPDRS Part III score (clinician rated motor examination) OFF and ON symptomatic medication state and MDS-UPDRS Part II score (patient-reported motor experiences of daily living). The Phase 2 PASADENA and Phase 2b PADOVA open-label extension studies will continue in order to further explore the observed effects in both studies. Roche will continue to evaluate the data and work together with health authorities to determine next steps.

Phase 2 PASADENA Clinical Trial

The results from the Phase 1 clinical trial further supported advancing prasinezumab into the Phase 2 PASADENA clinical trial. PASADENA was a two-part Phase 2 clinical trial in early Parkinson's disease patients conducted by Roche. Part 1 was a randomized, double-blind, placebo-controlled, three-arm trial and enrolled 316 patients to evaluate the efficacy and safety of prasinezumab in patients over 52 weeks. In part 1, patients were randomized on a 1:1:1 basis to receive one of two active doses (1500 mg or depending on body weight either 3500 mg or 4500 mg) of prasinezumab or placebo via intravenous infusion once every 4 weeks. Patients enrolled in the trial must not have been on dopaminergic therapy and were not expected to require dopaminergic therapy for at least 52 weeks. Part 2 of the trial was a 52-week blinded extension phase in which patients from the placebo arm of the trial were re-randomized onto one of two active doses on a 1:1 basis, so that all participants were on active treatment. Patients who were originally randomized to an active dose will continue at that dose level for the additional 52 weeks. In part 2, patients were allowed to use concomitant dopaminergic therapy. Any patient who medically required initiation of dopaminergic therapy during part 1 had their subsequent data censored for the primary endpoint analysis.

Results from Part 1 of the PASADENA clinical trial were presented in a Top Abstract oral presentation at the International Parkinson and Movement Disorder Society's MDS Virtual Conference 2020. While the trial did not meet the primary objective, signals of efficacy on multiple pre-specified secondary and exploratory clinical endpoints, including measures of motor function and biomarkers, were demonstrated in both of the prasinezumab arms when compared to placebo. In PASADENA, prasinezumab significantly reduced decline in motor function by 35% (pooled dose levels) vs. placebo after one year of treatment on the centrally rated assessment of Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III, a clinical examination of motor function. Motor symptoms associated with Parkinson's disease include slowness of movement (bradykinesia), tremor, rigidity, and gait. Prasinezumab-treated patients also demonstrated a significant delay in time to clinically meaningful worsening of motor progression on the site rated assessment of time to at least a 5-point progression on MDS-UPDRS Part III vs. placebo over one year, with a hazard ratio of 0.82 (pooled dose levels). The trial was designed with 80% power and a one-sided alpha of 0.10 to detect a 37.5% relative between group reduction from baseline to week 52.

The primary endpoint of the trial was the change from baseline in the MDS-UPDRS total score (Parts I, II and III) at 52 weeks in each treatment group vs. the placebo group (pooled dose levels: –14.0%, –1.30, 80% CI=(–3.18, 0.58), p=0.38; low dose level: –21.5%, –2.02, 80% CI=(–4.21, 0.18); and high dose level: –6.6%, –0.62, 80% CI=(–2.82, 1.58)). Signals of efficacy were observed on multiple pre-specified secondary and exploratory clinical endpoints including change from baseline in MDS-UPDRS Part III in prasinezumab-treated patients vs. placebo at 52 weeks by central rating (pooled dose levels: –35.0%, –1.88, 80% CI=(–3.31, –0.45), p=0.09; low dose level: –45.4%, –2.44, 80% CI=(–4.09, –0.78); and high dose level: –24.7%, –1.33, 80% CI=(–2.99, 0.34)) and by site rating (pooled dose levels: –25.0%, –1.44, 80% CI=(–2.83, –0.06), p=0.18; low dose level: –33.8%, –1.88, 80% CI=(–3.49, –0.27); and high dose level: –18.2%, –1.02, 80% CI=(–2.64, 0.61)). MDS-

UPDRS Part III is a clinical examination of motor function that assesses motor symptoms associated with Parkinson's disease. Prasinezumab also delayed time to clinically meaningful worsening of motor progression in prasinezumab-treated patients vs. placebo over 52 weeks as demonstrated by site rating of time to at least a 5-point progression in MDS-UPDRS Part III (pooled dose levels: HR=0.82, 80% CI=0.64 to 0.99, p=0.17; low dose level: HR=0.77, 80% CI=0.63 to 0.96; and high dose level: HR=0.87, CI=0.70 to 1.07).

Additional signals of efficacy on bradykinesia and, separately, a digital motor score developed by Roche using a novel smartphone technology further extended the results shown on MDS-UPDRS Part III.

In an analysis of cerebral blood flow, assessed by changes in magnetic resonance-arterial spin labeling (MRI-ASL) in a subset of patients, prasinezumab-treated patients showed improvement in cerebral blood flow in the putamen, an area of the brain associated with the loss of dopaminergic terminals and presence of alpha-synuclein pathology in Parkinson's disease, suggesting an impact on the underlying biology implicated in disease progression.

Prasinezumab was found to be generally safe and well tolerated, with the majority of adverse events reported as mild or moderate and similar across placebo and both treatment arms.

Phase 1 Clinical Trials

During 2014, together with Roche, we advanced prasinezumab into clinical development with the initiation of two Phase 1 clinical trials. Results of the first trial, a Phase 1 double-blind, placebo-controlled, single ascending dose trial demonstrated that prasinezumab was safe and well-tolerated in healthy volunteers, meeting the primary objective of the trial. Results of the second trial, a Phase 1b double-blind, placebo-controlled, multiple ascending dose trial demonstrated an acceptable safety and tolerability profile at all dose levels tested in patients with Parkinson's disease, meeting the primary objective of the trial. CNS penetration was demonstrated by a dose-dependent increase in prasinezumab levels in cerebrospinal fluid (CSF), and a mean concentration of prasinezumab in CSF of 0.3% relative to serum across all dose levels, which exceeded our expectations based on our preclinical experience. Data from the trial also demonstrated rapid, dose- and time-dependent mean reduction in levels of free serum α-synuclein of up to 97% after a single dose, which were statistically significant ($p<0.0001$), and maintained following two additional monthly doses.

In June 2018, we published results from the Phase 1b multiple ascending dose trial of prasinezumab in patients with Parkinson's disease in *JAMA Neurology*. The paper is entitled "Safety and Tolerability of Multiple Ascending Doses of PRX002/RG7935, an Anti-α-Synuclein Monoclonal Antibody, in Patients with Parkinson Disease: A Randomized Clinical Trial."

License, Development, and Commercialization Agreement with Roche

In December 2013, we entered into the License Agreement with Roche to develop and commercialize certain antibodies that target α-synuclein, including prasinezumab, which are referred to in this report collectively as "Licensed Products." The License Agreement became effective on January 17, 2014, which triggered an upfront payment to us of $30.0 million from Roche, which we received in February 2014. In July 2017, we announced that the first patient had been enrolled in PASADENA, a global Phase 2 clinical trial of prasinezumab in patients with early Parkinson's disease. The start of PASADENA triggered a $30.0 million milestone payment from Roche to Prothena, which was earned in the second quarter of 2017. In May 2021, we announced that the first patient had been enrolled in PADOVA, a global Phase 2b clinical trial of prasinezumab in patients with early Parkinson's disease. The start of PADOVA triggered a $60.0 million milestone payment from Roche to Prothena, which was earned in the second quarter of 2021.

Pursuant to the License Agreement, we are collaborating with Roche to develop antibody products targeting α-synuclein. Roche is primarily responsible for developing, obtaining and maintaining regulatory approval for, and commercializing Licensed Products under the collaboration, including prasinezumab. Roche is responsible for the clinical and commercial manufacture and supply of Licensed Products within a defined time period following the effective date of the License Agreement.

We have so far earned $135.0 million of a total $755.0 million in potential clinical, regulatory and sales milestones. In addition to the $$30.0 million upfront payment and clinical milestone payment of $15.0 million (both in 2014), the clinical milestone payment of $30.0 million in 2017, and the clinical milestone payment of $60.0 million in 2021, Roche is also obligated to pay:

- up to $290.0 million upon the achievement of additional development, regulatory and various first commercial sales milestones;
- up to $155.0 million upon the achievement of U.S. commercial sales milestones;
- up to $175.0 million upon achievement of ex-U.S. commercial sales milestones; and
- tiered, high single-digit to high double-digit royalties in the teens based on U.S. and ex-U.S. annual net sales, subject to certain adjustments, with respect to the applicable Licensed Product.

Roche bore 100% of the cost of conducting the research collaboration under the License Agreement during the research term, which expired December 31, 2017. In May 2021, the Company exercised its rights under the terms of License Agreement to receive potential U.S. commercial sales milestone and royalties, in lieu of a U.S. profit and loss share for prasinezumab in Parkinson's disease. Thus in the U.S. through May 28, 2021, the parties shared all development costs, all of which were allocated 70% to Roche and 30% to the Company, for prasinezumab in the Parkinson's disease indication. If the Company opts in to participate in co-development and co-funding for any other Licensed Products and/or indications, the parties will share all development and commercialization costs, as well as profits, all of which will be allocated 70% to Roche and 30% to the Company.

In addition, we have an option under the License Agreement to co-promote prasinezumab in the U.S. in the Parkinson's disease indication. If we exercise such option, we may also elect to co-promote additional licensed products in the U.S. approved for Parkinson's disease or other indications calling on the same prescriber. Outside the U.S., Roche has responsibility for developing and commercializing the licensed products.

Under the License Agreement with Roche, we granted to Roche an exclusive, worldwide license to develop, make, have made, use, sell, offer to sell, import and export the Licensed Products. The License Agreement continues on a country-by-country basis until the expiration of all payment obligations thereunder. The License Agreement may also be terminated (i) by Roche at will after the first anniversary of the effective date of the License Agreement, either in its entirety or on a Licensed Product-by-Licensed Product basis, upon 90 days' prior written notice to us prior to first commercial sale and 180 days' prior written notice to us after first commercial sale, (ii) by either party, either in its entirety or on a Licensed Product-by-Licensed Product or region-by-region basis, upon written notice in connection with a material breach uncured 90 days after initial written notice, and (iii) by either party, in its entirety, upon insolvency of the other party. The License Agreement may be terminated by either party on a patent-by-patent and country-by-country basis if the other party challenges a given patent in a given country. Our rights to co-develop licensed products under the License Agreement will terminate if we commence certain trials for certain types of competitive products. Our rights to co-promote licensed products under the License Agreement will terminate if we commence a Phase 3 trial for such competitive products.

Coramitug (formerly PRX004) for the Potential Treatment of ATTR Amyloidosis

Coramitug is an investigational antibody designed to deplete amyloid associated with disease pathology in hereditary and wild type ATTR amyloidosis, without affecting the native, normal tetrameric form of the protein.

ATTR amyloidosis is a rare, progressive and fatal disease characterized by deposition of abnormal, non-native forms of TTR protein (amyloid) in vital organs. ATTR amyloidosis can be hereditary (hATTR) when caused by a mutation in the TTR gene, or wild-type (wtATTR) when it occurs sporadically. In both forms of the disease, patients can experience a spectrum of clinical manifestations due to deposition of amyloid that can affect multiple organs, most commonly the heart and/or nervous system. The TTR protein is produced primarily in the liver and in its normal tetrameric form serves as a carrier for thyroxin and retinol binding protein (a transporter for vitamin A) and is also implicated in neuroprotective functions.

Wild-type ATTR (wtATTR) occurs sporadically and primarily involves cardiomyopathy. It is estimated that between 400,000 to 1.4 million patients suffer from ATTR-cardiomyopathy (ATTR-CM). Within this population, between 130,000 to 490,000 patients are estimated to be moderate-to-advanced and categorized as New York Heart Association Class III and IV.

In hereditary ATTR amyloidosis, mutations in the TTR gene causes non-native TTR to accumulate and damage body organs and tissue, such as the peripheral nerves and heart. This results in predominant symptoms of neuropathy (hATTR-PN) and/or cardiomyopathy (hATTR-CM), as well as other disease manifestations. It is estimated that there are approximately 50,000 patients with hATTR worldwide, with approximately 10,000 characterized as hATTR-PN and 40,000 characterized as hATTR-CM.

It is generally accepted that, at the time of diagnosis, affected organs in ATTR amyloidosis patients (both hATTR and wtATTR amyloidosis) contain extracellular amyloid deposits. These deposits, together with prefibrillar species, are believed to cause organ dysfunction and failure.

Current therapeutic approaches for ATTR amyloidosis have demonstrated benefit to patients by impacting the biological pathway leading to the formation of amyloid deposits. These approaches are designed to either reduce production of native forms of the TTR protein or bind to TTR and prevent tetramer dissociation but do not target the non-native, pathogenic form of TTR directly.

Coramitug's proposed mechanism of action is to deplete both circulating non-native TTR to prevent further deposition and deposited amyloid to improve organ function. Coramitug has been shown in preclinical studies to inhibit amyloid fibril formation, neutralize soluble aggregate forms of non-native TTR, and promote clearance of insoluble amyloid fibrils through antibody-mediated phagocytosis. This differentiated depleter mechanism of action could be developed as a monotherapy approach to ATTR amyloidosis and might also complement existing therapeutic approaches which either stabilize or reduce production of the native TTR tetramer.

We completed a Phase 1 clinical trial with coramitug in patients with hereditary forms of ATTR amyloidosis, in which coramitug was demonstrated to be safe and well tolerated. In October 2024, these Phase 1 results were published in *Amyloid*, the official journal of the International Society of Amyloidosis.

ATTR Amyloidosis Business Acquired by Novo Nordisk

In July 2021, we announced that we and Novo Nordisk entered into a definitive purchase agreement under which Novo Nordisk acquired our clinical stage antibody coramitug and broader ATTR amyloidosis business.

Under the terms of the definitive purchase agreement, Novo Nordisk acquired our wholly-owned subsidiary and gained full worldwide rights to the intellectual property and related rights of our ATTR amyloidosis business and pipeline. The aggregate purchase price consists of an upfront payment and development and sales milestone payments totaling up to $1.23 billion. We have earned approximately $100 million to date.

A Phase 2 clinical trial of coramitug in approximately 99 patients with ATTR amyloidosis with cardiomyopathy is being conducted by Novo Nordisk (NCT05442047).

BMS-986446 (formerly PRX005) for the Potential Treatment of Alzheimer's Disease

BMS-986446 *is* designed to be a best-in-class anti-tau antibody that specifically binds with high affinity the R1, R2, and R3 repeats within the microtubule binding region ("MTBR") of tau and targets both 3R and 4R tau isoforms. MTBR-tau has been shown in preclinical studies to be involved in the pathological spread of tau. Neurofibrillary tangles composed of misfolded tau proteins, along with amyloid beta plaques, are pathological hallmarks of Alzheimer's disease. Cell-to-cell transmission of pathogenic extracellular tau and the accumulation of pathogenic tau also correlate with the progression of symptomatology and clinical decline in patients with Alzheimer's disease. Recent publications suggest that during the course of Alzheimer's disease progression, tau appears to spread throughout the brain via synaptically-connected pathways; this propagation of pathology is thought to be mediated by tau "seeds" containing the MTBR of tau. Additionally, it has been recently reported that the presence of MTBR fragments in cerebrospinal fluid correlate with dementia stages and tau tangles in Alzheimer's disease to a higher degree than fragments of other tau regions. In preclinical research, antibodies targeting this region of tau were superior in blocking tau uptake and neurotoxicity, which has been associated with efficacy in relevant animal models. In these preclinical models, BMS-986446 demonstrated significant reduction of intraneuronal tau pathology and progression protection against behavioral deficit in a tau transgenic mouse model and complete blockade of neuronal tau internalization in vitro.

In July 2021, we entered into an exclusive US license agreement for BMS-986446 and we received an associated option exercise fee of $80 million. In July 2023, we entered into an exclusive global license agreement for BMS-986446, which as discussed above supersedes and replaces the US license agreement in its entirety and we received an associated option exercise fee of $55 million. We are eligible to receive regulatory and sales milestone payments of up to $563 million, as well as tiered royalties on annual, worldwide net sales.

Phase 1 Clinical Trial

In this first-in-human, randomized, placebo controlled, single ascending dose ("SAD") clinical trial, healthy volunteers (n=19) were enrolled into three BMS-986446 dose level cohorts (low, medium or high dose) and randomized in a 3:1 drug to placebo ratio. Trial participants received a single dose of BMS-986446 or placebo intravenously ("IV") and were followed for up to two months. The results of the trial found all three dose level cohorts of BMS-986446 to be generally safe and well tolerated, meeting the Phase 1 SAD trial primary objective. None of the treatment emergent adverse events ("TEAE") were serious. No clinically relevant changes were observed in other safety parameters. BMS-986446 also met key pharmacokinetic ("PK") and immunogenicity secondary endpoints. Plasma drug concentrations of BMS-986446 increased in a dose-proportional manner. Furthermore, BMS-986446 exposure in cerebrospinal fluid ("CSF") was measured in the high dose cohort and based on the robust exposure of BMS-986446 in the CSF (day 29 CSF:Plasma ratio=0.2%), substantial target engagement is expected in the CNS. BMS-986446 had a desirable immunogenicity profile with no persistent BMS-986446-induced antidrug antibodies ("ADA"s) observed.

A multiple ascending dose (MAD) portion of the Phase 1 clinical trial was ongoing at the time BMS acquired the global rights to the program and control of the Phase 1 trial. All program updates going forward, including results from ongoing and any future BMS-986446 clinical trials, will be reported by BMS.

Phase 2 Clinical Trial

In the first quarter of 2024, BMS advanced the anti-tau program BMS-986446 with the initiation of a Phase 2 clinical trial (NCT06268886). This is a randomized, double-blind, placebo-controlled, global, Phase 2 clinical trial designed to evaluate the efficacy, safety, and tolerability of BMS-986446, an anti-MTBR tau monoclonal antibody, in approximately 475 participants with early Alzheimer's disease. Participants will be randomized into one of three treatment arms including placebo, BMS-986446 Dose A, and BMS-986446 Dose B. The primary outcome measure is mean change from baseline to week 76 in Clinical Dementia Rating Scale Sum of Boxes ("CDR-SB").

PRX012 for the Potential Treatment of Alzheimer's Disease

PRX012 is an investigational antibody that targets Aβ, or amyloid beta, a protein implicated in Alzheimer's disease. Our scientists have advanced the understanding of the biology of Alzheimer's disease and made particularly impactful and fundamental discoveries that elucidated the role amyloid plays in the disease.

Monoclonal antibodies targeting key epitopes within the N-terminus of Aβ have demonstrated that reducing amyloid plaque burden is associated with the slowing of clinical decline in Alzheimer's disease. To address the growing prevalence of Alzheimer's disease with a therapeutic that can be made widely accessible to patients, we have developed highly potent anti-Aβ antibodies that retain or improve key attributes that are thought to underlie the observed efficacy of N-terminally directed therapeutics such as aducanumab, with the aim of offering similar or improved efficacy with convenient subcutaneous dosing regimens. In preclinical studies, our antibodies demonstrated a higher binding strength to amyloid than aducanumab; specifically, our lead candidate with an approximately 10-fold greater affinity/avidity for fibrillar Aβ than aducanumab that also neutralized soluble, toxic (i.e., oligomeric) Aβ species. Preclinical studies also showed that our antibodies recognize Aβ pathology to a greater extent than aducanumab, demonstrating more extensive plaque area binding at lower antibody concentrations, which are estimated to be clinically relevant exposures in the central nervous system following systemic dosing.

We are advancing our lead candidate, PRX012, as a next-generation approach for subcutaneous administration to address the unmet need of millions of patients with presymptomatic or early symptomatic Alzheimer's disease. In March 2022, we announced the FDA clearance of the IND for PRX012 and the initiation of a Phase 1 single ascending dose trial to investigate the safety, tolerability, immunogenicity, and pharmacokinetics of PRX012 in both healthy volunteers and patients with Alzheimer's disease. In April 2022, we announced that the FDA granted Fast Track designation for PRX012 for the treatment of Alzheimer's disease. The FDA's Fast Track designation program is designed to expedite the development and review of drugs intended to treat a serious condition, such as Alzheimer's disease, with evidence demonstrating the potential to address an unmet medical need. In January 2024, we announced that topline Phase 1 data from the single ascending dose trial and the initial multiple dose cohort (70 mg) supports single-injection once-monthly subcutaneous treatment and dose escalation. The ongoing Phase 1 trial continues as planned and we expect to report multiple clinical readouts starting in mid-2025 and continuing throughout the year.

PRX123, a Dual Aβ-Tau Vaccine for the Potential Treatment and Prevention of Alzheimer's Disease

We are developing a dual vaccine, PRX123, which concomitantly targets key epitopes within both the Aβ and tau proteins. Preclinical models suggest that Aβ and tau act synergistically in the development of Alzheimer's disease; however, the majority of vaccines and passive immunotherapies under development today target only one of these two pathological features.

PRX123 is being developed for the potential prevention and treatment of Alzheimer's disease. In preclinical studies, PRX123 has generated polyclonal responses against key epitopes within the N-terminal of Aβ and a key region of tau to promote amyloid clearance and blockade of tau transmission. Immunohistochemistry using sera from immunized animals demonstrated an appropriate and balanced immune response with antibodies that react to both Aβ plaques and tau tangles at concentrations expected to be reached in CNS following immunization and resultant titer generation.

In March 2022, we delivered an oral presentation at AD/PD 2022 on preclinical data demonstrating that PRX123 generated anti-Aβ and anti-tau antibodies to enable phagocytosis of Aβ and to neutralize tau. These findings provided proof of concept in multiple preclinical species.

In January 2024, we announced that the FDA has cleared the IND application for PRX123 and granted PRX123 Fast Track designation.

PRX019 for the Potential Treatment of Neurodegenerative Diseases

PRX019 is an investigational antibody for the potential treatment of neurodegenerative diseases in development in collaboration with BMS.

In December 2023, the FDA cleared the IND application for PRX019. In May 2024, we entered into an exclusive global license agreement for PRX019 and we received an associated option exercise fee of $80.0 million. We are eligible to receive development, regulatory, and sales milestone payments of up to $617.5 million as well as tiered royalties on annual, worldwide net sales.

In November 2024, we announced that we had initiated a Phase 1 first-in-human clinical trial to evaluate the safety, tolerability, immunogenicity, and pharmacokinetics of single ascending and multiple doses in healthy adults.

Our Discovery and Preclinical Programs

We are also advancing several discovery and preclinical-stage programs for neurological diseases with significant unmet medical needs.

If promising, we expect to advance our discovery programs into preclinical development. New target discovery will focus on areas where we can bring potential new therapies to patients expeditiously through our internal expertise and resources. Existing late discovery-stage or preclinical-stage programs may be partnered or out-licensed.

Regulation

We anticipate that if we commercialize any products, the U.S. market will ultimately be our most important market. For this reason, the laws and regulations discussed below focus on the requirements applicable to biologic products in the U.S.

Government Regulation

Governmental authorities, including the FDA, the EMA and comparable regulatory authorities in other countries, regulate the development, testing, use, labeling, manufacturing, storage, recordkeeping, reporting, marketing, advertising, promotion, tracking and tracing of pharmaceutical and biological products. The FDA does so under the U.S. Federal Food, Drug, and Cosmetic Act and its implementing regulations and guidance for industry, and the U.S. Public Health Service Act and its implementing regulations. Noncompliance with applicable requirements can result in warning and untitled letters, civil and criminal fines and other judicially imposed sanctions, including product seizures, import restrictions, injunctive actions and criminal prosecutions of both companies and individuals. In addition, administrative remedies can involve requests to recall violative products, the refusal of the government to enter into supply contracts; or the refusal to approve pending

applications for product approvals until manufacturing or other alleged deficiencies are brought into compliance. The FDA, the EMA and comparable regulatory authorities in other countries also have the authority to cause the revocation of approval of a marketed product or to impose additional labeling or distribution restrictions.

The pricing of pharmaceutical and biological products is regulated in many countries and the mechanism of price regulation varies. In the U.S., while there are limited indirect federal government price controls over private sector purchases of drugs, it is not possible to predict future regulatory action or private sector initiatives on the pricing of pharmaceutical products.

Product Approval

United States. In the U.S., our current drug candidates are regulated as biological products, or biologics. The FDA regulates biologics under the U.S. Food, Drug, and Cosmetics Act, the Public Health Service Act and their implementing regulations. Biologics are also subject to other federal, state and local statutes and regulations. The process required by the FDA before biologic product candidates may be marketed in the U.S. generally involves, and is not limited to, the following:

- completion of extensive nonclinical laboratory tests and animal studies, performed in accordance with the FDA's Good Laboratory Practice ("GLP") regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin and must be updated annually;
- performance of adequate and well-controlled human clinical trials to establish the efficacy and safety of the product for each proposed indication, all performed in accordance with FDA's current good clinical practices ("cGCP") requirements;
- completion of chemistry, manufacturing and control ("CMC") processes and procedures to establish the safety and quality of the product in accordance with FDA's current good manufacturing practices ("cGMP") regulations;
- submission to the FDA of a Biological License Application ("BLA") for a new biologic, after completion of all required clinical trials;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facilities at which the product is produced and tested to assess compliance with regulatory requirements, including cGMP regulations;
- referral of the BLA to an advisory committee for review, if deemed necessary; and
- FDA review and approval of a BLA for a new biologic, prior to any commercial marketing or sale of the product in the U.S.

Nonclinical tests assess the potential safety and pharmacologic effects of a product candidate in in vitro and/or in vivo studies. The results of these studies must be submitted to the FDA as part of an IND before human testing may proceed. An IND is a request for authorization from the FDA to manufacture and administer an investigational drug or biologic product to humans. The IND includes the proposed protocol(s) and general investigational plan for human studies. The IND also includes results of nonclinical studies and other human studies, as appropriate, as well as manufacturing information, analytical data and any other available data or literature to support the use of the investigational new drug. An IND must become effective before human clinical trials may be initiated. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises full or partial concerns or questions related to initiation of the proposed clinical trial(s). In such a case, the IND may be placed on a full or partial clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial(s) may begin. Accordingly, submission of an IND may or may not result in the FDA allowing a clinical trial(s) to commence as planned.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with cGCPs, which include the requirement that all research subjects provide their informed consent prior to their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety, and the efficacy criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. Additionally, approval must also be obtained from each clinical trial site's Institutional Review Board ("IRB") before the trials may be initiated, and the IRB must provide oversight of the trials until completed. There are also requirements governing the reporting of ongoing clinical trials and clinical trial results to public registries.

The clinical investigation of a pharmaceutical, including a biologic, is generally divided into three phases. Although the phases are usually conducted sequentially, they may overlap or be combined. The three phases of an investigation are as follows:

- *Phase 1.* Phase 1 includes the initial introduction of an investigational product into humans. Phase 1 clinical trials are typically more closely monitored and may be conducted in patients with the target disease or condition or in healthy volunteers. These studies are designed to evaluate the safety, appropriate dosage, metabolism and pharmacologic actions of the investigational product in humans, the side effects associated with increasing doses, and if possible, to gain early evidence on effectiveness. During Phase 1 clinical trials, sufficient information about the investigational product's pharmacokinetics and pharmacological effects may be obtained to permit the design of well-controlled Phase 2 and Phase 3 clinical trials. The total number of participants included in Phase 1 clinical trials varies, but is generally in the range of 20 to 80;

- *Phase 2.* Phase 2 includes controlled clinical trials conducted to preliminarily or further evaluate the efficacy and safety of the investigational product for a specific indication(s) in patients with the disease or condition under study, to determine dosage(s) for further studies, and to identify possible adverse side effects and safety risks associated with the product. Phase 2 clinical trials are typically well-controlled, closely monitored, and conducted in a patient population, usually involving no more than several hundred participants; and

- *Phase 3.* Phase 3 clinical trials are generally well controlled clinical trials conducted in an expanded patient population generally at geographically dispersed clinical trial sites. They are performed after preliminary evidence suggesting effectiveness and safety of the product has been obtained, and are intended to further evaluate efficacy and safety, to establish the overall benefit-risk relationship of the investigational product, and to provide an adequate basis for product approval. Phase 3 clinical trials usually involve several hundred to several thousand participants.

The clinical trial process can take many years to complete, and there can be no assurance that the data collected will support FDA approval of the product. During all phases of clinical development, regulatory agencies require extensive monitoring of clinical activities, clinical data, and clinical trial investigators. Clinical trials may not be completed successfully within any specified period, if at all. The FDA may place clinical trials on hold at any point in this process if, among other reasons, it concludes that clinical subjects are being exposed to an unreasonable and significant health risk or illness or injury. Trials may also be terminated by IRBs, which must review and approve all research involving human subjects. Side effects or adverse events that are reported during clinical trials can delay, impede or prevent further clinical testing and/or marketing authorization.

Information including the results of the nonclinical and clinical testing, and the chemistry, manufacturing and controls of the product are evaluated and, if determined to be adequate, submitted to the FDA to support the proposed product labeling through a BLA. The application includes all relevant data available from nonclinical and clinical trials, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other required information. Data from company-sponsored clinical trials intended to test the efficacy and safety of a proposed use of a product, and/or from alternative sources, including studies initiated by investigators may be included in a BLA.

Once the BLA submission has been accepted for filing, the FDA's goal is to review applications within ten months from the 60 day filing date for Standard Review (for a total of twelve months) or, in the case of Priority Review, six months from the 60 day-filing date (for a total of eight months).

The review process often may be significantly extended by the FDA's requests for additional information or clarification. The FDA reviews the BLA to determine, among other things, whether the proposed product is safe and effective, which includes determining whether it is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality, potency and purity. The FDA may refer the application to an advisory committee for evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it typically follows such recommendations.

In certain cases, the FDA may issue a SPA, which is a written agreement between a sponsor and the FDA that indicates concurrence between the parties regarding the adequacy and acceptability of specific design elements and planned analysis for a clinical trial intended to form the basis of a licensing application. An SPA does not indicate FDA concurrence on every detail in a particular trial protocol, and final marketing approval depends upon factors including the efficacy and safety results from the trial, the overall safety profile and an evaluation of the benefit/risk profile for the product candidate as demonstrated across clinical trials for the target patient population.

The FDA has four expedited program designations for serious conditions - Fast Track, Breakthrough Therapy, Accelerated Approval and Priority Review - to facilitate and expedite development and review of new drugs to address unmet medical needs or provide substantial improvements in the treatment of serious or life-threatening conditions.

The Fast Track designation provides pharmaceutical manufacturers with opportunities for frequent interactions with FDA during the product's development and for a rolling review of the BLA. A rolling review allows for completed portions of the application to be submitted and reviewed by the FDA prior to submission of the complete application.

The Breakthrough Therapy designation provides sponsors with all of the features of Fast Track designation as well as intensive guidance on implementing an efficient development program for the product and a commitment by the FDA to involve senior managers and experienced review staff in the review. This FDA designation requires preliminary clinical evidence that a product candidate intended to treat a serious or life-threatening condition, alone or in combination with other drugs or biologics, demonstrates substantial improvement over currently available therapy on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development.

FDA may grant Accelerated Approval to a product for a serious or life-threatening condition, upon a determination that the product has an effect on a surrogate or intermediate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA has required the sponsor to conduct post-approval confirmatory trials to verify the clinical benefit. In addition, the FDA requires pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

Any biologic product submitted to the FDA for approval, including a product with Fast Track or Breakthrough Therapy designation, may also be eligible for priority review. A product is eligible for priority review if it is intended to treat a serious condition, and if approved, would provide a significant improvement in safety or effectiveness, among other criteria. For original BLAs, the FDA goal to take action on an application granted Priority Review designation is within six months of the 60-day filing date (compared with ten months under standard review).

After the FDA evaluates the BLA and conducts pre-approval inspections of manufacturing facilities where the candidate product and/or its active pharmaceutical ingredient will be produced, of clinical sites and of the sponsor, if deemed necessary, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the biologic with specific labeling for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter may require additional clinical data and/or an additional Phase 3 clinical trial(s), and/or other significant, expensive and time-consuming requirements related to clinical trials, nonclinical studies or manufacturing. Even if such additional information is submitted, the FDA may ultimately decide that the BLA does not satisfy the criteria for approval.

The FDA may also require a Risk Evaluation and Mitigation Strategy ("REMS") plan as a condition of approval to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. A REMS or a separate medication guide, if required, must be submitted to the FDA for review and approval.

The FDA also may impose other conditions for approval including but not limited to, changes to proposed labeling, changes to manufacturing controls and specifications, or a commitment or requirement to conduct one or more post-marketing studies or additional clinical trials. Such post-marketing commitments or requirements may include Phase 4 clinical trials and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

European Union. In the EU, our current drug candidates are regulated as biological products, or biologics. The EU regulates biologics under Directive 2001/83/EC, Regulation (EC) No 726/2004, their implementing regulations and scientific guidelines.

In the EU, there are several pathways for marketing approval, depending on the type of product for which approval is sought. Under the centralized procedure, which is mandatory for *inter alia*, medicinal products (i) derived from certain biotechnology processes, (ii) contain new active substances to treat certain diseases such as auto-immune and other immune dysfunctions, or (iii) designated orphan medicines, a sponsor submits a single application to the EMA and an authorization granted under this procedure is valid in all EEA member states (i.e., the EU member states, Iceland, Liechtenstein, and Norway). The centralized procedure is optional for certain other medicines, including medicines that constitute a significant innovation or the authorization of which would be in the interest of patients at EU level. The marketing application is similar to the BLA submitted to the FDA in the U.S. and is evaluated by the Committee for Medicinal Products for Human Use (the

"CHMP"), the expert scientific committee of the EMA. If the CHMP determines that the marketing application fulfills the requirements for efficacy, safety and quality (equivalent to chemistry, manufacturing and controls in the US), it will submit a favorable opinion to the European Commission (the "EC"). The CHMP opinion is not binding, but is typically adopted by the EC. A marketing application approved by the EC is valid in all EEA member states.

National marketing authorization are available for product candidates not falling within the mandatory scope of the centralized procedure, namely: (i) national authorization procedures, which requires a separate application in and approval determination by each country; (ii) a decentralized procedure, whereby applicants submit identical applications to several countries and receive simultaneous approval; and (iii) a mutual recognition procedure, where applicants submit an application to one country for review and approval, and other countries may accept or reject the decision in the initial country. Regardless of the approval process employed, various regulatory authorities share responsibilities for the monitoring, detection, and evaluation of adverse events post-approval, including national authorities, the EMA, the EC, and the marketing authorization holder.

Post-Approval Requirements

Any products manufactured or distributed by us or on our behalf pursuant to FDA approvals are subject to continuing regulation by the FDA, including requirements for recordkeeping, reporting of adverse events, and submitting product deviation reports to notify the FDA of unanticipated changes in distributed products. Additionally, any significant change in the approved product or in how it is manufactured, including changes in formulation or the site of manufacture, generally require prior FDA approval of a supplemental BLA. The packaging and labeling of all products developed by us are also subject to FDA approval and ongoing regulation and oversight.

Sponsors are required to register their facilities with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP standards, which impose, among other things, certain quality processes, manufacturing controls and documentation requirements upon us and our third-party manufacturers in order to ensure that the product is safe, and has the identity, strength, quality, purity and potency characteristics that it purports to have. Certain states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Noncompliance with cGMP or other requirements can result in issuance of warning or untitled letters, civil and criminal penalties, seizures, and injunctive action, as well as FDA not approving pending supplemental applications or withdrawing prior approvals, and product recalls.

FDA regulations also require, among other things, investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers and sponsors must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

The FDA and other federal and state agencies closely regulate the labeling, marketing and promotion of drugs. While doctors are free to prescribe any product approved by the FDA for any use, a company can only make claims relating to safety and efficacy of a product that are consistent with the FDA approved labeling, and the company is allowed to market a drug only for the particular use(s) approved by the FDA. In addition, any claims we make for our products in advertising or promotion must be appropriately balanced with important safety information and otherwise be adequately substantiated. Failure to comply with these requirements can result in, among other things, adverse publicity, warning or untitled letters, corrective advertising, injunctions, potential civil and criminal penalties, criminal prosecution, and agreements with governmental agencies that materially restrict the manner in which a company promotes or distributes drug products. Government regulators, including the Department of Justice and the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities, have increased their scrutiny of the promotion and marketing of drugs.

The FDA also enforces the requirements of the U.S. Prescription Drug Marketing Act, which, among other things, imposes various requirements in connection with the distribution of product samples to physicians. Sales, marketing and scientific/educational grant programs must comply with the U.S. Anti-Kickback Statute, the U.S. False Claims Act, and similar state laws. Pricing and rebate programs must comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act. We may also be subject to the U.S. Physician Payment Sunshine Act (the "Sunshine Act") which regulates disclosure of payments to healthcare professionals and providers.

The U.S. Foreign Corrupt Practices Act (the "FCPA"), the Irish Criminal Justice (Corruption Offences) Act 2018 (the "Irish Corruption Act") and the U.K. Bribery Act prohibit companies and their representatives from offering, promising, authorizing or making payments to governmental officials (and certain private individuals under the Irish Corruption Act and

the U.K. Bribery Act) for the purpose of obtaining or retaining business abroad. In many countries, the healthcare professionals we interact with may meet the definition of a government official for purposes of the FCPA. Failure to comply with domestic or non-domestic laws could result in various adverse consequences, including possible delay in approval or refusal to approve a product, recalls, seizures, withdrawal of an approved product from the market, the imposition of civil or criminal sanctions and the prosecution of executives overseeing our international operations.

Orphan Drugs

Under the U.S. Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally defined as a disease or condition that affects fewer than 200,000 individuals in the U.S., or more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making available in the U.S. a drug or biologic for this type of disease or condition will be recovered from sales in the U.S. for that drug or biologic. Orphan drug designation must be requested before submitting a BLA. In the U.S., orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user fee waivers. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The first BLA applicant to receive FDA approval for a particular active ingredient to treat a particular disease with FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the U.S. for that product, for that indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market the same drug for the same orphan indication, except in limited circumstances, such as demonstration of clinical superiority to the product with orphan exclusivity or if FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. As a result, even if one of our drug candidates receives orphan exclusivity, the FDA can still approve other drugs that have a different active ingredient for use in treating the same indication or disease. In addition, another company may obtain orphan exclusivity for the same drug for the same use before we do, which would block FDA from approving our product until the end of the exclusivity period unless we can demonstrate clinical superiority or the first-approved company is unable to assure supply. Furthermore, the FDA can waive orphan exclusivity if we are unable to manufacture sufficient supply of our product.

In the EU, the EMA's Committee for Orphan Medicinal Products ("COMP") grants orphan drug designation to promote the development of products intended for the diagnosis, prevention, or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the EU. Additionally, designation is granted for products intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition when, without incentives, it is unlikely that sales of the drug in the EU would be sufficient to justify the necessary investment in developing the drug or biological product or where there is no satisfactory method of diagnosis, prevention, or treatment, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition. In the EU, a sponsor must apply for maintenance of the orphan drug designation at the time of marketing authorization. If successful, the orphan drug designation entitles the sponsor to ten years of market exclusivity following drug or biological product approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Pharmaceutical Coverage, Pricing and Reimbursement

Sales of our products will depend, in part, on the extent to which our products will be covered by third-party payors, such as federal, state and other government health care programs, commercial insurance and managed healthcare organizations. In order to secure coverage and reimbursement for any product that may be approved for sale, a company may need to conduct additional pharmacoeconomic, real-world, or other outcomes studies to demonstrate the medical necessity, value and cost-effectiveness of the product (in addition to the costs incurred to obtain FDA or other comparable marketing approvals).

A decision by a third-party payor to limit or not cover a product candidate could reduce physician utilization once the product is approved and have an adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that adequate reimbursement will be approved at a rate that covers our costs, including research, development, manufacture, sale and distribution. Further, one payor's determination to provide coverage for a drug product does not ensure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

We expect our products, if and when approved, may be eligible for coverage under Medicare, the U.S. federal health care program that provides health care benefits to the aged and disabled. We also expect to participate in the Medicaid Drug Rebate Program ("MDRP"),which requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. Under the MDRP, manufacturers must pay a rebate to each state Medicaid program for quantities of products utilized on an outpatient basis (with some exceptions) that are dispensed

to Medicaid beneficiaries and paid for by a state Medicaid program. MDRP rebates are calculated using a statutory formula, state-reported utilization data, and pricing data that are calculated and reported by manufacturers on a monthly and quarterly basis to CMS. These data include the average manufacturer price ("AMP") and, in the case of single source and innovator multiple source products, the best price for each drug.

We also anticipate participating in the 340B drug pricing program in the U.S., which requires participating manufacturers to agree to charge statutorily-defined covered entities no more than the 340B "ceiling price" for the manufacturer's covered outpatient drugs. These 340B covered entities include health care organizations that have certain federal designations or receive funding from specific federal programs, including Federally Qualified Health Centers, Ryan White HIV/AIDS Program grantees, and certain types of hospitals and specialized clinics, as well as certain hospitals that serve a disproportionate share of low-income patients. The U.S. Patient Protection and Affordable Care Act, as amended by the U.S. Health Care and Education Reconciliation Act (collectively, the "ACA"), expanded the 340B program to also include certain children's hospitals, certain free-standing cancer hospitals, critical access hospitals, certain rural referral centers and certain sole community hospitals, each as defined by ACA. The 340B ceiling price is calculated using a statutory formula, which is based on the AMP and rebate amount for the covered outpatient drug as calculated under the MDRP, and in general, products subject to the MDRP are also subject to the 340B ceiling price calculation and discount requirement. Any changes to the definition of Medicaid AMP and the Medicaid rebate amount also could affect our 340B ceiling price calculation for our products and could negatively impact our results of operations.

U.S. federal law further requires that for a company to be eligible to have its products paid for with federal funds under the MDRP and Medicare Part B programs, as well as to be purchased by certain federal agencies and grantees, it also must participate in the Department of Veterans Affairs ("VA") Federal Supply Schedule ("FSS") pricing program. To participate, manufacturers are required to enter into an FSS contract and other agreements with the VA for any covered drugs. Under these agreements, manufacturers must make such products available to the "Big Four" federal agencies—the VA, the Department of Defense ("DoD"), the Public Health Service (including the Indian Health Service), and the Coast Guard—at pricing that is capped pursuant to a statutory federal ceiling price ("FCP"), formula set forth in Section 603 of the Veterans Health Care Act of 1992 ("VHCA"). The FCP is based on a weighted average non-federal average manufacturer price ("Non-FAMP"), which manufacturers are required to report on a quarterly and annual basis to the VA.

Governments and third-party payors have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Increasingly, the third-party payors who reimburse patients or healthcare providers, such as the federal healthcare programs described above and private insurance plans, are requiring that drug companies provide them with predetermined discounts from list prices, and are seeking to reduce the prices charged or the amounts reimbursed for medical products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

The containment of healthcare costs, including drug pricing, has also become a priority of federal, state and foreign governments action and legislation. For example, in the U.S, there have been several recent Congressional inquiries and proposed federal legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies for drugs. This includes the American Rescue Plan Act of 2021, which included among its provisions a sunset of the provision in the ACA that capped pharmaceutical manufacturers' rebate liability under the MRDP. Under the ACA, manufacturers' rebate liability was capped at 100% of the AMP for a covered outpatient drug. As of January 1, 2024, manufacturers' MDRP rebate liability is no longer capped, potentially resulting in a manufacturer paying more in MDRP rebates than it receives on the sale of certain covered outpatient drugs.

At the state level in the U.S., legislatures are increasingly passing laws and implementing regulations designed to control pharmaceutical and biological product pricing, including limitations on reimbursement, discounts, restrictions on certain product access and marketing, cost disclosure (including disclosures for certain price increases or launches of costly drugs), and transparency measures, and, in some cases, to encourage importation from other countries and bulk purchasing. It is likely that additional state and federal healthcare reform measures will continue to be adopted in the future, which could limit the amounts that federal and state governments will pay for healthcare products and services, potentially reducing demand for a pharmaceutical manufacturer's products or adding additional pricing pressure.

Other Healthcare Laws

Although we currently do not have any products on the market, if our drug candidates are approved and we begin commercialization, we may be subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and other jurisdictions in which we conduct our business. These laws extensively govern how pharmaceutical companies, like Prothena, are operated and regulate activities related to pharmaceutical products. These laws and regulations may require administrative guidance to implement. Failure to comply could subject the Company to legal and/or administrative actions, which may include substantial fines and/or penalties; orders to stop non-compliant activities; criminal charges; warning letters; product recalls or seizures; delays in product approvals; and exclusion from participation in government reimbursement programs or contracts as well as limitations on conducting business in applicable jurisdictions.

Such laws include, without limitation:

- The U.S. federal Anti-Kickback Statute, or AKS, which is a criminal law that prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order, or recommendation of, any good or service for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid. The AKS has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, pharmacies, purchasers, and formulary managers on the other, including, for example, consulting/speaking arrangements, discount and rebate offers, grants, charitable contributions, and patient support offerings, among others. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Violations of the federal Anti-Kickback Statute can result in significant civil monetary penalties and criminal fines, as well as imprisonment and exclusion from participation in government healthcare programs;

- The U.S. federal civil False Claims Act, or the FCA, which may be enforced through civil whistleblower or *qui tam* actions and imposes significant civil penalties, treble damages and potential exclusion from government healthcare programs against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or for making a false record or statement material to an obligation to pay the federal government or for knowingly and improperly avoiding, decreasing or concealing an obligation to pay money to the federal government. Pharmaceutical companies have been investigated and/or subject to government enforcement actions asserting liability under the False Claims Act for a variety of alleged activities, including alleged off-label promotion of drugs, purportedly concealing price concessions in the pricing information submitted to the government for government price reporting purposes, and allegedly providing free product to customers with the expectation that the customers would bill federal healthcare programs for the product. FCA liability is potentially significant in the healthcare industry because the statute provides for treble damages and significant mandatory penalties per false or fraudulent claim or statement for violations, which are currently set at $14,308 up to $28,619 per false claim or statement for penalties assessed after January 15, 2025. Further, a violation of the federal Anti-Kickback Statute can serve as a basis for liability under the federal civil False Claims Act. There is also the federal criminal False Claims Act, which is similar to the federal civil False Claims Act and imposes criminal liability on those that make or present a false, fictitious or fraudulent claim to the federal government;

- The U.S. federal Civil Monetary Penalties Law, which authorizes the imposition of substantial civil monetary penalties against an entity that engages in activities including, among others (1) knowingly presenting, or causing to be presented, a claim for services not provided as claimed or that is otherwise false or fraudulent in any way; (2) arranging for or contracting with an individual or entity that is excluded from participation in federal healthcare programs to provide items or services reimbursable by a federal healthcare program; (3) violations of the federal Anti-Kickback Statute; or (4) failing to report and return a known overpayment;

- The U.S. federal Physician Payments Sunshine Act, implemented as the Open Payments Program, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, among others, to track and report annually to CMS information related to payments and other transfers of value made by that entity to US-licensed physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists, certified nurse midwives, and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to timely, accurately, and completely submit the required information for all payments, transfers of value and ownership or investment interests may result in civil monetary penalties;

- The U.S. federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") which imposes criminal and civil liability for, among other things, executing or attempting to execute a scheme to defraud any healthcare benefit

program, including any third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statements or representations, or making false statements relating to healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, which mandates, among other things, the adoption of uniform standards for the electronic exchange of information in common healthcare transactions as well as standards relating to the privacy and security of individually identifiable health information. These standards require the adoption of administrative, physical and technical safeguards to protect such information. In addition, many states have enacted comparable laws addressing the privacy and security of health information, some of which are more stringent than HIPAA. Failure to comply with these laws can result in the imposition of significant civil and criminal penalties;

- U.S. state laws that require the reporting of certain pricing information, including information pertaining to and justifying price increases, prohibit prescription drug price gouging; or impose payment caps on certain pharmaceutical products deemed by the state to be "high cost"; and

- Analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures.

Efforts to ensure that our business arrangements will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations, or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, disgorgement, monetary fines, individual imprisonment, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, possible exclusion from participation in federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Intellectual Property

We seek to protect our proprietary technology and other intellectual property that we believe is important to our business, including by seeking, maintaining and defending patents. We also rely on trade secrets and know-how to protect our business. We may seek licenses from others as appropriate to enhance or maintain our competitive position.

Our intellectual property is primarily directed to therapeutic product candidates and related methods for the treatment of diseases that involve protein dysregulation, amyloidosis, or neurodegeneration, and other proprietary technologies and processes related to our lead product development candidates.

We own or hold exclusive licenses to a number of issued patents and pending patent applications in the U.S. and other jurisdictions, including Patent Cooperation Treaty applications. As of December 31, 2024, our patent portfolio included the following families of patents or patent applications that we own or have exclusively licensed from other parties:

- Approximately 9 patent families related to AL or AA amyloidosis, including our birtamimab program, including a composition of matter patent anticipated to expire 2029 (subject to potential adjustments in patent term as described below);

- Approximately 16 patent families related to passive immunotherapy for Parkinson's disease and other synucleinopathies, including our prasinezumab program, including a composition of matter patent anticipated to expire in 2032 (subject to potential adjustments in patent term as described below);

- Approximately 14 patent families related to passive immunotherapy for Alzheimer's disease, including our PRX005 and PRX012 programs; and
- Approximately 20 patent families related to other potential targets of intervention and diseases and other product candidates, including PRX019 and vaccines.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the date of filing the non-provisional application. In the U.S., a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier-filed patent.

The term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration of a U.S. patent as compensation for the patent term lost during diligent clinical development and the FDA regulatory review process, which together are the regulatory review period. The U.S. Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under a regulatory review period. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent can be extended for each first regulatory review period for a product. Moreover, a patent can only be extended once, and thus, if a single patent is applicable to multiple products, it can only be extended based on one product. Similar provisions are available in Europe and other jurisdictions to extend the term of a patent that covers an approved drug. When possible, depending upon the length of clinical trials and other factors involved in the filing of a BLA or NDA, we expect to apply for patent term extensions for patents covering our product candidates and their methods of use, however, there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and if granted, the length of such extensions.

University of Tennessee License Agreement: Under a License Agreement with the University of Tennessee Research Foundation, we have exclusively licensed from the University of Tennessee its joint ownership interest in certain patents jointly owned with us. Those patents relate to our program targeting amyloidosis (birtamimab). Under that sublicensable, worldwide license, we are required to pay to the University of Tennessee an amount equal to 1% of net sales of any product covered by any licensed patent, plus certain additional payments in the event that all or a portion of the license is sublicensed. To date, we have not paid or incurred any royalties to the University of Tennessee under our agreement. The agreement is effective on a country-by-country basis for the longer of (i) a period of twenty years from the effective date of the agreement, or (ii) in each country in which a valid claim for any licensed patent or patent application exists, expiration of such valid claim. The agreement will terminate prior to the end of its term if we become insolvent unless the University of Tennessee elects to allow the agreement to remain in effect. The University of Tennessee may terminate the agreement prior to the end of its term upon our failure to make payment under the agreement within 120 days of notice of such failure or upon our material breach of the agreement, which breach has not been cured within 60 days of written notice of such breach. We may terminate the agreement prior to the end of its term if we have paid all amounts due to the University of Tennessee through the effective date of the termination and provide three months' written notice to the University of Tennessee or upon material breach of the agreement by the University of Tennessee, which breach has not been cured within 60 days of written notice of such breach.

University of California License Agreement: Under a License Agreement with The Regents of the University of California, we have exclusively licensed from the University of California its joint ownership interest in certain patents jointly owned with us. Those patents relate to our program targeting Parkinson's disease and other synucleinopathies (prasinezumab). Under that sublicensable, worldwide license, we are required to pay to the University of California an amount equal to 1% of net sales of any product covered by any licensed patent, plus certain additional payments for milestones achieved and sublicense revenue. To date, we have not paid or incurred any royalties to the University of California under our agreement. The agreement is effective until the expiration date of the last to expire licensed patent. The obligation to pay royalties continues on a country-by-country basis until the expiration of the last to expire patent containing a valid claim covering the applicable product. The agreement will terminate prior to the end of its term without prior written notice if (i) we, or third parties on our behalf or at our written urging, file a claim including an assertion that any portion of the licensed patents is invalid or unenforceable, or (ii) upon the filing of a petition for relief under the U.S. Bankruptcy Code by or against us as a debtor or alleged debtor. The University of California may terminate the agreement prior to the end of its term upon our default, if we fail to cure the default within 60 days of written notice of such default. We may terminate the agreement prior to the end of its term upon a 90 day written notice to the University of California.

Elan License Agreement: Under an Amended and Restated Intellectual Property License and Contribution Agreement with Elan and certain of its affiliates, we have exclusively licensed from Elan and those affiliates certain patents and patent applications owned by them, and exclusively sublicensed from Elan and those affiliates certain patents and patent applications owned by Janssen Alzheimer Immunotherapy. Those licenses are worldwide, fully paid, royalty-free, perpetual and irrevocable, and relate to our program targeting α-synuclein. Subsequent to entering into this Agreement, Elan was acquired by Perrigo Company plc.

Competition

The pharmaceutical industry is highly competitive. Our principal competitors consist of major international companies, all of which are larger and have greater financial resources, technical staff, manufacturing, R&D and marketing capabilities than we have. We also compete with smaller research companies and generic drug and biosimilar manufacturers. The degree of competition varies for each of our programs.

A drug may be subject to competition from alternative therapies during the period of patent protection or regulatory exclusivity and thereafter it may be subject to further competition from generic products or biosimilars. Governmental and other pressures toward the dispensing of generic products or biosimilars may rapidly and significantly reduce, slow or reverse the growth, sales and profitability of any product not protected by patents or regulatory exclusivity, and may adversely affect our future results and financial condition. If we successfully discover, develop and commercialize any products, the launch of competitive products, including generic or biosimilar versions of any such products, may have a material adverse effect on our revenues and results of operations.

Our competitive position depends in part upon our ability to discover and develop innovative and cost-effective new products. If we fail to discover and develop new products, our business, financial condition and results of operations will be materially and adversely affected.

Manufacturing

Birtamimab - Boehringer Ingelheim Biopharmaceuticals GmbH ("BI") manufactured clinical supplies of our drug candidate birtamimab for our prior Phase 1, Phase 2 (PRONTO) and Phase 3 (VITAL) clinical trials. Rentschler Biopharma SE ("Rentschler") is our third-party manufacturer of drug substance for our Phase 3 (AFFIRM-AL) clinical trial. Such drug substance manufactured by Rentschler has been demonstrated to be comparable to the drug substance manufactured by BI. Catalent Indiana, LLC ("Catalent Indiana") is our third-party manufacturer of drug product for our Phase 3 (AFFIRM-AL) clinical trial, and this drug product has been demonstrated to be comparable to the drug product produced by BI. We are dependent on Rentschler and Catalent Indiana to manufacture clinical supplies for our Phase 3 (AFFIRM-AL) clinical trial.

PRX012 - Catalent Pharma Solutions, LLC ("Catalent Pharma") is our third-party manufacturer for drug substance and Sharp Sterile Manufacturing, LLC (formerly known as "Berkshire Sterile Manufacturing, LLC" and hereinafter referred to as "Sharp Sterile") is our third-party manufacturer for drug product for our drug candidate PRX012. We are dependent on Catalent Pharma and Sharp Sterile to manufacture clinical supplies for our Phase 1 clinical trials and any subsequent clinical trials for PRX012.

Prasinezumab - BI manufactured clinical supplies of our drug candidate prasinezumab for our completed Phase 1a single ascending dose and Phase 1b multiple ascending dose clinical trials. Roche, with whom we are collaborating on development of prasinezumab, is manufacturing clinical supplies for the ongoing Phase 2 and any subsequent clinical trials for prasinezumab. We are dependent on Roche, and its third-party manufacturers if applicable, to manufacture these clinical supplies.

Coramitug (formerly PRX004) - Rentschler manufactured clinical supplies of our drug candidate coramitug for our completed Phase 1 clinical trial. In July 2021, we sold shares of one of our wholly-owned subsidiaries to Novo Nordisk. In connection with the transaction, Novo Nordisk acquired our ATTR amyloidosis business, including our drug candidate coramitug. We are dependent on Novo Nordisk, and its third-party manufacturers if applicable, to manufacture clinical supplies of coramitug.

BMS-986446 (formerly PRX005) - Catalent Pharma was our third-party manufacturer for drug substance and Sharp Sterile was our third-party manufacturer for drug product for our drug candidate BMS-986446 for our Phase 1 clinical trial. BMS, with whom we are collaborating on development of BMS-986446, is responsible for manufacturing clinical supplies for any subsequent clinical trials for BMS-986446. We are dependent on BMS, and its third-party manufacturers if applicable, to manufacture these clinical supplies.

PRX019 - Lonza Ltd ("Lonza") is our third-party manufacturer for drug substance and drug product for our drug candidate PRX019. We are dependent on Lonza to manufacture clinical supplies for our Phase 1 clinical trial.

Research and Development

Our research and development expenses totaled $222.5 million, $220.6 million, and $135.6 million in 2024, 2023, and 2022, respectively. For more information, see "Management's Discussion and Analysis of Financial Condition and Results of Operations."

Employees and Human Capital Management

As of December 31, 2024, we had 163 employees, including 27 holding M.D. and/or Ph.D. degrees. Of our employees, 116 were engaged in research and development activities and the remainder were working in general and administrative areas.

To attract and retain qualified employees, we offer a total rewards package consisting of base salary and cash target bonus, a comprehensive benefit and wellness package, and equity compensation for every employee. An objective of our equity incentive program has been, and continues to be, to align the interests of equity incentive plan participants with those of our shareholders. We benchmark and survey the market to ensure we maintain competitive compensation and benefits programs for our employees.

As of December 31, 2024, we employed approximately 63% women and 37% men, and approximately 43% of our employees are racially or ethnically diverse. Our executive team, including employees at or above the vice president level, includes approximately 44% women, and approximately 26% who are racially or ethnically diverse. These figures were estimated by our human resources department.

The well-being, health, and safety of our employees are integral to the success of our business. We utilize numerous policies and strategies to ensure a safe workplace and laboratory environment, and also provide programs for employee wellness. Additionally, because we have a geographically-dispersed workforce, including remote working arrangements, we have efforts focused on engagement and integration of our existing and new employees.

Our Board of Directors has delegated to the Nominating and Corporate Governance Committee the responsibility to oversee and monitor our strategies and policies related to human capital management within our workforce.

Information about Segment and Geographic Revenue

Information about segment and geographic revenue is set forth in Note 2 to the Consolidated Financial Statements included in this report.

Available information

Our principal executive office is at 77 Sir John Rogerson's Quay, Block C, Grand Canal Docklands, Dublin 2, D02 VK60, Ireland, and our telephone number at that address is +353-1-236-2500. We are subject to the information and periodic reporting requirements of the Securities Exchange Act of 1934, as amended, and, in accordance therewith, file periodic reports, proxy statements and other information with the U.S. Securities and Exchange Commission (the "SEC"). Such periodic reports, proxy statements and other information are available for inspection and copying at the SEC's Public Reference Room at 100 F Street, NE., Washington, DC 20549 or may be obtained by calling the SEC at 1-800-SEC-0330. In addition, the SEC maintains a website at www.sec.gov that contains reports, proxy statements and other information regarding issuers that file electronically with the SEC. We also post on the Investors page of our website, www.prothena.com, a link to our filings with the SEC, our Corporate Governance Guidelines and Code of Conduct, which applies to all directors and employees, and the charters of the Audit, Compensation and Nominating and Corporate Governance Committees of our Board of Directors. Our filings with the SEC are posted on our website and are available free of charge as soon as reasonably practical after they are filed electronically with the SEC. Please note that information contained on our website is not incorporated by reference in, or considered to be a part of, this report. You can also obtain copies of these documents free of charge by writing or telephoning us at: Prothena Corporation plc, 77 Sir John Rogerson's Quay, Block C, Grand Canal Docklands, Dublin 2, D02 VK60, Ireland, +353-1-236-2500, or through the Investors page of our website.

ITEM 1A. RISK FACTORS

You should carefully consider the risks described below, together with all of the other information included in this Form 10-K, in considering our business and prospects. Set forth below and elsewhere in this Form 10-K and in other documents we file with the SEC are descriptions of certain risks, uncertainties, and other factors that could cause our actual results to differ materially from those anticipated. If any of the following risks, other unknown risks, or risks that we think are immaterial occur, our business, financial condition, results of operations, cash flows, or growth prospects could be adversely impacted, in which case, the market price of our ordinary shares could decline, and you may lose all or part of your investment in our ordinary shares. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations.

Risks Relating to Our Financial Position, Our Need for Additional Capital, and Our Business

We anticipate that we will incur losses for the foreseeable future and we may never sustain profitability.

We may not generate the cash that is necessary to finance our operations in the foreseeable future. We incurred net losses of $122.3 million, $147.0 million and $116.9 million for the years ended December 31, 2024, 2023, and 2022, respectively. As of December 31, 2024, we had an accumulated deficit of $1.1 billion. We expect to continue to incur substantial losses for the foreseeable future as we:

- support the Phase 3 AFFIRM-AL clinical trial for birtamimab, the Phase 1 clinical trials for PRX012, the Phase 1 clinical trial for PRX019, and potential additional clinical trials for these and other programs, including PRX123;
- develop and possibly commercialize our drug candidates, including birtamimab, PRX012, and PRX123;
- undertake nonclinical development of other drug candidates and initiate clinical trials, if supported by nonclinical data;
- pursue our early stage research and seek to identify additional drug candidates; and
- potentially acquire rights from third parties to drug candidates or technologies through licenses, acquisitions, or other means.

We must generate significant revenue to achieve and maintain profitability. Even if we succeed in discovering, developing, and commercializing one or more drug candidates, we may not be able to generate sufficient revenue and we may never be able to achieve or sustain profitability.

We will require additional capital to fund our operations, and if we are unable to obtain such capital, we will be unable to successfully develop and commercialize drug candidates.

As of December 31, 2024, we had cash and cash equivalents of $471.4 million. The majority of such cash is held in accounts at U.S. banking institutions that we believe are of high quality. Cash held in depository accounts may exceed the $250,000 Federal Deposit Insurance Corporation insurance limits. If such banking institutions were to fail, we could lose all or a portion of those amounts held in excess of such insurance limitations. Although we believe, based on our current business plans, that our existing cash and cash equivalents will be sufficient to meet our obligations for at least the next twelve months, we anticipate that we will require additional capital in order to continue the research and development, and eventual commercialization, of our drug candidates. Our future capital requirements will depend on many factors that are currently unknown to us, including, without limitation:

- the timing of progress, results, and costs of our clinical trials, including the Phase 3 clinical trial for birtamimab, the Phase 2 clinical trial for prasinezumab being conducted by Roche, the Phase 2b clinical trial for prasinezumab being conducted by Roche, the Phase 2 clinical trial for coramitug (formerly PRX004) being conducted by Novo Nordisk, the Phase 2 clinical trial for BMS-986446 being conducted by BMS, the Phase 1 clinical trials for PRX012, and the Phase 1 clinical trial for PRX019;
- the timing, initiation, progress, results, and costs of these and our other research, development, and possible commercialization activities;
- the results of our research, nonclinical studies, and clinical trials;

- the costs of manufacturing our drug candidates for clinical development as well as for future commercialization needs;
- if and when appropriate, the costs of preparing for commercialization of our drug candidates;
- the costs of preparing, filing, and prosecuting patent applications, and maintaining, enforcing, and defending intellectual property-related claims;
- our ability to establish strategic collaborations, licensing, or other arrangements;
- the timing, receipt, and amount of any capital investments, cost-sharing contributions or reimbursements, milestone payments, or royalties that we might receive under current or potential future collaborations;
- 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 have based our expectations relating to liquidity and capital resources on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our drug candidates, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with completing the development and commercialization of our current drug candidates.

In the pharmaceutical industry, the research and development process is lengthy and involves a high degree of risk and uncertainty. This process is conducted in various stages and, during each stage, there is substantial risk that drug candidates in our research and development pipeline will experience difficulties, delays or failures. This makes it difficult to estimate the total costs to complete our clinical trials and to estimate anticipated completion dates with any degree of accuracy, which raises concerns that attempts to quantify costs and provide estimates of timing may be misleading by implying a greater degree of certainty than actually exists.

In order to develop and obtain regulatory approval for our drug candidates we will need to raise substantial additional funds. We expect to raise any such additional funds through public or private equity or debt financings, collaborative agreements with corporate partners, or other arrangements. Our ability to raise additional capital, including our ability to secure new collaborations, may also be adversely impacted by global economic conditions, including any disruptions to, and volatility in, the credit and financial markets in the United States and worldwide, geopolitical turmoil, and the ongoing conflict in Israel and any potential escalation or geographic expansion of such conflict, which could heighten other risks identified in this report. We cannot assure that additional funds will be available when we need them on terms that are acceptable to us or at all. If we raise additional funds by issuing equity securities, including pursuant to our Amended Distribution Agreement (as may be further amended from time to time, and as discussed below), substantial dilution to existing shareholders would result. If we raise additional funds by incurring debt financing, the terms of the debt may involve significant cash payment obligations as well as covenants and specific financial ratios that may restrict our ability to operate our business. We may be required to relinquish rights to our technologies or drug candidates or grant licenses on terms that are not favorable to us in order to raise additional funds through strategic alliances, joint ventures, or licensing arrangements.

If adequate funds are not available on a timely basis, we may be required to:

- terminate or delay clinical trials or other development activities for one or more of our drug candidates;
- delay arrangements for activities that may be necessary to commercialize our drug candidates;
- curtail or eliminate our drug research and development programs that are designed to identify new drug candidates; or
- cease operations.

In addition, if we do not meet our payment obligations to third parties as they come due, we may be subject to litigation claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and distract management and may have unfavorable results that could further adversely impact our financial condition.

Our future success depends on our ability to retain key personnel and to attract, retain, and motivate qualified personnel.

We are highly dependent on key personnel, including Dr. Gene G. Kinney, our President and Chief Executive Officer. There can be no assurance that we will be able to retain Dr. Kinney or any of our key personnel. The loss of the services of Dr. Kinney or any other person on whom we are highly dependent might impede the achievement of our research, development, and commercial objectives. We do not carry "key person" insurance covering any members of our senior management.

Attracting and retaining qualified scientific and other personnel are critical to our growth and future success. Competition for qualified personnel in our industry is intense. We may not be able to attract and retain these personnel on acceptable terms given that competition. Additionally, we may not be able to integrate and motivate qualified personnel to enable them to succeed in their positions. Failure to attract, integrate, retain, and motivate qualified personnel could have a material adverse effect on our business, financial condition, results of operations, and/or growth prospects.

Our collaborators, prospective collaborators, and suppliers may need assurances that our financial resources and stability on a stand-alone basis are sufficient to satisfy their requirements for doing or continuing to do business with us.

Some of our collaborators, prospective collaborators, and suppliers may need assurances that our financial resources and stability on a stand-alone basis are sufficient to satisfy their requirements for doing or continuing to do business with us. If our collaborators, prospective collaborators or suppliers are not satisfied with our financial resources and stability, it could have a material adverse effect on our ability to develop our drug candidates, enter into licenses or other agreements and on our business, financial condition or results of operations.

The agreements we entered into with Elan involve conflicts of interest and therefore may have materially disadvantageous terms to us.

We entered into certain agreements with Elan in connection with our separation from Elan, which set forth the main terms of the separation and provided a framework for our initial relationship with Elan. These agreements may have terms that are materially disadvantageous to us or are otherwise not as favorable as those that might be negotiated between unaffiliated third parties. In December 2013, Elan was acquired by Perrigo Company plc ("Perrigo"), and in February 2014 Perrigo caused Elan to sell all of its shares of Prothena in an underwritten offering. As a result of the acquisition of Elan by Perrigo and the subsequent sale of all of its shares of Prothena, Perrigo may be less willing to collaborate with us in connection with the agreements to which we and Elan are a party and other matters.

We have been, and may in the future be, adversely affected by business disruptions beyond our control, including outbreaks of epidemic, pandemic, or contagious disease, geopolitical turmoil, earthquakes or other natural disasters, and adverse weather events, including as a result of climate change.

The operational and financial impact of a business disruption beyond our control, such as a public health crisis, geopolitical turmoil, or an adverse weather event has, and could, adversely affect our business in the following ways:

- As we have seen with the outbreak of the COVID-19 pandemic, outbreaks of epidemic, pandemic, or contagious disease or other public health emergencies have historically and may in the future disrupt our operations, including clinical trials, research and nonclinical studies, the manufacture or shipment of both drug substance and finished drug product for drug candidates for preclinical testing and clinical trials, and access to stable credit and financial markets in the United States and worldwide. For example, the Phase 3 clinical trial for birtamimab and the Phase 2 clinical trial for prasinezumab conducted by Roche were disrupted by the COVID-19 pandemic as a result of (i) the inability or unwillingness of study participants, site investigators or other study personnel to travel to clinical trial sites or otherwise follow study protocols and (ii) the diversion of healthcare resources away from the conduct of clinical trials.

- Geographic regions where we operate may be affected by war, terrorism, or political instability, and our operations may be vulnerable to disruption, including disturbances to the credit and financial markets (in such region or worldwide), or to services generally, including healthcare services. For example, the Phase 3 clinical trial for birtamimab has clinical trial sites located globally, including in Israel and Eastern Europe, and operations at such clinical trial sites may be disrupted by ongoing conflicts and/or new conflicts, which could result in (i) the inability or unwillingness of study participants, site investigators or other study personnel to travel to such clinical trial sites or otherwise follow study protocols, (ii) the diversion of healthcare resources away from the conduct of clinical trials, or (iii) the complete or partial cessation of operations at such clinical trial sites.

- Our key research facility and a significant portion of our operations are in the San Francisco Bay Area of Northern California, which in the past has experienced severe earthquakes. If an earthquake, other natural disaster, or similar event were to occur and prevent us from using all or a significant portion of those operations or local critical infrastructure, or that otherwise disrupts our operations, it could be difficult or impossible for us to continue our business for a substantial period of time. We have disaster recovery and business continuity plans, but they may prove to be inadequate in the event of a natural disaster or similar event. We may incur substantial expenses if our disaster recovery and business continuity plans prove to be inadequate. We do not carry earthquake insurance. Furthermore, third parties upon which we are materially dependent upon, including our clinical trial sites, may be vulnerable to natural disasters or similar events.

- Climate change could have an impact on longer-term natural weather trends. Extreme weather events that are linked to rising temperatures, changing global weather patterns, sea, land and air temperatures, as well as sea levels, rain and snow could result in increased occurrence and severity of adverse weather events.

Any one or more of these force majeure events could have a material adverse effect on our liquidity, results of operations, financial condition or business, including the progress of, and timelines for, our nonclinical and clinical development programs, and may create safety challenges for our employees and safe occupancy of our job sites, financial market volatility and significant macroeconomic uncertainty in global markets. Furthermore, any governmental or business actions, or any actions taken by individuals in response to any such events (including mandatory quarantines, travel restrictions, delay in operations of the U.S. FDA and comparable foreign regulatory agency, and interruptions to healthcare services), may divert healthcare resources away from the conduct of clinical trials and development programs.

We may experience breaches or similar disruptions of our information technology systems or data.

Our business is increasingly dependent on critical, complex, and interdependent information technology systems to support business processes as well as internal and external communications. Despite the implementation of security measures, our internal computer systems, and those of our current and any future CROs and other contractors, consultants, and collaborators, have been subject to and remain vulnerable to damage from cyberattacks, "phishing" attacks, ransomware, computer viruses, unauthorized access, natural disasters, terrorism, war, and telecommunication or electrical failures. Attacks upon information technology systems are increasing in their frequency, levels of persistence, sophistication, and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. As a result of the COVID-19 pandemic, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to or to sabotage systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. Any breakdown, malicious intrusion, or computer virus could result in the impairment of key business processes or breach of data security, which could result in a material disruption of our development programs and cause interruptions in our business operations, whether due to a loss of our trade secrets or other intellectual property or lead to unauthorized disclosure of personal data of our employees, third parties with which we do business, clinical trial participants, or others. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, such a breach may require notification to governmental agencies, the media, or individuals pursuant to applicable data privacy and security law and regulations. Such an event could have an adverse effect on our business, financial condition, or results of operations.

Changes in and failures to comply with U.S. and foreign privacy and data protection laws, regulations, and standards may adversely affect our business, operations, and financial performance.

We and our partners are subject to certain federal, state, and foreign data privacy and security laws and regulations. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues, which may affect our business and may increase our compliance costs and exposure to liability. In the United States, numerous federal and state laws and regulations, including state security breach notification laws, federal and state health information privacy laws (including U.S. Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), as amended by the Health Information Technology for Economic and Clinical Health Act, and regulations promulgated thereunder), and federal and state consumer protection laws (including Section 5 of the Federal Trade Commission Act), govern the collection, use, disclosure, and protection of personal information. Each of these laws is subject to varying interpretations by courts and government agencies, creating complex compliance issues. State privacy laws in particular are evolving, with more than a dozen new state privacy laws passed in recent years, along with additional health privacy specific laws. These laws may further increase our compliance obligations, and potential legal privacy risks. For example, Washington

recently passed the My Health My Data Act, which has a broader scope than HIPAA and includes a private right of action. In addition, we may obtain health information from third parties, including research institutions from which we obtain clinical trial data, that are subject to privacy and security requirements under HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and the regulations promulgated thereunder. Depending on the facts and circumstances, we could be subject to significant penalties if we obtain, use or disclose individually identifiable health information in a manner that is not authorized or permitted by HIPAA.

Compliance with these and any other applicable privacy and data security laws and regulations is a rigorous and time-intensive process, and we may be required to substantially amend existing procedures and policies or put in place additional procedures and policies to ensure compliance with privacy and data protection rules and requirements. These changes could adversely impact our business by increasing operational and compliance costs or impact business practices. Further, there is a risk that the amended policies and procedures will not be implemented correctly or that individuals within the business will not be fully compliant with the new procedures. If we fail to comply with any such laws or regulations, we may face significant litigation, government investigations, fines and penalties as well as reputational damage which could adversely affect our business, operations, financial condition and prospects. Furthermore, the laws are not consistent, and compliance in the event of a widespread data breach is costly. In addition, states are constantly adopting new laws or amending existing laws, requiring attention to frequently changing regulatory requirements. For example, the California Consumer Privacy Act (the "CCPA") went into effect January 1, 2020. The CCPA, among other things, imposes new data privacy obligations on covered companies and provides expanded privacy rights to California residents, including the right to access, delete, and opt out of certain disclosures of their information. The CCPA provides for civil penalties for violations, as well as a private right of action with statutory damages for certain data breaches, which may increase the frequency and likelihood of data breach litigation. Although the law includes limited exceptions for health-related information, including clinical trial data, such exceptions may not apply to all of our operations and processing activities. Further, the California Privacy Rights Act (the "CPRA") imposes additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It also creates a California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions went into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. Although the CCPA currently exempts certain health-related information, including clinical trial data, the CCPA and the amendments under the CPRA may increase our compliance costs and potential liability.

Multiple states have followed California to legislate comprehensive privacy laws with data privacy rights. For example, Virginia passed the Virginia Consumer Data Protection Act, which went into effect on January 1, 2023, and affords consumers similar rights to the CCPA, along with additional rights, such as the right to opt-out of processing for profiling and targeted advertising purposes. Additionally, the Colorado Privacy Act and Connecticut Personal Data Privacy and Online Monitoring Act went into effect on July 1, 2023. While these new laws generally include exemptions for HIPAA-covered and clinical trial data, they impact the overall privacy landscape. Several other states have followed suit and passed similar legislation which will go into effect in the coming years. Further, additional privacy laws that are similar in nature have been proposed in other states and at the federal level and, if passed, such laws may have potentially conflicting requirements that would make compliance challenging.

We are also or may become subject to rapidly evolving data protection laws, rules, and regulations in foreign jurisdictions. For example, in the European Union ("EU"), the EU General Data Protection Regulation (the "EU GDPR") governs the collection of, and other processing activities involving, personal data (i.e., data which identifies an individual or from which an individual is identifiable), including clinical trial data, and grants individuals various data protection rights (e.g., the right to the erasure of personal data). The EU GDPR imposes a number of obligations on companies, including inter alia: (i) accountability and transparency requirements, and enhanced requirements for obtaining valid consent; (ii) obligation to consider data protection when any new products or services are developed, and to limit the amount of personal data processed; and (iii) obligations to implement appropriate technical and organizational measures to safeguard personal data and to report certain personal data breaches to: (x) the data protection supervisory authority without undue delay (and no later than 72 hours, where feasible) after becoming aware of the personal data breach, unless the personal data breach is unlikely to result in a risk to the data subjects' rights and freedoms; and (y) affected data subjects where the personal data breach is likely to result in a high risk to their rights and freedoms. In addition, the EU GDPR prohibits the transfer of personal data from the European Economic Area ("EEA") to jurisdictions that the European Commission does not recognize as having "adequate" data protection laws unless a data transfer mechanism has been put in place or a derogation under the EU GDPR can be relied on. In July 2020, the Court of Justice of the EU limited how organizations could lawfully transfer personal data from the EEA to the United States by invalidating the EU-US Privacy Shield Framework for purposes of international transfers and imposing further restrictions on the use of standard contractual clauses ("EU SCCs") including, a requirement for companies to carry out a transfer privacy impact assessment ("TIA"), which, among other things, assesses the laws governing access to personal data in the recipient

country and considers whether supplementary measures that provide privacy protections additional to those provided under the EU SCCs will need to be implemented to ensure an "essentially equivalent" level of data protection to that afforded in the EEA. On July 31, 2023, the European Commission adopted its Final Implementing Decision granting the United States adequacy ("Adequacy Decision"), for EU-U.S. transfers of personal data for entities self-certified to the EU-U.S. Data Privacy Framework ("DPF"). Entities relying on EU SCCs for transfers to the United States are also able to rely on the analysis in the Adequacy Decision as support for their TIA regarding the equivalence of U.S. national security safeguards and redress. The EU GDPR imposes substantial fines for breaches and violations (up to the greater of €20 million or 4% of the noncompliant company's total annual global turnover). The EU GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with data protection supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the EU GDPR.

The EU GDPR has been implemented (as implemented, the "UK GDPR") in the United Kingdom ("UK"). The UK GDPR sits alongside the UK Data Protection Act 2018 which implements certain derogations in the EU GDPR into UK law. Under the UK GDPR, companies not established in the UK but which process personal data in relation to the offering of goods or services to individuals in the UK, or the monitoring of their behavior will be subject to the UK GDPR – the requirements of which are (at this time) largely aligned with those under the EU GDPR and as such, may lead to similar compliance and operational costs with potential fines up to the greater of £17.5 million or 4% of the noncompliant company's total annual global turnover. The UK GDPR also imposes similar restrictions on international transfers of personal data from the UK to jurisdictions that the UK Government does not consider "adequate". The UK's Information Commissioner's Office published: (i) its own form of EU SCCs, known as the International Data Transfer Agreement for transfers to outside the UK; (ii) a "UK addendum" to the new EU SCCs which amends the relevant provisions of such clauses to work in a UK context; and (iii) its own version of the TIA (although entities may choose to adopt either the EU or UK-style TIA). Further, on September 21, 2023, the UK Secretary of State for Science, Innovation and Technology established a UK-U.S. data bridge (i.e., a UK equivalent of the Adequacy Decision) and adopted UK regulations to implement the UK-U.S. data bridge ("UK Adequacy Regulations"). Personal data may now be transferred from the UK under the UK-U.S. data bridge through the UK extension to the DPF to organizations self-certified under the UK extension to the DPF. The above-described changes may lead to additional costs and increase our overall risk exposure.

Compliance with U.S. and foreign data privacy and security laws, rules, and regulations have required us, and may require us in the future, to take on more onerous obligations in our contracts, require us to engage in costly compliance exercises, restrict our ability to collect, use and disclose data, or in some cases, impact our or our partners' or suppliers' ability to operate in certain jurisdictions. Each of these constantly evolving laws can be subject to varying interpretations. If we fail to comply with any such laws, rules, or regulations, we may face government investigations and/or enforcement actions, fines, civil or criminal penalties, private litigation, or adverse publicity that could adversely affect our business, financial condition, and results of operations.

Risks Related to the Discovery, Development, and Regulatory Approval of Drug Candidates

Our success is largely dependent on the success of our research and development programs. Our drug candidates are in various stages of development and we may not be able to successfully discover, develop, obtain regulatory approval for, or commercialize any drug candidates.

The success of our business depends substantially upon our ability to discover, develop, obtain regulatory approval for and commercialize our drug candidates successfully. Our research and development programs are prone to the significant and likely risks of failure inherent in drug development, which can result from the failure of the drug candidate to be sufficiently effective, the safety profile of the drug candidate, a clinical trial that is not sufficiently enrolled or powered or adequately designed to detect a drug effect, or other reasons. We intend to continue to invest most of our time and financial resources in our research and development programs.

There is no assurance that the results of the Phase 3 clinical trial for birtamimab, the Phase 2 clinical trial for prasinezumab, the Phase 2b clinical trial for prasinezumab, the Phase 2 clinical trial for coramitug, the Phase 2 clinical trial for BMS-986446, the Phase 1 clinical trials for PRX012, and the Phase 1 clinical trial for PRX019 will support further development of these drug candidates. In addition, we currently do not, and may never, have any other drug candidates in clinical trials, and we have not identified drug candidates for many of our research programs.

Before obtaining regulatory approvals for the commercial sale of any drug candidate for a target indication, we must demonstrate with substantial evidence gathered in adequate and well-controlled clinical trials that the drug candidate is safe and effective for use for that target indication. In the U.S., this must be done to the satisfaction of the FDA; in the EU, this must be

done to the satisfaction of the European Medicines Agency (the "EMA"); and in other countries this must be done to the satisfaction of comparable regulatory authorities.

Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain, and subject to unanticipated delays. Despite our efforts, our drug candidates may not:

- offer improvement over existing treatment options;
- be proven safe and effective in clinical trials; or
- meet applicable regulatory standards.

Positive results in nonclinical studies of a drug candidate may not be predictive of similar results in humans during clinical trials, and promising results from early clinical trials of a drug candidate may not be replicated in later clinical trials. Interim results of a clinical trial do not necessarily predict final results. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in early-stage development. Accordingly, the results from completed nonclinical studies and early clinical trials for our drug candidates may not be predictive of the results we may obtain in later stage studies or trials. Our nonclinical studies or clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional nonclinical studies or clinical trials, or to discontinue clinical trials altogether.

Furthermore, we have not marketed, distributed, or sold any products. Our success will, in addition to the factors discussed above, depend on the successful commercialization of any drug candidates that obtain regulatory approval. Successful commercialization may require:

- obtaining and maintaining commercial manufacturing arrangements with third-party manufacturers;
- developing the marketing and sales capabilities, internal and/or in collaboration with pharmaceutical companies or contract sales organizations, to market and sell any approved drug; and
- acceptance of any approved drug in the medical community and by patients and third-party payers.

Many of these factors are beyond our control. We do not expect any of our drug candidates to be commercially available for several years and some or all may never become commercially available. Accordingly, we may never generate revenues through the sale of products.

We have entered into collaborations with Roche and BMS and may enter into additional collaborations in the future, and we might not realize the anticipated benefits of such collaborations.

Research, development, commercialization and/or strategic collaborations, including those that we have with Roche and BMS, are subject to numerous risks, which include the following:

- collaborators may have significant control or discretion in determining the efforts and resources that they will apply to a collaboration, and might not commit sufficient efforts and resources or might misapply those efforts and resources;
- we may have limited influence or control over the approaches to research, development, and/or commercialization of products candidates in the territories in which our collaboration partners lead research, development, and/or commercialization;
- collaborators might not pursue research, development, and/or commercialization of collaboration drug candidates or might elect not to continue or renew research, development, and/or commercialization programs based on nonclinical and/or clinical trial results, changes in their strategic focus due to the acquisition of competing products, availability of funding, or other factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators might delay, provide insufficient resources to, or modify or stop research or clinical development for collaboration drug candidates or require a new formulation of a drug candidate for clinical testing;
- collaborators could develop or acquire products outside of the collaboration that compete directly or indirectly with our drug candidates or require a new formulation of a drug candidate for nonclinical and/or clinical testing;

- collaborators with sales, marketing, and distribution rights to one or more drug candidates might not commit sufficient resources to sales, marketing, and distribution or might otherwise fail to successfully commercialize those drug candidates;

- collaborators might not properly maintain or defend our intellectual property rights or might use our intellectual property improperly or in a way that jeopardizes our intellectual property or exposes us to potential liability;

- collaboration activities might result in the collaborator having intellectual property covering our activities or drug candidates, which could limit our rights or ability to research, develop, and/or commercialize our drug candidates;

- collaborators might not be in compliance with laws applicable to their activities under the collaboration, which could impact the collaboration or us;

- disputes might arise between us and a collaborator that could cause a delay or termination of the collaboration or result in costly litigation that diverts management attention and resources; and

- collaborations might be terminated, which could result in a need for additional capital to pursue further research, development, and/or commercialization of our drug candidates.

In addition, funding provided by a collaborator might not be sufficient to advance drug candidates under the collaboration.

If a collaborator terminates a collaboration or a program under a collaboration, including by failing to exercise a license or other option under the collaboration, whether because we fail to meet a milestone or otherwise, any potential revenue from the collaboration would be significantly reduced or eliminated. In addition, we will likely need to either secure other funding to advance research, development, and/or commercialization of the relevant drug candidate or abandon that program, the development of the relevant drug candidate could be significantly delayed, and our cash expenditures could increase significantly if we are to continue research, development, and/or commercialization of the relevant drug candidates.

Any one or more of these risks, if realized, could reduce or eliminate future revenue from drug candidates under our collaborations, and could have a material adverse effect on our business, financial condition, results of operations, and/or growth prospects.

If clinical trials of our drug candidates are prolonged, delayed, suspended, or terminated, we may be unable to commercialize our drug candidates on a timely basis, if at all, which would require us to incur additional costs and delay or prevent our receipt of any revenue from potential product sales.

We cannot predict whether we, or our partners (as applicable), will encounter problems with the Phase 3 clinical trial for birtamimab, the Phase 2 clinical trial for prasinezumab, the Phase 2b clinical trial for prasinezumab, the Phase 2 clinical trial for coramitug, the Phase 2 clinical trial for BMS-986446, the Phase 1 clinical trials for PRX012, the Phase 1 clinical trial for PRX019, or any other future clinical trials that will cause us or any regulatory authority to delay, suspend or terminate those clinical trials or delay the analysis of data derived from them. A number of events, including any of the following, could delay the completion of our ongoing or planned clinical trials and negatively impact our ability to obtain regulatory approval for, and to market and sell, a particular drug candidate:

- conditions imposed on us by the FDA, the EMA, or other comparable regulatory authorities regarding the scope or design of our clinical trials;

- delays in obtaining, or our inability to obtain, required approvals from institutional review boards ("IRBs") or other reviewing entities at clinical sites selected for participation in our clinical trials;

- insufficient supply or deficient quality of our drug candidates or other materials necessary to conduct our clinical trials;

- delays in obtaining regulatory authority authorization for the conduct of our clinical trials;

- lower than anticipated enrollment and/or retention rate of subjects in our clinical trials, which can be impacted by a number of factors, including size of patient population, design of trial protocol, trial length, eligibility criteria, perceived risks and benefits of the drug candidate, patient proximity to trial sites, patient referral practices of physicians, availability of other treatments for the relevant disease, and competition from other clinical trials;

- slower than expected rates of events in trials with a primary endpoint that is event-based;
- serious and unexpected drug-related side effects experienced by subjects in clinical trials; or
- failure of our third-party contractors and collaborators to meet their contractual obligations to us or otherwise meet their development or other objectives in a timely manner.

Further, conducting clinical trials in foreign countries, as we do and may continue do for our drug candidates, presents potential additional risks for our clinical trials. These risks include the failure in foreign countries to adhere to clinical protocol as a result of differences in regional or local healthcare services or customs, obtaining clinical data and/or clinical samples from sites in such foreign countries, managing additional administrative burdens associated with foreign regulatory requirements, as well as political and economic risks relevant to such foreign countries.

We are dependent upon Roche with respect to further development of prasinezumab. Under the terms of our collaboration with Roche, Roche is responsible for that further development, including the conduct of the ongoing Phase 2 and Phase 2b clinical trials and any future clinical trial of that drug candidate.

We are dependent upon Novo Nordisk with respect to further development of coramitug, including the Phase 2 clinical trial and any future clinical trial of that drug candidate.

We are dependent upon BMS with respect to further development of BMS-986446, including the Phase 2 clinical trial and any future clinical trial of that drug candidate.

Clinical trials may also be delayed or terminated as a result of ambiguous or negative data or results. In addition, a clinical trial may be delayed, suspended or terminated by us, the FDA, the EMA or other comparable regulatory authorities, the IRBs for the sites where the IRBs are overseeing a trial, or the safety oversight committee overseeing the clinical trial at issue due to a number of factors, including:

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;
- inspection of the clinical trial operations or trial sites by the FDA, the EMA, or other regulatory authorities resulting in the imposition of a clinical hold on or imposition of additional conditions for the conduct of the trial;
- interpretation of data by the FDA, the EMA, or other regulatory authorities;
- requirement by the FDA, the EMA, or other regulatory authorities to perform additional studies;
- failure to achieve primary or secondary endpoints or other failure to demonstrate efficacy or adequate safety;
- unforeseen safety issues; or
- lack of adequate funding to continue the clinical trial.

Additionally, changes in regulatory requirements and guidance may occur and we may need to amend clinical trial protocols to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to regulatory authorities and IRBs for reexamination, which may impact the cost, timing, or successful completion of a clinical trial. For example, the FDA may modify or enhance clinical trial requirements which could affect enrollment and retention of patients. Such effects on recruitment and retention of patients may hinder or delay a clinical trial, which could increase costs and delay clinical programs.

We do not know whether our clinical trials will be conducted as planned, will need to be restructured, or will be completed on schedule, if at all. Delays in our clinical trials will result in increased development costs for our drug candidates. In addition, if we experience delays in the completion of, or if we terminate, any of our clinical trials, the commercial prospects for our drug candidates may be delayed or harmed and our ability to generate product revenues will be delayed or jeopardized. Furthermore, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of a drug candidate.

The regulatory approval processes of the FDA, the EMA, and other comparable regulatory authorities are lengthy, time consuming, and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our drug candidates, our business will be substantially harmed.

The time required to obtain approval by the FDA, the EMA, and other comparable regulatory authorities is inherently unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a drug candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any drug candidate, and it is possible that none of our existing drug candidates or any drug candidates we may seek to develop in the future will ever obtain regulatory approval.

Our drug candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA, the EMA, or comparable regulatory authorities may disagree with the design, implementation, or conduct of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA, the EMA, or comparable regulatory authorities that a drug candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA, the EMA, or comparable regulatory authorities for approval;
- we may be unable to demonstrate that a drug candidate's clinical and other benefits outweigh its safety risks;
- the FDA, the EMA, or comparable regulatory authorities may disagree with our interpretation of data from nonclinical studies or clinical trials;
- the data collected from clinical trials of our drug candidates may not be sufficient to support the submission of an NDA or a BLA to the FDA, a Marketing Authorization Application ("MAA") to the EMA, or similar applications to comparable regulatory authorities;
- the FDA, the EMA, or comparable regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; or
- the approval policies or regulations of the FDA, the EMA, or comparable regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our drug candidates, which would significantly harm our business, results of operations, and/or growth prospects.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our drug candidates for fewer or more limited indications than we request, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a drug candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that drug candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our drug candidates.

The FDA or other comparable foreign regulatory authorities may not accept data from trials conducted in locations outside of their jurisdiction.

We are and may choose to conduct international clinical trials in the future. The acceptance of study data by the FDA or other comparable foreign regulatory authority from clinical trials conducted outside of their respective jurisdictions may be subject to certain conditions. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (1) the data are applicable to the United States population and United States medical practice; (2) the trials are performed by clinical investigators of recognized competence; and (3) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. In addition, such foreign trials would be subject to the applicable local laws of

the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any other comparable foreign regulatory authority will accept data from trials conducted outside of its applicable jurisdiction. If the FDA or any other comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our product candidates not receiving approval for commercialization in the applicable jurisdiction.

Even if our drug candidates receive regulatory approval in one country or jurisdiction, we may never receive approval or commercialize our products in other countries or jurisdictions.

In order to market drug candidates in a particular country or jurisdiction, we must establish and comply with numerous and varying regulatory requirements of that country or jurisdiction, including with respect to safety and efficacy. Approval procedures vary among countries and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from that required to obtain, for example, FDA approval in the U.S. or EMA approval in the EU. The regulatory approval process in other countries may include all of the risks detailed above regarding FDA approval in the U.S. and EMA approval in the EU as well as other risks. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another country or jurisdiction, but a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. Failure to obtain regulatory approval in one country or jurisdiction or any delay or setback in obtaining such approval would impair our ability to develop other markets for that drug candidate.

Although we have obtained agreement with the FDA on a special protocol assessment ("SPA") with regard to our Phase 3 AFFIRM-AL clinical trial of birtamimab, a SPA does not guarantee approval of birtamimab or any other particular outcome from regulatory review.

On January 27, 2021, the FDA agreed to a SPA for our Phase 3 AFFIRM-AL clinical trial of birtamimab. The FDA's SPA process is designed to facilitate the FDA's review and approval of drugs by allowing the FDA to evaluate proposed critical design features of certain clinical trials that are intended to form the primary basis for determining a drug candidate's efficacy and safety. Upon specific request by a clinical trial sponsor, the FDA will evaluate the study protocol and statistical analysis plan and respond to a sponsor's questions regarding protocol design and scientific and regulatory requirements. FDA aims to complete SPA reviews within 45 days of receipt of the request. The FDA ultimately assesses whether specific elements of the protocol design for the trial, such as entry criteria, endpoints, size, duration, and planned analyses, are acceptable to support an application for regulatory approval of the drug candidate with respect to the effectiveness of and safety for the indication studied. All agreements and disagreements between the FDA and the sponsor regarding a SPA must be clearly documented in a SPA letter or the minutes of a meeting between the sponsor and the FDA.

Although the FDA has agreed to the SPA for our Phase 3 AFFIRM-AL clinical trial with respect to the primary endpoint and certain other aspects of the clinical trial, a SPA agreement does not guarantee approval of a drug candidate. The FDA may limit the scope of its agreement to a SPA agreement to certain, specific aspects of the clinical trial design. Even if the FDA agrees to the design, execution, and analysis proposed in a protocol reviewed under the SPA process, the FDA may revoke or alter its agreement in certain circumstances. In particular, a SPA agreement is not binding on the FDA if public health concerns emerge that were unrecognized at the time of the SPA agreement, other new scientific concerns regarding product safety or efficacy arise, the sponsor fails to comply with the agreed upon study protocol, or the relevant data, assumptions, or information provided by the sponsor in a request for the SPA change or are found to be false or to omit relevant facts. In addition, even after a SPA agreement is finalized, the SPA agreement may be modified, and such modification will be deemed binding on the FDA review division, except under the circumstances described above, if the FDA and the sponsor agree in writing to the modification of the study protocol and/or statistical analysis plan. Generally, such modification is intended to improve the study. The FDA retains significant latitude and discretion in interpreting the terms of the SPA agreement and the data and results from any study that is the subject of the SPA agreement.

Moreover, if the FDA revokes or alters its agreement under the SPA, or interprets the data collected from the clinical trial differently than the sponsor, the FDA may not deem the data sufficient to support an application for regulatory approval.

Both before and after marketing approval, our drug candidates are subject to ongoing regulatory requirements and continued regulatory review, and if we fail to comply with these continuing requirements, we could be subject to a variety of sanctions and the sale of any approved products could be suspended.

Both before and after regulatory approval to market a particular drug candidate, adverse event reporting, manufacturing, labeling, packaging, storage, distribution, advertising, promotion, record keeping, and reporting related to the product are subject to extensive, ongoing regulatory requirements. These requirements include submissions of safety and other post-

marketing information and reports, as well as continued compliance with current good manufacturing practice ("cGMP") requirements and current good clinical practice ("cGCP") requirements for any clinical trials that we conduct. Any regulatory approvals that we receive for our drug candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the drug candidate. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or not previously observed in clinical trials, or problems with our third-party manufacturers or manufacturing processes, or failure to comply with the regulatory requirements of the FDA, the EMA, or other comparable regulatory authorities could subject us to administrative or judicially imposed sanctions, including:

- restrictions on the marketing of our products or their manufacturing processes;
- warning letters;
- civil or criminal penalties;
- fines;
- injunctions;
- product seizures or detentions;
- import or export bans;
- voluntary or mandatory product recalls and related publicity requirements;
- suspension or withdrawal of regulatory approvals;
- total or partial suspension of production; and
- refusal to approve pending applications for marketing approval of new products or supplements to approved applications.

The policies of the FDA, the EMA, or other comparable regulatory authority may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

If side effects are identified during the time our drug candidates are in development, or, if they are approved by applicable regulatory authorities, after they are on the market, we may choose to or be required to perform lengthy additional clinical trials, discontinue development of the affected drug candidate, change the labeling of any such products, or withdraw any such products from the market, any of which would hinder or preclude our ability to generate revenues.

Undesirable side effects caused by our drug candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, the EMA, or other comparable regulatory authorities. Drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete a trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly. Even if any of our drug candidates receives marketing approval, as greater numbers of patients use a drug following its approval, an increase in the incidence or severity of side effects or the incidence of other post-approval problems that were not seen or anticipated during pre-approval clinical trials could result in a number of potentially significant negative consequences, including:

- regulatory authorities may withdraw their approval of the product;
- regulatory authorities may require the addition of labeling statements, such as contraindications, warnings, or precautions; or impose additional safety monitoring or reporting requirements;
- we may be required to change the way the product is administered, or to conduct additional clinical trials;

- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could substantially increase the costs and expenses of developing, commercializing and marketing any such drug candidates or could harm or prevent sales of any approved products.

We deal with hazardous materials and must comply with environmental laws and regulations which can be expensive and restrict how we do business.

Some of our research and development activities involve the controlled storage, use, and disposal of hazardous materials. We are subject to U.S. federal, state, local, and other countries' and jurisdictions' laws and regulations governing the use, manufacture, storage, handling, and disposal of these hazardous materials. Although we believe that our safety procedures for the handling and disposing of these materials comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental contamination or injury from these materials. In the event of an accident, state or federal authorities may curtail our use of these materials, and we could be liable for any civil damages that result, which may exceed our financial resources and may seriously harm our business. Because we believe that our laboratory and materials handling policies and practices sufficiently mitigate the likelihood of materials liability or third-party claims, we currently carry no insurance covering such claims. An accident could damage, or force us to shut down, our operations.

Risks Related to the Commercialization of Our Drug Candidates

Even if any of our drug candidates receives regulatory approval, if such approved product does not achieve broad market acceptance, the revenues that we generate from sales of the product will be limited.

Even if any drug candidates we may develop or acquire in the future obtain regulatory approval, they may not gain broad market acceptance among physicians, healthcare payers, patients and the medical community. The degree of market acceptance for any approved drug candidate will depend on a number of factors, including:

- the indication and label for the product and the timing of introduction of competitive products;
- demonstration of clinical safety and efficacy compared to other products;
- prevalence, frequency, and severity of adverse side effects;
- availability of coverage and adequate reimbursement from managed care plans and other third-party payers;
- convenience and ease of administration;
- cost-effectiveness;
- other potential advantages of alternative treatment methods; and
- the effectiveness of marketing and distribution support of the product.

Consequently, even if we discover, develop, and commercialize a product, the product may fail to achieve broad market acceptance and we may not be able to generate significant revenue from the product.

The success of prasinezumab in the United States, if approved, will be dependent upon the strength and performance of our collaboration with Roche. If we fail to maintain our existing collaboration with Roche, such termination would likely have a material adverse effect on our ability to develop and commercialize prasinezumab and our business. Furthermore, in May 2021, we opted out of profit and loss sharing with Roche for prasinezumab in Parkinson's disease; however if we opt out of profit and loss sharing for any other Licensed Products and/or indications, our revenues from such other Licensed Products and/or indications will be reduced.

The success of sales of prasinezumab in the U.S. will be dependent on the ability of Roche to successfully develop in collaboration with us, and launch and commercialize prasinezumab, if approved by the FDA, pursuant to the License Agreement we entered into in December 2013. Our collaboration with Roche is complex, particularly with respect to future U.S. commercialization of prasinezumab, with respect to financial provisions, allocations of responsibilities, cost estimates, and

the respective rights of the parties in decision making. Accordingly, significant aspects of the development and commercialization of prasinezumab require Roche to execute its responsibilities under the arrangement, or require Roche's agreement or approval, prior to implementation, which could cause significant delays that may materially impact the potential success of prasinezumab in the U.S. In addition, Roche may under some circumstances independently develop products that compete with prasinezumab, or Roche may decide to not commit sufficient resources to the development, commercialization, marketing and distribution of prasinezumab. If we are not able to collaborate effectively with Roche on plans and efforts to develop and commercialize prasinezumab, our business could be materially adversely affected.

Furthermore, the terms of the License Agreement provide that Roche has the ability to terminate such arrangement for any reason after the first anniversary of the License Agreement at any time upon 90 days' notice (if prior to first commercial sale) or 180 days' notice (if after first commercial sale). For example, even if prasinezumab was approved by the FDA, Roche may determine that the outcomes of clinical trials made prasinezumab a less attractive commercial product and terminate our collaboration. If the License Agreement is terminated, our business and our ability to generate revenue from sales of prasinezumab could be substantially harmed as we will be required to develop, commercialize, and build our own sales and marketing organization, or enter into another strategic collaboration in order to develop and commercialize prasinezumab in the U.S. Such efforts may not be successful and, even if successful, would require substantial time and resources to carry out.

The manner in which Roche launches prasinezumab, if approved by the FDA, including the timing of launch and potential pricing, will have a significant impact on the ultimate success of prasinezumab in the U.S., and the success of the overall commercial arrangement with Roche. If launch of commercial sales of prasinezumab in the U.S. by Roche is delayed or prevented, our revenue will suffer and our stock price may decline. Further, if launch and resulting sales by Roche are not deemed successful, our business would be harmed and our stock price may decline. Any lesser effort by Roche in its prasinezumab sales and marketing efforts may result in lower revenue and thus lower profits with respect to the U.S. The outcome of Roche's commercialization efforts in the U.S. could also have a negative effect on investors' perception of potential sales of prasinezumab outside of the U.S., which could also cause a decline in our stock price.

In May 2021, we opted out of profit and loss sharing with Roche for prasinezumab in Parkinson's disease. However, pursuant to the License Agreement, we are responsible for 30% of all development and commercialization costs for any future Licensed Products and/or indications (other than Parkinson's disease with prasinezumab) that we opt to co-develop, in each case unless we elect to opt out of profit and loss sharing. If we elect to opt out of profit and loss sharing, we will instead receive sales milestones and royalties, and our revenue, if any, from such other Licensed Products and/or indications will be reduced.

Our right to co-develop Licensed Products and/or indications under the License Agreement (other than Parkinson's disease with prasinezumab for which we have opted out of co-development) will terminate if we commence certain studies for a competitive product that treats Parkinson's disease or other indications that we opted to co-develop. In addition, our right to co-promote prasinezumab and other Licensed Products will terminate if we commence a Phase 3 study for a competitive product that treats Parkinson's disease.

Moreover, under the terms of the License Agreement, we rely on Roche to provide us estimates of their costs, revenue, and revenue adjustments and royalties, which estimates we use in preparing our quarterly and annual financial reports. If the underlying assumptions on which Roche's estimates were based prove to be incorrect, actual results or revised estimates supplied by Roche that are materially different from the original estimates could require us to adjust the estimates included in our reported financial results. If material, these adjustments could require us to restate previously reported financial results, which could have a negative effect on our stock price.

Our ability to receive any significant revenue from prasinezumab will be dependent on Roche's efforts and may result in lower levels of income than if we marketed or developed our drug candidates entirely on our own. Roche may not fulfill its obligations or carry out marketing activities for prasinezumab as diligently as we would like. We could also become involved in disputes with Roche, which could lead to delays in or termination of development or commercialization activities and time-consuming and expensive litigation or arbitration. If Roche terminates or breaches the License Agreement, or otherwise decides not to complete its obligations in a timely manner, the chances of successfully developing, commercializing, or marketing prasinezumab would be materially and adversely affected.

Outside of the United States, we are solely dependent on the efforts and commitments of Roche, either directly or through third parties, to further develop and, if prasinezumab is approved by applicable regulatory authorities, commercialize prasinezumab. If Roche's efforts are unsuccessful, our ability to generate future product sales from prasinezumab outside the United States would be significantly reduced.

Under our License Agreement, outside of the U.S., Roche has responsibility for developing and commercializing prasinezumab and any future Licensed Products targeting α-synuclein. As a consequence, any progress and commercial success outside of the U.S. is dependent solely on Roche's efforts and commitment to the program. For example, Roche may delay, reduce, or terminate development efforts relating to prasinezumab outside of the U.S., or under some circumstances independently develop products that compete with prasinezumab, or decide not to commit sufficient resources to the commercialization, marketing, and distribution of prasinezumab.

In the event that Roche does not diligently develop and commercialize prasinezumab, the License Agreement provides us the right to terminate the License Agreement in connection with a material breach uncured for 90 days after notice thereof. However, our ability to enforce the provisions of the License Agreement so as to obtain meaningful recourse within a reasonable timeframe is uncertain. Further, any decision to pursue available remedies including termination would impact the potential success of prasinezumab, including inside the U.S., and we may choose not to terminate as we may not be able to find another partner and any new collaboration likely will not provide comparable financial terms to those in our arrangement with Roche. In the event of our termination, this may require us to develop and commercialize prasinezumab on our own, which is likely to result in significant additional expense and delay. Significant changes in Roche's business strategy, resource commitment and the willingness or ability of Roche to complete its obligations under our arrangement could materially affect the potential success of the drug candidate. Furthermore, if Roche does not successfully develop and commercialize prasinezumab outside of the U.S., our potential to generate future revenue outside of the U.S. would be significantly reduced.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell approved products, we may be unable to generate product revenue.

We do not currently have a fully-scaled organization for the sales, marketing, and distribution of pharmaceutical products. In order to market any products that may be approved by the FDA, the EMA, or other comparable regulatory authorities, we must build our sales, marketing, managerial, and other non-technical capabilities or make arrangements with third parties to perform these services.

We have entered into the License Agreement with Roche for the development of prasinezumab and may develop our own sales force and marketing infrastructure to co-promote prasinezumab in the U.S. for the treatment of Parkinson's disease and any future Licensed Products approved for Parkinson's disease in the U.S. If we exercise our co-promotion option and are unable to develop our own sales force and marketing infrastructure to effectively commercialize prasinezumab or other Licensed Products, our ability to generate additional revenue from potential sales of prasinezumab or such products in the U.S. may be harmed. In addition, our right to co-promote prasinezumab and other Licensed Products will terminate if we commence a Phase 3 study for a competitive product that treats Parkinson's disease.

For any other products that may be approved, if we are unable to establish adequate sales, marketing, and distribution capabilities, whether independently or with third parties, we may not be able to generate product revenue and may not become profitable.

If government and third-party payers fail to provide coverage and adequate reimbursement rates for any of our drug candidates that receive regulatory approval, our revenue and prospects for profitability will be harmed.

In both U.S. and non-U.S. markets, our sales of any future products will depend in part upon the availability of reimbursement from third-party payers. Such third-party payers include government health programs such as Medicare and Medicaid, managed care providers, private health insurers, and other organizations. There is significant uncertainty related to the third-party coverage and reimbursement of newly approved drugs. Coverage and reimbursement may not be available for any drug that we or our collaborators commercialize and, even if these are available, the level of reimbursement may not be satisfactory. Third-party payers often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Third-party payers are also increasingly attempting to contain healthcare costs by demanding price discounts or rebates limiting both coverage and the amounts that they will pay for new drugs, and, as a result, they may not cover or provide adequate payment for our drug candidates. We might need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any future products to such payers' satisfaction. Such studies might require us to commit a significant amount of management time and financial and other resources. Our future products might not ultimately be considered cost-effective. Adequate third-party reimbursement might not be available to enable us to maintain price levels

sufficient to realize an appropriate return on investment in product development. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we or our collaborators may not be able to successfully commercialize any drug candidates for which marketing approval is obtained.

Additionally, pursuant to the Medicaid Drug Rebate Statute, we will be required to participate in the Medicaid Drug Rebate Program in order for federal payment to be available for our products under Medicaid and Medicare Part B. Under the Medicaid Drug Rebate Program, we will be required to, among other things, pay a rebate to each state Medicaid program for quantities of our products utilized on an outpatient basis (with some exceptions) that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program. Medicaid Drug Rebate Program rebates are calculated using a statutory formula, state-reported utilization data, and pricing data that are calculated and reported by us on a monthly and quarterly basis to the Centers for Medicare and Medicaid Services ("CMS"). These data include the average manufacturer price and, in the case of single source and innovator multiple source products, the best price for each drug.

The regulations that govern marketing approvals, pricing, coverage, and reimbursement for new drugs vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or licensing approval is granted. In some countries, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we or our collaborators might obtain marketing approval for a drug in a particular country, but then be subject to price regulations that delay commercial launch of the drug, possibly for lengthy time periods, and negatively impact our ability to generate revenue from the sale of the drug in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more drug candidates, even if our drug candidates obtain marketing approval.

U.S. and other governments continue to propose and pass legislation designed to reduce the cost of healthcare. In the U.S., we expect that there will continue to be federal and state proposals to implement similar governmental controls. In addition, recent changes in the Medicare program and increasing emphasis on managed care in the U.S. will continue to put pressure on pharmaceutical product pricing. For example, in 2010, the U.S. Patient Protection and Affordable Care Act, as amended by the U.S. Health Care and Education Reconciliation Act (collectively, the "ACA"), was enacted. The ACA substantially changed the way healthcare is financed by both governmental and private insurers and significantly affects the pharmaceutical industry. Among the provisions of the ACA of importance to the pharmaceutical industry are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- an increase in the minimum rebates a manufacturer must pay under the U.S. Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- expansion of healthcare fraud and abuse laws, including the U.S. False Claims Act ("FCA") and the U.S. Anti-Kickback Statute, new government investigative powers and enhanced penalties for non-compliance;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- a licensure framework for follow-on biologic products;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- implementation of the federal Physician Payments Sunshine Act, which requires pharmaceutical manufacturers, among others, to annually track and report all payments and other transfers of value they make to certain healthcare providers, as well as physician ownership held in the company;
- a requirement for manufacturers and distributors to annually report drug samples that they provide to physicians; and

- establishment of the Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect in 2013 and will stay in effect through the first six months of the FY 2032 sequestration order, unless additional congressional action is taken, with the exception of a temporary suspension from May 1, 2020, through March 31, 2022, and a subsequent 1% cut in Medicare payments in effect from March 31, 2022 to July 1, 2022, due to the COVID-19 pandemic. In 2013, the U.S. American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our drugs, if approved, and, accordingly, our financial operations.

Since its enactment, there have been judicial, executive, and Congressional challenges to certain aspects of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been signed into law, including the repeal, effective January 1, 2019, of the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states who argued that, without the individual mandate, the entire ACA was unconstitutional. The Supreme Court's dismissal of the lawsuit did not specifically rule on the constitutionality of the ACA.

Moreover, President Biden signed into law the Inflation Reduction Act (IRA) on August 16, 2022, which allows Medicare to: beginning in 2026, establish a "maximum fair price" for a fixed number of pharmaceutical and biological products covered under Medicare Parts B and D following a price negotiation process with CMS; and, beginning in 2023, penalize drug companies that raise prices for products covered under Medicare Parts B and D faster than inflation, among other reforms. CMS has also taken steps to implement the IRA, including: on October 2, 2024, releasing final guidance outlining the process for the second round of price negotiations for products subject to the "maximum fair price" provision; on December 20, 2024, releasing a list of 64 Medicare Part B products that had an adjusted coinsurance rate based on the inflationary rebate provisions of the IRA for the time period of January 1, 2025 to March 31, 2025; and on January 17, 2025, releasing a list of fifteen additional drugs covered under Medicare Part D subject to price negotiations during 2025. It is unclear how future regulatory actions to implement the IRA, as well as the outcome of pending litigation against the IRA brought against the Department of Health and Human Services (HHS), the Secretary of HHS, CMS, and the CMS Administrator challenging the constitutionality and administrative implementation of the IRA's drug price negotiation provisions, may affect our products and future profitability.

Additionally, on October 14, 2022, President Biden issued an Executive Order on Lowering Prescription Drug Costs for Americans, which instructed the Secretary of HHS to consider whether to select for testing by the CMS Innovation Center new health care payment and delivery models that would lower drug costs and promote access to innovative drug therapies for beneficiaries enrolled in the Medicare and Medicaid programs. On February 14, 2023, HHS issued a report in response to the October 14, 2022 Executive Order, which, among other things, selects three potential drug affordability and accessibility models to be tested by the CMS Innovation Center. Specifically, the report addresses: (1) a model that would allow Part D Sponsors to establish a "high-value drug list" setting the maximum co-payment amount for certain common generic drugs at $2.00; (2) a Medicaid-focused model that would establish a partnership between CMS, manufacturers, and state Medicaid agencies that would result in multi-state outcomes-based agreements or certain cell and gene therapy drugs; and (3) a model that would adjust Medicare Part B payment amounts for Accelerated Approval Program drugs to advance the developments of novel treatments.

We expect that other healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved drug. Legislation and regulations affecting the pricing of pharmaceuticals might change before our drug candidates are approved for marketing. Any reduction in reimbursement from Medicare or other government healthcare programs may result in a similar reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our drugs.

There can be no assurance that our drug candidates, if they are approved for sale in the U.S. or in other countries, will be considered medically reasonable and necessary for a specific indication, that they will be considered cost-effective by third-party payers, that coverage or an adequate level of reimbursement will be available, or that third-party payers' reimbursement policies will not adversely affect our ability to sell our drug candidates profitably if they are approved for sale.

The markets for our drug candidates are subject to intense competition. If we are unable to compete effectively, our drug candidates may be rendered noncompetitive or obsolete.

The research, development, and commercialization of new drugs is highly competitive. We will face competition with respect to all drug candidates we may develop or commercialize in the future from pharmaceutical and biotechnology companies worldwide. The key factors affecting the success of any approved product will be its indication, label, efficacy, safety profile, drug interactions, method of administration, pricing, coverage, reimbursement, and level of promotional activity relative to those of competing drugs.

Furthermore, many large pharmaceutical and biotechnology companies, academic institutions, governmental agencies, and other public and private research organizations are pursuing the development of novel drugs that target the same indications we are targeting with our research and development program. We face, and expect to continue to face, intense and increasing competition as new products enter the market and advanced technologies become available. Many of our competitors have:

- significantly greater financial, technical and human resources than we have and may be better equipped to discover, develop, manufacture, and commercialize drug candidates;
- more extensive experience in nonclinical testing and clinical trials, obtaining regulatory approvals, and manufacturing and marketing pharmaceutical products;
- drug candidates that have been approved or are in late-stage clinical development; and/or
- collaborative arrangements in our target markets with leading companies and research institutions.

Competitive products may render our research and development program obsolete or noncompetitive before we can recover the expenses of developing and commercializing our drug candidates. Furthermore, the development of new treatment methods and/or the widespread adoption or increased utilization of any vaccine or development of other products or treatments for the diseases we are targeting could render any of our drug candidates noncompetitive, obsolete or uneconomical. If we successfully develop and obtain approval for a drug candidate, we will face competition based on the safety and effectiveness of the approved product, the timing of its entry into the market in relation to competitive products in development, the availability and cost of supply, marketing and sales capabilities, coverage, reimbursement, price, patent position and other factors. Even if we successfully develop drug candidates but those drug candidates do not achieve and maintain market acceptance, our business will not be successful.

Our drug candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated.

Our current drug candidates are regulated by the FDA as biologic products and we intend to seek approval for these products pursuant to the BLA pathway. The U.S. Biologics Price Competition and Innovation Act of 2009 (the "BPCIA") created an abbreviated pathway for the approval of biosimilar and interchangeable biologic products. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an existing brand product.

Under the BPCIA, an application for a biosimilar product cannot be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA, and cannot be approved by the FDA until 12 years after the original branded product was approved under a BLA. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. However, during the 12-year period of reference product exclusivity, another company may obtain FDA licensure and market a competing version of the reference product if the FDA approves a full de novo BLA, not an abbreviated BLA for a biosimilar product, for the competing product containing that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product.

The law is complex and is still being interpreted and implemented by the FDA. Any processes adopted by the FDA to implement the BPCIA could have a material adverse effect on the future commercial prospects for our biologic products. In addition, there has been discussion of whether Congress should reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate implementation of the BPCIA is subject to significant uncertainty.

We believe that any of our drug candidates approved as a biologic product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise,

or that the FDA will not consider our drug candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biologic products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

We may be unable to maintain the benefits associated with Orphan Drug Designation, including the potential for supplemental market exclusivity.

Birtamimab has been granted Orphan Drug Designation by both the FDA and EMA for the treatment of AL amyloidosis. In addition, we may seek Orphan Drug Designation for one or more of our current or future drug candidates. Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drug products for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may grant orphan designation to a drug product intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 in the United States. In the United States, Orphan Drug Designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. Orphan Drug Designation does not convey any advantage in, or shorten the duration of, the regulatory review and licensure process.

If a drug product that has Orphan Drug Designation subsequently receives the first FDA approval or licensure for a particular active ingredient for the disease for which it has such designation, the drug product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including an NDA or BLA, to market the same drug product for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the biological product was designated. As a result, even if one of our drug candidates receives orphan exclusivity, the FDA can still approve or license other drug products that have a different active ingredient for use in treating the same indication or disease. Further, the FDA can waive orphan exclusivity if we are unable to manufacture sufficient supply of our drug product.

A Fast Track designation by the FDA, even if granted for current or future drug candidates, may not lead to a faster development or regulatory review, licensure process and does not increase the likelihood that our drug candidates will receive marketing licensure.

Birtamimab, for the treatment of AL amyloidosis, and PRX012 and PRX123, each for the treatment of Alzheimer's disease, have each been granted Fast Track Designation by the FDA. In addition, we may seek Fast Track designation for one or more of our future drug candidates. If a drug candidate is intended for the treatment of a serious condition and demonstrates the potential to address an unmet medical need for this condition, the sponsor may apply for FDA Fast Track designation for a particular indication. We may seek Fast Track designation for our drug candidates, but there is no assurance that the FDA will grant this status to any of our drug candidates. The FDA has broad discretion whether or not to grant Fast Track designation, and even if we consider a particular drug candidate to be eligible for this designation, there is no assurance that it will be granted by the FDA. Even if we do receive Fast Track designation, we may not experience a faster review or approval compared to other, non-expedited FDA procedures, and receiving a Fast Track designation does not provide assurance of ultimate FDA approval. In addition, the FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our applicable clinical development program. Marketing applications filed by sponsors of products granted Fast Track designation may qualify for priority review under FDA policies and procedures, but Fast Track designation does not assure any such review or ultimate marketing approval by the FDA.

We are subject to healthcare and other laws and regulations, including anti-bribery, anti-kickback, fraud and abuse, false claims, and physician payment transparency laws and regulations, which could expose us to criminal, civil and/or administrative sanctions and penalties; exclusion from governmental healthcare programs or reimbursements; contractual damages; and reputational harm.

Our operations and activities are directly, or indirectly through our service providers and collaborators, subject to numerous healthcare and other laws and regulations, including, without limitation, those relating to anti-bribery, anti-kickback, fraud and abuse, false claims, physician payment transparency, and health information privacy and security, in the U.S., the EU, and other countries and jurisdictions in which we conduct our business. These laws include:

- the U.S. federal Anti-Kickback Statute, an intent-based federal criminal statute which prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering, providing, or paying remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or

the purchase, lease, order or arrangement for, or recommendation of an item or service for which payment may be made, in whole or in part, by a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. The term remuneration has been interpreted broadly to include anything of value. Further, courts have found that if any "one purpose" of an arrangement involving remuneration is to induce referrals of federal healthcare program business, the federal Anti-Kickback Statute has been violated. The federal Anti-Kickback Statute applies to arrangements between pharmaceutical manufacturers on the one hand and individuals, such as prescribers, patients, purchasers, and formulary managers on the other hand, including, for example, consulting/speaking arrangements, discount and rebate offers, grants, charitable contributions, and patient support offerings, among others. Although there are several statutory exceptions and regulatory safe harbors to the federal Anti-Kickback Statute that protect certain common industry activities from prosecution, these exceptions and safe harbors are narrowly drawn. Arrangements that do not fully satisfy all elements of an available exception or safe harbor are evaluated based on the specific facts and circumstances and are typically subject to increased scrutiny;

- U.S. federal false claims laws, including the civil FCA, which impose criminal and civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other third-party payers that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the ACA specified that any claims submitted as a result of a violation of the federal Anti-Kickback Statute constitute false claims and are subject to enforcement under the federal False Claims Act. Violations of the FCA may be subject to significant civil fines and penalties for each false claim, currently ranging from $13,946-$27,894 per false claim, treble damages, and potential exclusion from participation in federal healthcare programs;

- HIPAA, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and making false statements in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- the U.S. federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, among others, to track and report annually to CMS information related to "payments or other transfers of value" made to U.S.-licensed physicians (defined to include doctors, dentists, optometrists, podiatrists and licensed chiropractors), physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists, anesthesiology assistants, certified nurse midwives, and teaching hospitals; as well as tracking and reporting of ownership and investment interests held by the U.S.-licensed physicians (as defined by statute) and their immediate family members;

- analogous state laws and regulations that may apply to sales or marketing arrangements and claims for healthcare items or services reimbursed by non-governmental third-party payers, including private insurers, that may be broader in scope than their federal equivalents; state laws and regulations that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state laws and regulations that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or require the disclosure of marketing expenditures and other pricing information; and

- similar and other laws and regulations in the U.S. (federal, state and local), in the EU (including member countries), and other countries and jurisdictions.

Ensuring our compliance with applicable laws and regulations involves substantial costs, and it is possible that governmental authorities or third parties will assert that our business practices fail to comply with these laws and regulations. If our actions are found to be in violation of any laws and regulations, we may be subject to significant civil, criminal, and administrative damages, penalties, and fines, as well as exclusion from participation in government healthcare programs, curtailment or restructuring of our operations, and reputational harm, any of which could have a material adverse effect on our business, financial condition, or results of operations.

If a successful product liability or clinical trial claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, we could incur substantial liability.

The use of our drug candidates in clinical trials and the sale of any products for which we obtain marketing approval will expose us to the risk of product liability and clinical trial liability claims. Product liability claims might be brought against us by consumers, healthcare providers, or others selling or otherwise coming into contact with our products. Clinical trial liability claims may be filed against us for damages suffered by clinical trial subjects or their families. If we cannot successfully defend ourselves against product liability claims, we could incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- decreased demand for any approved drug candidates;
- impairment of our business reputation;
- withdrawal of clinical trial participants;
- costs of related litigation;
- distraction of management's attention;
- substantial monetary awards to patients or other claimants;
- loss of revenues; and
- the inability to successfully commercialize any approved drug candidates.

We currently have clinical trial liability insurance coverage for all of our clinical trials. However, our insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If and when we obtain marketing approval for any of our drug candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain this product liability insurance on commercially reasonable terms. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us could cause our ordinary share price to decline and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

Risks Related to Our Dependence on Third Parties

We rely on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet established deadlines for the completion of any such clinical trials.

We do not have the ability to independently conduct clinical trials for our drug candidates, and we rely on third parties, such as consultants, contract research organizations, medical institutions, and clinical investigators to assist us with these activities. Our reliance on these third parties for clinical development activities results in reduced control over these activities. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. Although we have and will enter into agreements with these third parties, we will be responsible for confirming that our clinical trials are conducted in accordance with their general investigational plans and protocols. Moreover, the FDA, the EMA, and other comparable regulatory authorities require us to comply with regulations and standards, commonly referred to as cGCPs, for conducting, recording, and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the trial participants are adequately protected. Our reliance on third parties does not relieve us of these responsibilities and requirements. If we or any of our third-party contractors fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the EMA, or other comparable regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with cGCP regulations. In addition, our clinical trials must be conducted with product produced under cGMPs. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. Requirements regarding clinical trial data may evolve, and any such changes to data requirements may cause the FDA or comparable foreign regulatory authorities to disagree with data from preclinical studies or clinical trials, and to require further studies.

To date, we believe our consultants, contract research organizations, and other third parties with which we are working have generally performed satisfactorily; however, if these third parties do not successfully carry out their contractual duties, meet expected deadlines, or comply with applicable regulations, we have been, and may be, required to replace them. Although we believe that there are a number of other third-party contractors we could engage to continue these activities, we may not be able to enter into arrangements with alternative third-party contractors or to do so on commercially reasonable terms, which may result in a delay of our planned clinical trials. Accordingly, we may be delayed in obtaining regulatory approvals for our drug candidates and may be delayed in our efforts to successfully develop our drug candidates.

In addition, our third-party contractors are not our employees, and except for remedies available to us under our agreements with such third-party contractors, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical and nonclinical programs. If third-party contractors do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our drug candidates. As a result, our results of operations and the commercial prospects for our drug candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

If we do not establish additional strategic collaborations, we may have to alter our research, development, and/or commercialization plans.

Research, development, and potential commercialization of our drug candidates will require substantial additional cash to fund expenses. Our strategy includes potentially collaborating with additional leading pharmaceutical and biotechnology companies to assist us in furthering research, development, and/or potential commercialization of some of our drug candidates in some or all geographies. It may be difficult to enter into one or more of such collaborations in the future. We face significant competition in seeking appropriate collaborators and these collaborations are complex and time-consuming to negotiate and document. We may not be able to negotiate collaborations on acceptable terms, or at all, in which case we may have to curtail the development of a particular drug candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we will need to obtain additional capital, which may not be available to us on acceptable terms, or at all. If we do not have sufficient funds, we will not be able to bring our drug candidates to market and generate product revenue.

We have no manufacturing capacity and depend on third-party manufacturers to supply us with nonclinical and clinical trial supplies of all of our drug candidates, and we will depend on third-party manufacturers to supply us with any drug product for commercial sale if we obtain marketing approval from the FDA, the EMA, or any other comparable regulatory authority for any of our drug candidates.

We do not own or operate facilities for the manufacture, packaging, labeling, storage, testing, or distribution of nonclinical or clinical supplies of any of our drug candidates. We instead contract with and rely on third parties to manufacture, package, label, store, test, and distribute nonclinical and clinical supplies of our drug candidates, and we plan to continue to do so for the foreseeable future. We also rely on third-party consultants to assist us with managing these third parties and with our manufacturing strategy. Certain of these third parties have failed to perform these activities for us and any of these third parties may fail to perform these activities for us in the future, which could cause nonclinical or clinical development of our drug candidates to be delayed, which could have an adverse effect on our business, financial condition, results of operations, and/or growth prospects.

If the FDA, the EMA, or any other comparable regulatory authority approves any of our drug candidates for commercial sale, we expect to continue to rely, at least initially, on third parties to manufacture, package, label, store, test, and distribute commercial supplies of such approved drug product. Significant scale-up of manufacturing may require additional comparability validation studies, which the FDA, the EMA, or other comparable regulatory authorities must review and approve. Our third-party manufacturers might not be able to successfully establish such comparability or increase their manufacturing capacity in a timely or economic manner, or at all. If our third-party manufacturers are unable to successfully establish comparability or increase their manufacturing capacity for any drug product, and we are unable to timely establish our own manufacturing capabilities, the commercial launch of that drug candidate could be delayed or there could be a shortage in supply, which could have an adverse effect on our business, financial condition, results of operations, and/or growth prospects.

Our third-party manufacturers' facilities could be damaged by fire, power interruption, information system failure, natural disaster or other similar event, which could cause a delay or shortage in supplies of our drug candidates, which could have an adverse effect on our business, financial condition, results of operations, and/or growth prospects.

Our drug candidates require, and any future drug product will require, precise, high quality manufacturing, packaging, labeling, storage, and testing that meet stringent cGMP, other regulatory requirements and other standards. Our third-party manufacturers are subject to ongoing periodic and unannounced inspections by the FDA, the EMA, and other comparable regulatory authorities to ensure compliance with these cGMPs, other regulatory requirements and other standards. We do not have control over, and are dependent upon, our third-party manufacturers' compliance with these cGMPs, regulations and standards. Any failure by a third-party manufacturer to comply with these cGMPs, regulations or standards or that compromises the safety of any of our drug candidates or any drug product could cause a delay or suspension of production of nonclinical or clinical supplies of our drug candidates or commercial supplies of drug product, cause a delay or suspension of nonclinical or clinical development, product approval and/or commercialization of our drug candidates or drug product, result in seizure or recall of clinical or commercial supplies, result in fines and civil penalties, result in liability for any patient injury or death or otherwise increase our costs, any of which could have an adverse effect on our business, financial condition, results of operations, and/or growth prospects. If a third-party manufacturer cannot or fails to perform its contractual commitments, does not have sufficient capacity to meet our nonclinical, clinical or eventual commercial requirements or fails to meet cGMPs, regulations or other standards, we have been, and may be, required to replace it or qualify an additional third-party manufacturer. Although we believe there are a number of potential alternative manufacturers, the number of manufacturers with the necessary manufacturing and regulatory expertise and facilities to manufacture biologics like our antibodies is limited. In addition, we have incurred, and could incur, significant additional costs and delays in identifying and qualifying any new third-party manufacturer, due to the technology transfer to such new manufacturer and because the FDA, the EMA, and other comparable regulatory authorities must approve any new manufacturer prior to manufacturing our drug candidates. Such approval would require successful technology transfer, comparability and other testing and compliance inspections. Transferring manufacturing to a new manufacturer could therefore interrupt supply, delay our clinical trials and any commercial launch, and/or increase our costs for our drug candidates, any of which could have an adverse effect on our business, financial condition, results of operations, and/or growth prospects.

Rentschler Biopharma SE ("Rentschler") and Catalent Indiana, LLC ("Catalent Indiana") are our third-party manufacturers of clinical supplies of birtamimab. We are dependent on Rentschler and Catalent Indiana to manufacture these clinical supplies.

Catalent Pharma Solutions, LLC ("Catalent Pharma") and Sharp Sterile Manufacturing, LLC ("Sharp Sterile") are our third-party manufacturers of clinical supplies of our drug candidate PRX012. We are dependent on Catalent Pharma and Sharp Sterile to manufacture these clinical supplies.

Lonza Ltd ("Lonza") is our third-party manufacturer of clinical supplies of our drug candidate PRX019. We are dependent on Lonza to manufacture these clinical supplies.

We are dependent on Roche, and its third-party manufacturers if applicable, to manufacture clinical supplies of prasinezumab.

We are dependent on Novo Nordisk, and its third-party manufacturers if applicable, to manufacture clinical supplies of coramitug.

We are dependent on BMS, and its third-party manufacturers if applicable, to manufacture clinical supplies of BMS-986446.

In July 2021, the Company sold the equity interests of a subsidiary that owns and has exclusive licenses to intellectual property rights and other assets pertaining to the investigational humanized monoclonal antibody known as coramitug (formerly PRX004), and we might not realize the anticipated benefits of such transaction.

On July 8, 2021, the Company, together with its wholly owned subsidiary, Prothena Biosciences Limited ("PBL"), entered into a Share Purchase Agreement with Novo Nordisk and NNRE (together with Novo Nordisk, "Buyer"), pursuant to which PBL sold and transferred to NNRE, all issued and outstanding ordinary shares of Neotope Neuroscience Limited, a wholly owned subsidiary of PBL, for an aggregate purchase price of up to $1.23 billion. The aggregate purchase price consists of an upfront payment of $60 million in cash, subject to customary purchase price adjustments, and an aggregate of $1.17 billion in cash, payable on Buyer's achievement of certain development, commercialization and net sales-based milestones. On November 21, 2022, we earned a $40 million milestone payment. There can be no assurance that such remaining milestones

will be met. If we do not receive additional milestone payments as a result of the transaction in anticipated amounts or at all, we may need to seek additional sources of capital to pursue further research, development, and/or commercialization of our drug candidates, and this could have a material adverse effect on our business, financial condition, results of operations, and/or growth prospects.

We depend on third-party suppliers for key raw materials used in our manufacturing processes, and the loss of these third-party suppliers or their inability to supply us with adequate raw materials could harm our business.

We rely on third-party suppliers for the raw materials required for the production of our drug candidates. Our dependence on these third-party suppliers and the challenges we may face in obtaining adequate supplies of raw materials involve several risks, including limited control over pricing, availability, quality, and delivery schedules. We cannot be certain that our suppliers will continue to provide us with the quantities of these raw materials that we require or satisfy our anticipated specifications and quality requirements. Any supply interruption in limited or sole sourced raw materials could materially harm our ability to manufacture our products until a new source of supply, if any, could be identified and qualified. Although we believe there are currently several other suppliers of these raw materials, we may be unable to find a sufficient alternative supply channel in a reasonable time or on commercially reasonable terms. Any performance failure on the part of our suppliers could delay the development and potential commercialization of our drug candidates, including limiting supplies necessary for clinical trials and regulatory approvals, which would have a material adverse effect on our business.

Risks Related to Our Intellectual Property

If we are unable to adequately protect or enforce the intellectual property relating to our drug candidates our ability to successfully commercialize our drug candidates will be harmed.

Our success depends in part on our ability to obtain patent protection both in the U.S. and in other countries for our drug candidates. Our ability to protect our drug candidates from unauthorized or infringing use by third parties depends in substantial part on our ability to obtain and maintain valid and enforceable patents. Due to evolving legal standards relating to the patentability, validity and enforceability of patents covering pharmaceutical inventions and the scope of claims made under these patents, our ability to obtain, maintain and enforce patents is uncertain and involves complex legal, factual and scientific questions. Accordingly, rights under any issued patents may not provide us with sufficient protection for our drug candidates or provide sufficient protection to afford us a commercial advantage against competitive products or processes. Additionally, our ability to obtain patent protection for our drug candidates also depends on our collaborators, partners, contractors, and employees involved in the generation of intellectual property to carry out their contractual duties, including those to assign or license relevant intellectual property rights developed on our behalf to us.

In addition, the strength of patents in the biotechnology and pharmaceutical field can be uncertain, and evaluating the scope of such patents involves complex legal, factual, and scientific analyses and has in recent years been the subject of much litigation, resulting in court decisions, including Supreme Court decisions, which have increased uncertainties as to the ability to enforce patent rights in the future. We cannot guarantee that any patents will issue from any pending or future patent applications owned by or licensed to us or our affiliates. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Consequently, we may not obtain or maintain adequate patent protection for any of our programs and product candidates. Even if patents have issued or will issue, we cannot guarantee that the claims of these patents are or will be valid or enforceable or will provide us with any significant protection against competitive products or otherwise be commercially valuable to us. Patent applications in the U.S. are maintained in confidence for up to 18 months after their filing. In some cases, however, patent applications remain confidential in the U.S. Patent and Trademark Office (the "USPTO") for the entire time prior to issuance as a U.S. patent. Similarly, publication of discoveries in the scientific or patent literature often lags behind actual discoveries. Consequently, we cannot be certain that we or our licensors or co-owners were the first to invent, or the first to file patent applications on, our drug candidates or their use as drugs. In the event that a third party has also filed a U.S. patent application relating to our drug candidates or a similar invention, we may have to participate in interference or derivation proceedings declared by the USPTO to determine priority of invention in the U.S. The costs of these proceedings could be substantial and it is possible that our efforts would be unsuccessful, resulting in a loss of our U.S. patent position. Furthermore, we may not have identified all U.S. and non-U.S. patents or published applications that affect our business either by blocking our ability to commercialize our drugs or by covering similar technologies. Composition-of-matter patents on the biological or chemical active pharmaceutical ingredient are generally considered to be the strongest form of intellectual property protection for pharmaceutical products, as such patents provide protection without regard to any method of use. We cannot be certain that the claims in our patent applications covering composition-of-matter of our drug candidates will be considered patentable by the USPTO and courts in the U.S. or by the patent offices and courts in other countries, nor can we be certain that the claims in our issued composition-of-matter patents will not be found invalid or unenforceable if challenged. Method-of-use patents protect the use of a product

for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products "off-label." Although off-label prescriptions may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent or prosecute.

We cannot guarantee that any of our patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our drug candidates in any jurisdiction. The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our products. We may incorrectly determine that our products are not covered by a third-party patent or may incorrectly predict whether a third-party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our drug candidates. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our products.

We may be subject to a third-party preissuance submission of prior art to the USPTO and foreign patent agencies, or become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review, or other patent office proceedings or litigation, in the U.S. or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could result in loss of exclusivity or in patent claims being narrowed, invalidated, or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. In addition, given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. Any failure to obtain or maintain patent protection with respect to our drug candidates could have a material adverse effect on our business, financial condition, results of operations, and/or growth prospects.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is costly, time-consuming, and inherently uncertain. Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs, and may diminish our ability to protect our inventions, obtain, maintain, and enforce our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our owned and licensed patents. Recent patent reform legislation in the United States and other countries, including the Leahy-Smith America Invents Act, or the Leahy-Smith Act, signed into law on September 16, 2011, could increase those uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. These include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. After March 2013, under the Leahy-Smith Act, the United States transitioned to a first inventor to file system in which, assuming that the other statutory requirements are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013, but before we file an application covering the same invention, could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or our licensors were the first to either (i) file any patent application related to our drug candidates and other proprietary technologies we may develop or (ii) invent any of the inventions claimed in our or our licensor's patents or patent applications. Even where we have a valid and enforceable patent, we may not be able to exclude others from practicing the claimed invention where the other party can show that they used the invention in commerce before our filing date or the other party benefits from a compulsory license. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued

patents, all of which could have a material adverse effect on our business, financial condition, results of operations, and/or growth prospects.

Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained. Depending on decisions by Congress, the federal courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. We cannot predict how future decisions by Congress, the federal courts or the USPTO may impact the value of our patents.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment, and other similar provisions during the patent application process. Although an inadvertent lapse, including due to the effect of geopolitical conflict on us or our patent maintenance vendors, can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application or invalidity of an issued patent include failure to respond to official actions within prescribed time limits, non-payment of fees, failure to properly legalize and submit formal documents, and failure to submit certain prior art. In any such event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

The lives of our patents may not be sufficient to effectively protect our products and business.

Patents have a limited lifespan. In the United States, if all maintenance fees are paid timely, the natural expiration of a patent is generally 20 years after its first effective filing date. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Given the amount of time required for the development, testing, and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such drug candidates are commercialized. Even if patents covering our drug candidates are obtained, once a patent covering a drug candidate has expired, we may be open to competition, including biosimilar or generic medications. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing drug candidates similar or identical to ours. Our patents issued as of December 31, 2024, are anticipated to expire on dates ranging from 2025 to 2042, subject to any patent extensions that may be available for such patents. If patents are issued on our patent applications pending as of December 31, 2024, the resulting patents are projected to expire on dates ranging from 2025 to 2045. In addition, although upon issuance in the United States a patent's life can be increased based on certain delays caused by the USPTO, this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. A patent term extension based on regulatory delay may be available in the United States. However, only a single patent can be extended for each first regulatory review period for a product, and any patent can be extended only once, for a single product. Moreover, the scope of protection during the period of the patent term extension does not extend to the full scope of the claim, but instead only to the scope of the product as approved. Laws governing analogous patent term extensions in foreign jurisdictions vary widely, as do laws governing the ability to obtain multiple patents from a single patent family. Additionally, we may not receive an extension if we fail to exercise due diligence during the testing phase or regulatory review process, apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following our patent expiration and may take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data to launch their product earlier than might otherwise be the case, and our revenue could be reduced, possibly materially. If we do not have sufficient patent life to protect our products, our business and results of operations will be adversely affected.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We may be subject to claims that former employees, collaborators, or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. Inventorship disputes may arise from conflicting views regarding the

contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third parties involved in developing our drug candidates or as a result of questions regarding co-ownership of potential joint inventions. For example, we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our drug candidates. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

We or our licensors may have relied on third-party consultants or collaborators or on funds from third parties, such as the U.S. government, such that we or our licensors are not the sole and exclusive owners of the patents we in-licensed. If other third parties have ownership rights or other rights to our patents, including in-licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements have been, and may be, breached, and we have been, and may be, forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. We may not have adequate remedies for any breach of our assignment agreements or related claims. Such claims related to the ownership of what we regard as our intellectual property could have a material adverse effect on our business, financial condition, results of operations, and/or growth prospects.

We may not be able to protect our intellectual property rights throughout the world.

Patents are of national or regional effect, and filing, prosecuting, maintaining, and defending patents on drug candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can have a different scope and strength than do those in the United States. In addition, the laws of some foreign countries, particularly certain developing countries, do not currently, or may not in the future, protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement rights are not as strong as those in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or adequate to prevent them from competing.

We license patent rights from third-party owners. Such licenses may be subject to early termination if we fail to comply with our obligations in our licenses with third parties, which could result in the loss of rights or technology that are material to our business.

We are a party to licenses that give us rights to third-party intellectual property or technology that is necessary or useful for our business, and we may enter into additional licenses in the future. Under these license agreements we are obligated to pay the licensor fees, which may include annual license fees, milestone payments, royalties, a percentage of revenues associated with the licensed technology and a percentage of sublicensing revenue. In addition, under certain of such agreements, we are required to diligently pursue the development of products using the licensed technology. If we fail to comply with these obligations, including due to our use of the intellectual property licensed to us in an unauthorized manner, and fail to cure our breach within a specified period of time, the licensor may have the right to terminate the applicable license, in which event we could lose valuable rights and technology that are material to our business, harming our ability to develop, manufacture, and/or commercialize our platform or drug candidates.

In addition, the agreements under which we license intellectual property or technology to or from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology or increase what we believe to be our financial or other obligations under the relevant

agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and/or growth prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected drug candidates. Our business also would suffer if any current or future licensors fail to abide by the terms of the license, if the licensors fail to enforce licensed patents against infringing third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights.

In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability.

If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant research programs or drug candidates and our business, financial condition, results of operations, and/or growth prospects could suffer.

Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues and is complicated by the rapid pace of scientific discovery in our industry. Disputes may also arise between us and our licensors regarding intellectual property subject to a license agreement, including those relating to:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the license agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- whether we are complying with our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our drug candidates, and what activities satisfy those diligence obligations;
- the priority of invention of patented technology;
- the amount and timing of payments owed under license agreements; and
- the allocation of ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and by us and our partners.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected drug candidates. We are generally also subject to all of the same risks with respect to protection of intellectual property that we license as we are for intellectual property that we own, which are described below. If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize our products could suffer.

We depend, in part, on our licensors to file, prosecute, maintain, defend, and enforce patents and patent applications that are material to our business.

If the licensor retains control of prosecution of the patents and patent applications licensed to us, we may have limited or no control over the manner in which the licensor chooses to prosecute or maintain its patents and patent applications and have limited or no right to continue to prosecute any patents or patent applications that the licensor elects to abandon. If our licensors or any future licensees having rights to file, prosecute, maintain, and defend our patent rights fail to conduct these activities for patents or patent applications covering any of our drug candidates, including due to the impact of geopolitical conflict on our licensors' business operations, our ability to develop and commercialize those drug candidates may be adversely affected and we may not be able to prevent competitors from making, using, or selling competing products. We cannot be certain that such activities by our licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents or other intellectual property rights. Pursuant to the terms of the license agreements with some of

our licensors, the licensors may have the right to control enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents and, even if we are permitted to pursue such enforcement or defense, we cannot ensure the cooperation of our licensors. We cannot be certain that our licensors will allocate sufficient resources or prioritize their or our enforcement of such patents or defense of such claims to protect our interests in the licensed patents. Even if we are not a party to these legal actions, an adverse outcome could harm our business because it might prevent us from continuing to license intellectual property that we may need to operate our business. In addition, even when we have the right to control patent prosecution of licensed patents and patent applications, enforcement of licensed patents, or defense of claims asserting the invalidity of those patents, we may still be adversely affected or prejudiced by actions or inactions of our licensors and their counsel that took place prior to or after our assuming control. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensing partners.

We may wish to form collaborations in the future with respect to our drug candidates, but may not be able to do so or to realize the potential benefits of such transactions, which may cause us to alter or delay our development and commercialization plans.

Our drug candidates may also require specific components to work effectively and efficiently, and rights to those components may be held by others. We may be unable to in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, which would harm our business. If we fail to obtain licenses to necessary third-party intellectual property rights, we may need to cease use of the compositions or methods covered by such third-party intellectual property rights and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology. Any delays in entering into new collaborations or strategic partnership agreements related to our drug candidates could delay the development and commercialization of our drug candidates in certain geographies, which could harm our business prospects, financial condition, and results of operations.

The licensing and acquisition of third-party intellectual property rights is a competitive practice, and companies that may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our drug candidates. More established companies may have a competitive advantage over us due to their larger size and cash resources or greater clinical development and commercialization capabilities. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional drug candidates that we may seek to acquire.

Moreover, some of our owned and in-licensed patents or patent applications or future patents are or may be co-owned with third parties. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such patents or patent applications, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we may need the cooperation of any such co-owners of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us. Furthermore, our owned and in-licensed patents may be subject to a reservation of rights by one or more third parties. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

Litigation regarding patents, patent applications, and other proprietary rights may be expensive and time consuming. If we are involved in such litigation, it could cause delays in bringing drug candidates to market and harm our ability to operate.

Our success will depend in part on our ability to operate without infringing the proprietary rights of third parties. Although we are not currently aware of any litigation or other proceedings or third-party claims of intellectual property infringement related to our drug candidates, the pharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights, as well as administrative proceedings for challenging patents, including interference, derivation, *inter partes* review, post-grant review, and reexamination proceedings before the USPTO, or oppositions and other comparable proceedings in foreign jurisdictions, as well as administrative proceedings for challenging patents, including interference, derivation, *inter partes* review, post-grant review, and reexamination proceedings before the USPTO, or oppositions and other comparable proceedings in foreign jurisdictions. Other parties may hold or obtain patents in the future and allege that the use of our technologies infringes these patent claims or that we are employing their proprietary technology without authorization. Furthermore, patent reform and changes to patent laws add uncertainty to the possibility of

challenge to our patents in the future. We cannot assure you that our drug candidates and other proprietary technologies we may develop will not infringe existing or future patents owned by third parties.

In addition, third parties may challenge our existing or future patents. Competitors may also infringe our patents or other intellectual property or the intellectual property of our licensors. To cease such infringement or unauthorized use, we may be required to file patent infringement claims, which can be expensive and time-consuming and divert the time and attention of our management and scientific personnel. Proceedings involving our patents or patent applications or those of others could result in adverse decisions regarding:

- the patentability of our inventions relating to our drug candidates; and/or
- the enforceability, validity or scope of protection offered by our patents relating to our drug candidates; and/or
- findings that our drug candidates, products, or activities infringe third-party patents or other intellectual property rights.

Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time consuming and, even if resolved in our favor, is likely to divert significant resources from our core business including distracting our technical and management personnel from their normal responsibilities. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Third parties asserting their patent or other intellectual property rights against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our drug candidates or force us to cease some of our business operations. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of management and other employee resources from our business, cause development delays, and may impact our reputation. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

In the event we are able to establish third-party infringement of our patents, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our ordinary shares.

If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action, or challenge the validity of the patents in court. Patent litigation is costly and time consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, if we do not obtain a license, develop or obtain non-infringing technology, fail to defend an infringement action successfully, or have infringed patents declared invalid, we may:

- incur substantial monetary damages, including treble damages and attorneys' fees for willful infringement;
- obtain one or more licenses from third parties and potentially pay royalties;
- redesign our infringing products, which may be impossible on a cost-effective basis or require substantial time and monetary expenditure;
- encounter significant delays in bringing our drug candidates to market; and/or
- be precluded from participating in the manufacture, use, or sale of our drug candidates or methods of treatment requiring licenses.

In that event, we would be unable to further develop and commercialize our drug candidates, which could harm our business significantly.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our current or future trademarks or trade names may be challenged, infringed, circumvented, declared generic or descriptive, or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. During trademark registration proceedings, we may receive rejections of our applications by the USPTO or in other foreign jurisdictions. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names.

Moreover, any name we have proposed to use with our drug candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. Similar requirements exist in Europe. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA (or an equivalent administrative body in a foreign jurisdiction) objects to any of our proposed proprietary product names, it may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. Furthermore, in many countries, owning and maintaining a trademark registration may not provide an adequate defense against a subsequent infringement claim asserted by the owner of a senior trademark. At times, competitors or other third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. If we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

We may be unable to adequately prevent disclosure of trade secrets and other proprietary information.

We rely on trade secrets to protect our proprietary technologies, especially where we do not believe patent protection is appropriate or obtainable; however, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers, and other advisors to protect our trade secrets and other proprietary information. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. Any disclosure, either intentional or unintentional, by our employees, the employees of third parties with whom we share our facilities or third-party consultants and vendors that we engage to perform research, clinical trials or manufacturing activities, or misappropriation by third parties (such as through a cybersecurity breach) of our trade secrets or proprietary information could enable competitors to duplicate or surpass our technological achievements, thus eroding our competitive position in our market. In addition, others may independently discover our trade secrets and proprietary information, and we would have no right to prevent them from using that technology or information to compete with us. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, or misappropriation of our intellectual property by third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results, and financial condition.

We may be subject to claims that our employees, collaborators, partners, contractors, or advisors have wrongfully used or disclosed alleged trade secrets of third parties.

Many of our employees were previously employed at universities, Elan or Elan subsidiaries, or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Likewise, our collaborators, partners, contractors, and advisors may have in the past, or may currently, work with or for universities, or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know-how of third parties is not disclosed to us or used in their work for us, we may be subject to claims that we or our employees, collaborators, partners, contractors, or advisors have used or disclosed intellectual property, including trade secrets or other proprietary information, of third parties. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees. If our defenses to these claims fail, in addition to requiring us to pay monetary damages, a court could prohibit us from using technologies or features that are essential to our drug candidates, if such technologies or features are found to incorporate, be derived from, or benefited from the knowledge of the trade secrets or other proprietary information of third parties. Moreover, any such litigation or the threat thereof may adversely affect our reputation, our ability to form strategic alliances or sublicense our rights to collaborators, engage with scientific advisors or hire employees or consultants, each of which would have an adverse effect on our business, results of operations and financial condition. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make drug candidates that are similar to ours but that are not covered by the claims of the patents that we own or have exclusively licensed;
- we or our licensors or future collaborators might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed;
- we or our licensors or future collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or have exclusively licensed may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- we cannot predict the scope of protection of any patent issuing based on our patent applications, including whether the patent applications that we own or in-license will result in issued patents with claims that cover our drug candidates or uses thereof in the United States or in other foreign countries;
- the claims of any patent issuing based on our patent applications may not provide protection against competitors or any competitive advantages, or may be challenged by third parties;
- if enforced, a court may not hold that our patents are valid, enforceable and infringed;
- we may need to initiate litigation or administrative proceedings to enforce and/or defend our patent rights which will be costly whether we win or lose;

- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property;
- we may fail to adequately protect and police our trademarks and trade secrets; and
- the patents of others may have an adverse effect on our business, including if others obtain patents claiming subject matter similar to or improving that covered by our patents and patent applications.

Should any of these events occur, they could significantly harm our business, results of operations, and prospects.

Risks Related to Our Ordinary Shares

The market price of our ordinary shares may fluctuate widely.

Our ordinary shares commenced trading on the Nasdaq Global Market on December 21, 2012 and currently trade on the Nasdaq Global Select Market. We cannot predict the prices at which our ordinary shares may trade. The market price of our ordinary shares may fluctuate widely, depending upon many factors, some of which may be beyond our control, including:

- our ability to obtain financing as needed;
- progress in and results from our ongoing or future nonclinical research and clinical trials;
- the execution of our agreements with third parties, including with Roche, BMS, and Novo Nordisk;
- failure or delays in advancing our nonclinical drug candidates or other drug candidates we may develop in the future into clinical trials;
- results of clinical trials conducted by others, including on drugs that would compete with our drug candidates;
- issues in manufacturing our drug candidates;
- regulatory developments or enforcement in the U.S. and other countries;
- developments or disputes concerning patents or other proprietary rights;
- introduction of technological innovations or new commercial products by our competitors;
- changes in estimates or recommendations by securities analysts, if any, who cover our company;
- public concern over our drug candidates;
- litigation;
- future sales of our ordinary shares by us or by existing shareholders;
- general market conditions;
- changes in the structure of healthcare payment systems;
- failure of any of our drug candidates, if approved, to achieve commercial success;
- economic and other external factors or other disasters or crises;
- period-to-period fluctuations in our financial results;
- overall fluctuations in U.S. equity markets;
- our quarterly or annual results, or those of other companies in our industry;

- announcements by us or our competitors of significant acquisitions or dispositions;
- the operating and ordinary share price performance of other comparable companies;
- investor perception of our company and the drug development industry;
- natural or environmental disasters that investors believe may affect us;
- changes in tax laws or regulations applicable to our business or the interpretations of those tax laws and regulations by taxing authorities; or
- fluctuations in the budgets of federal, state and local governmental entities around the world.

These and other external factors may cause the market price and demand for our ordinary shares to fluctuate substantially, which may limit or prevent investors from readily selling their ordinary shares and may otherwise negatively affect the liquidity of our ordinary shares. In particular, stock markets in general have experienced volatility that has often been unrelated to the operating performance of a particular company. These broad market fluctuations may adversely affect the trading price of our ordinary shares. Some companies that experienced volatility in the trading price of their stock have been the subject of securities class action litigation. If any of our shareholders brought a lawsuit against us, we could incur substantial costs defending the lawsuit. Such a lawsuit could also divert the time and attention of our management.

Your percentage ownership in Prothena may be diluted in the future.

As with any publicly traded company, your percentage ownership in us may be diluted in the future because of equity issuances for acquisitions, capital raising transactions (including the sale of ordinary shares pursuant to our Amended Distribution Agreement, as may be further amended from time to time, and as discussed below), or otherwise. We may need to raise additional capital in the future. If we are able to raise additional capital, we may issue equity or convertible debt instruments, which may severely dilute your ownership interest in us. In addition, we intend to continue to grant option awards to our directors, officers and employees, which would dilute your ownership stake in us. As of December 31, 2024, the number of ordinary shares available for issuance pursuant to outstanding and future equity awards under our equity plans was 15,332,174.

If we are unable to maintain effective internal controls, our business could be adversely affected.

We are subject to the reporting and other obligations under the U.S. Securities Exchange Act of 1934, as amended, including the requirements of Section 404 of the U.S. Sarbanes-Oxley Act, which require annual management assessments of the effectiveness of our internal control over financial reporting. In addition, under Section 404(b) of the U.S. Sarbanes-Oxley Act, if we are either an "accelerated filer" or "large accelerated filer," our independent registered public accounting firm must attest to the effectiveness of our internal control over financial reporting. The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation to meet the detailed standards under the rules. During the course of its testing, our management may identify material weaknesses or deficiencies which may not be remedied in time to meet the deadline imposed by the Sarbanes-Oxley Act. These reporting and other obligations place significant demands on our management and administrative and operational resources, including accounting resources.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of our financial statements for external purposes in accordance with accounting principles generally accepted in the U.S. During the course of our review and testing of our internal controls, we have identified, and may identify in the future, deficiencies and may be unable to remediate them before we must provide the required reports. Furthermore, if we have a material weakness in our internal controls over financial reporting, we may not detect errors on a timely basis and our consolidated financial statements may be materially misstated. We, or our independent registered public accounting firm (if required), may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall.

We cannot provide assurance that a material weakness will not occur in the future, or that we will be able to conclude on an ongoing basis that we have effective internal controls over financial reporting in accordance with Section 404 and the related rules and regulations of the SEC when required. A material weakness in internal control over financial reporting is a deficiency,

or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of a company's annual or interim consolidated financial statements will not be prevented or detected on a timely basis by the company's internal controls. If we cannot in the future favorably assess, or our independent registered public accounting firm (if required), is unable to provide an unqualified attestation report on, the effectiveness of our internal controls over financial reporting, investor confidence in the reliability of our financial reports may be adversely affected, which could have a material adverse effect on our share price. In addition, any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from the Nasdaq Global Select Market or other adverse consequences that would have an adverse effect on our business, financial position and results of operations.

If we were treated as a passive foreign investment company for U.S. federal income tax purposes, it could result in adverse U.S. federal income tax consequences to United States holders of our ordinary shares.

Significant potential adverse U.S. federal income tax implications generally apply to U.S. investors owning shares of a passive foreign investment company ("PFIC"), directly or indirectly. In general, we would be a PFIC for a taxable year if either (i) 75% or more of our income constitutes passive income, or (ii) 50% or more of our assets produce passive income or are held for the production of passive income. Changes in the composition of our active or passive income, passive assets or changes in our fair market value may cause us to become a PFIC. A separate determination must be made each taxable year as to whether we are a PFIC (after the close of each taxable year).

We do not believe we were a PFIC for U.S. federal income tax purposes for our taxable year ended December 31, 2024. However, the application of the PFIC rules is subject to uncertainties in a number of respects, and we cannot assure that the U.S. Internal Revenue Service (the "IRS") will not take a contrary position. We also cannot assure that we will not be a PFIC for U.S. federal income tax purposes for the current taxable year or any future taxable year.

We may not be able to successfully maintain our tax rates, which could adversely affect our business and financial condition, results of operations and growth prospects.

We are incorporated in Ireland and maintain subsidiaries or offices in Ireland and the U.S. We are able to achieve a low average tax rate through the performance of certain functions and ownership of certain assets in tax-efficient jurisdictions, together with intra-group service agreements. However, changes in tax laws or interpretations thereof in any of these jurisdictions could adversely affect our ability to do so in the future. Taxing authorities, such as the IRS and the Irish Revenue Commissioners ("Irish Revenue"), actively audit and otherwise challenge these types of arrangements, and have done so in our industry. We are subject to reviews and audits by the IRS, Irish Revenue and other taxing authorities from time to time, and the IRS, Irish Revenue or other taxing authorities may challenge our structure and inter-group arrangements. The Company's U.S. subsidiaries are currently under examination by the IRS for the tax year 2021. Responding to or defending against challenges from taxing authorities may be expensive and time consuming, and may divert management's time and focus away from operating our business. We cannot predict whether and when taxing authorities will conduct an audit, challenge our tax structure or the cost involved in responding to any such audit or challenge. If we are unsuccessful, we may be required to pay taxes for prior periods, interest, fines or penalties, and may be obligated to pay increased taxes in the future, all of which could have an adverse effect on our business, financial condition, results of operations, and/or growth prospects. In addition to the impact of changes in tax laws, our provision for income tax can be materially impacted, for example, by the geographical mix of our profits and losses, changes in our business, such as internal restructuring and acquisitions, changes and accounting guidance and other regulatory, legislative or judicial developments changes in tax rates, tax audit determinations, changes in our uncertain tax positions, changes in our intent and capacity to permanently reinvest foreign earnings, changes to our transfer pricing practices, tax deductions attributed to equity compensation and changes in our need for a valuation allowance for deferred tax assets.

Future changes to the tax laws relating to multinational corporations could adversely affect us.

Under current law, we are treated as a foreign corporation for U.S. federal tax purposes. However, changes to the U.S. Internal Revenue Code, U.S. Treasury Regulations or other IRS guidance thereunder could adversely affect our status as a foreign corporation or otherwise affect our effective tax rate. For example, in 2017 the United States enacted tax reform that contained significant changes to corporate taxation, including a provision that requires capitalization and amortization of research and development costs over five years for tax years beginning after December 31, 2021. In addition, the Irish Government, Irish Revenue, U.S. Congress, the IRS, the Organization for Economic Co-operation and Development ("OECD"), and other governments and agencies in jurisdictions where we do business have recently focused on issues related to the taxation of multinational corporations, including the OECD's Global Anti-Base Erosion Model Rules (Pillar Two), which apply a 15% global minimum tax rate on a jurisdiction-by-jurisdiction basis to groups with turnover of not less than €750 million in at least two of the four prior fiscal years. Pillar Two has been implemented into Irish law with effect for periods

beginning on or after December 31, 2023. As a result of Pillar Two or other policy changes, whether at national or supranational level, the tax laws in Ireland, the U.S., and other countries in which we do business could change on a prospective or retroactive basis, and any such changes could have an adverse effect on our business, financial condition, results of operations, and/or growth prospects.

Irish law differs from the laws in effect in the United States and may afford less protection to holders of our ordinary shares.

It may not be possible to enforce court judgments obtained in the U.S. against us in Ireland based on the civil liability provisions of the U.S. federal or state securities laws. In addition, there is uncertainty as to whether the courts of Ireland would recognize or enforce judgments of U.S. courts obtained against us or our directors or officers based on the civil liabilities provisions of the U.S. federal or state securities laws or hear actions against us or those persons based on those laws. We have been advised that the U.S. currently does not have a ratified treaty providing for the reciprocal recognition and enforcement of judgments in civil and commercial matters with Ireland. Therefore, a final judgment for the payment of money rendered by any U.S. federal or state court based on civil liability, whether or not based solely on federal or state securities laws, would not automatically be enforceable in Ireland.

As an Irish incorporated company, we are governed by the Irish Companies Act 2014, as amended (the "Companies Act"), which differs in some material respects from laws generally applicable to U.S. corporations and shareholders, including, among others, differences relating to interested director and officer transactions and shareholder lawsuits. Likewise, the duties of directors and officers of an Irish company generally are owed to the company only. Shareholders of Irish companies generally do not have a personal right of action against directors or officers of the company and may exercise such rights of action on behalf of the company only in limited circumstances. Accordingly, holders of our ordinary shares may have more difficulty protecting their interests than would holders of securities of a corporation incorporated in a jurisdiction of the U.S.

The operation of the Irish Takeover Rules may affect the ability of certain parties to acquire our ordinary shares.

Under the Irish Takeover Panel Act, 1997, Takeover Rules, 2022 (the "Irish Takeover Rules"), if an acquisition of ordinary shares were to increase the aggregate holding of the acquirer and its concert parties to ordinary shares that represent 30% or more of the voting rights of the company, the acquirer and, in certain circumstances, its concert parties would be required (except with the consent of the Irish Takeover Panel) to make an offer for the outstanding ordinary shares at a price not less than the highest price paid for the ordinary shares by the acquirer or its concert parties during the previous 12 months. This requirement would also be triggered by an acquisition of ordinary shares by a person holding (together with its concert parties) ordinary shares that represent between 30% and 50% of the voting rights in the company if the effect of such acquisition were to increase that person's percentage of the voting rights by 0.05% within a 12 month period. Under the Irish Takeover Rules, certain separate concert parties are presumed to be acting in concert. Our board of directors and their relevant family members, related trusts and "controlled companies" are presumed to be acting in concert with any corporate shareholder who holds 20% or more of our shares. The application of these presumptions may result in restrictions upon the ability of any of the concert parties and/or members of our board of directors to acquire more of our securities, including under the terms of any executive incentive arrangements. In the future, we may consult with the Irish Takeover Panel with respect to the application of this presumption and the restrictions on the ability to acquire further securities, although we are unable to provide any assurance as to whether the Irish Takeover Panel will overrule this presumption. Accordingly, the application of the Irish Takeover Rules may restrict the ability of certain of our shareholders and directors to acquire our ordinary shares.

Irish law differs from the laws in effect in the United States with respect to defending unwanted takeover proposals and may give our board of directors less ability to control negotiations with hostile offerors.

We are subject to the Irish Takeover Rules, pursuant to which our Board is not permitted to take any action that might frustrate an offer for our ordinary shares once our Board has received an approach that may lead to an offer or has reason to believe that such an offer is or may be imminent, subject to certain exceptions. Potentially frustrating actions such as (i) the issue of ordinary shares, options or convertible securities, (ii) material acquisitions or disposals, (iii) entering into contracts other than in the ordinary course of business, or (iv) any action, other than seeking alternative offers, which may result in frustration of an offer, are prohibited during the course of an offer or at any earlier time during which our Board has reason to believe an offer is or may be imminent. These provisions may give our Board less ability to control negotiations with hostile offerors and protect the interests of holders of ordinary shares than would be the case for a corporation incorporated in a jurisdiction of the U.S.

Irish law requires that our shareholders renew every five years the authority of our Board of Directors to issue shares and to do so for cash without applying the statutory pre-emption right, and if our shareholders do not renew these authorizations by May 17, 2027 (or any renewal is subject to limitations), our ability to raise additional capital to fund our operations would be limited.

As an Irish incorporated company, we are governed by the Companies Act. The Companies Act requires that every five years our shareholders renew the separate authorities of our Board to (a) allot and issue shares, and (b) opt out of the statutory pre-emption right that otherwise applies to share issuances for cash (which pre-emption right would require that shares issued for cash be offered to our existing shareholders on a pro rata basis before the shares may be issued to new shareholders). At our shareholders' annual general meeting held on May 17, 2022, our shareholders authorized our Board to issue ordinary shares up to the amount of our authorized share capital, and to opt out of the statutory pre-emption right for such issuances. Under Irish law, these authorizations will expire on May 17, 2027, five years after our shareholders last renewed these authorizations. Irish law requires that our shareholders renew the authority for our Board to issue ordinary shares by a resolution approved by not less than 50% of the votes cast at a general meeting of our shareholders. Irish law requires that our shareholders renew the authority of our Board to opt out of the statutory pre-emption right in share issuances for cash by a resolution approved by not less than 75% of the votes cast at a general meeting of our shareholders. If these authorizations are not renewed before May 17, 2027, or are renewed with limitations, our Board would be limited in its ability to issue shares, which would limit our ability to raise additional capital to fund our operations, including the research, development and potential commercialization of our drug candidates.

Transfers of our ordinary shares may be subject to Irish stamp duty.

Irish stamp duty may be payable in respect of transfers of our ordinary shares (currently at the rate of 1% of the price paid or the market value of the shares acquired, if greater).

Under the Irish Stamp Duties Consolidation Act, 1999 (the "Stamp Duties Act"), a transfer of our ordinary shares from a seller who holds shares through The Depository Trust Company ("DTC") to a buyer who holds the acquired shares through DTC will not be subject to Irish stamp duty. Shareholders may also transfer their shares into or out of DTC without giving rise to Irish stamp duty provided that there is no change in the beneficial ownership of such shares and the transfer into or out of DTC is not effected in contemplation of a subsequent sale of such shares to a third party; in order to benefit from this exemption from Irish stamp duty, the seller must confirm to us that there is no change in the ultimate beneficial ownership of the shares as a result of the transfer and there is no agreement for the sale of the shares by the beneficial owner to a third party being contemplated.

A transfer of our ordinary shares (i) by a seller who holds shares outside of DTC to any buyer, or (ii) by a seller who holds the shares through DTC to a buyer who holds the acquired shares outside of DTC, may be subject to Irish stamp duty. Payment of any Irish stamp duty is generally a legal obligation of the transferee.

Any Irish stamp duty payable on transfers of our ordinary shares could adversely affect the price of those shares.

We do not anticipate paying cash dividends, and accordingly, shareholders must rely on ordinary share appreciation for any return on their investment.

We anticipate losing money for the foreseeable future and, even if we do turn a profit, we do not anticipate declaring or paying any cash dividends for the foreseeable future. Therefore, the success of an investment in our ordinary shares will depend upon appreciation in their value and in order to receive any income or realize a return on your investment, you will need to sell your Prothena ordinary shares. There can be no assurance that our ordinary shares will maintain their price or appreciate in value.

Dividends paid by us may be subject to Irish dividend withholding tax.

Although we do not currently anticipate paying cash dividends, if we were to do so in the future, an Irish dividend withholding tax (currently at a rate of 25%) may arise. A number of exemptions from Irish dividend withholding tax exist such that shareholders resident in the U.S. and shareholders resident in other countries that have entered into a double taxation treaty with Ireland may be entitled to exemptions from Irish dividend withholding tax subject to the completion of certain dividend withholding tax declaration forms.

Shareholders entitled to an exemption from Irish dividend withholding tax on any dividends received from us will not be subject to Irish income tax in respect of those dividends, unless they have some connection with Ireland other than their

shareholding (for example, they are resident in Ireland). Non-Irish resident shareholders who receive dividends subject to Irish dividend withholding tax will generally have no further liability to Irish income tax on those dividends.

Prothena ordinary shares received by means of a gift or inheritance could be subject to Irish capital acquisitions tax.

Irish capital acquisitions tax ("CAT") could apply to a gift or inheritance of our ordinary shares irrespective of the place of residence, ordinary residence or domicile of the parties. This is because our ordinary shares will be regarded as property situated in Ireland. The person who receives the gift or inheritance has primary liability for CAT. Gifts and inheritances passing between spouses are exempt from CAT. It is recommended that each shareholder consult his or her own tax advisor as to the tax consequences of holding our ordinary shares or receiving dividends from us.

ITEM 1B. UNRESOLVED STAFF COMMENTS.

None.

ITEM 1C. CYBERSECURITY

Processes for Assessing, Identifying and Managing Risks from Cybersecurity Threats

We, like any other organization operating in the biotechnology and pharmaceutical space, are subject to cybersecurity threats. In order to be prepared to respond to a potential cybersecurity threat, we have implemented an Information Technology ("IT") Security Guidelines Policy. Such policy sets forth a framework for management of all Company-managed IT systems and equipment. In connection with such policy, we have also implemented an IT Security Incident Response Plan, which sets forth processes in the event of a suspected cybersecurity incident. The processes set forth in such IT Security Incident Response Plan are part of our overall enterprise risk management system. As set forth in the IT Security Incident Response Plan, we may engage third-party consultants to assist us with the response to any suspected cybersecurity incident. We engage third parties on a periodic basis in connection with our overall enterprise risk management assessment. With respect to third-party service providers that we may engage in connection with our day-to-day operations, we attempt to assess such service provider's processes regarding potential cybersecurity threats in connection with first engaging such service provider.

Oversight of Risks Related to Cybersecurity Threats

Both our Board of Directors and members of our management team are responsible for oversight of risks related to cybersecurity threats. Our Audit Committee reviews our major risk exposures, including risks related to cybersecurity threats. Our Head of IT, who reports to our Chief Legal Officer, is primarily responsible for assessing and managing risks related to cybersecurity threats. Our Head of IT has approximately 30 years of experience managing IT systems for organizations similarly situated to ours. As set forth in the IT Security Incident Response Plan, the Chief Legal Officer and the Head of Human Resources would be informed of any cybersecurity incident, and depending on the severity of the cybersecurity incident, many other functions of the management team would be informed as well. At the discretion of the Chief Legal Officer, the Audit Committee would be informed of a cybersecurity incident. Additionally, our Head of IT presents an annual report, which sets forth risks related to cybersecurity threats, to the Audit Committee and is available to the committee to discuss any aspect of the report.

As of the date of this report, we have not identified any risks from cybersecurity threats, including as a result of any previous cybersecurity incidents, that have materially affected us, our business strategy, results of operation or financial condition for the years of financial statements presented in this report.

Notwithstanding the approach we take to cybersecurity threats, we may not be successful in preventing or mitigating a cybersecurity incident that could have a material adverse effect on us. See Item 1A. "Risk Factors" for a discussion of risks related to cybersecurity threats.

ITEM 2. PROPERTIES

Our corporate registered address and office is in Dublin, Ireland and our U.S. operations are in Brisbane, California.

In Dublin, Ireland, we occupy approximately 920 square feet of office spaces under two leases which expire on July 31, 2025.

In Brisbane, California, we occupy approximately 31,157 square feet of office and laboratory space under a sublease with Arcus Biosciences, Inc. which expires on September 30, 2028, unless terminated earlier.

We believe that our facilities are sufficient to meet our current needs.

ITEM 3. LEGAL PROCEEDINGS

We are not currently a party to any material legal proceedings. We may at times be party to ordinary routine litigation incidental to our business. When appropriate in management's estimation, we may record reserves in our financial statements for pending legal proceedings.

ITEM 4. MINE SAFETY DISCLOSURES

Not Applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES.

Market Information for Ordinary Shares

Our ordinary shares commenced trading on The Nasdaq Global Market under the symbol "PRTA" on December 21, 2012 and currently trade on The Nasdaq Global Select Market.

Holders

There were approximately 5,177 shareholders of record of our ordinary shares as of February 20, 2025. Because many of our shares are held by brokers and other institutions on behalf of shareholders, we are unable to estimate the total number of shareholders represented by these record holders.

Dividend Policy

We have not paid dividends in the past and do not anticipate paying dividends in the foreseeable future. Any future determination to pay dividends will be at the discretion of our Board of Directors and will be dependent upon our financial condition, results of operations, capital requirements, and such other factors as our Board of Directors deems relevant.

Under Irish law, dividends and distributions may only be made from distributable reserves. Distributable reserves generally means accumulated realized profits, to the extent not previously utilized by distribution or capitalization, less accumulated realized losses, to the extent not previously written off in a reduction or re-organization of capital. In addition, no distribution or dividend may be made unless the net assets of Prothena are equal to, or in excess of, the aggregate of our called up share capital plus undistributable reserves and the distribution does not reduce our net assets below such aggregate. Undistributable reserves include undenominated capital, the share premium account, the capital redemption reserve fund and the amount by which Prothena's accumulated unrealized profits, so far as not previously utilized by any capitalization, exceed our accumulated unrealized losses, so far as not previously written off in a reduction or reorganization of capital.

The determination as to whether or not we have sufficient distributable reserves to fund a dividend must be made by reference to the "relevant financial statements" of Prothena. The "relevant financial statements" are either the last set of unconsolidated annual audited financial statements or other financial statements properly prepared in accordance with the Irish Companies Act 2014, which give a "true and fair view" of our unconsolidated financial position and accord with accepted accounting practice. The relevant financial statements must be filed in the Companies Registration Office (the official public registry for companies in Ireland).

Securities Authorized for Issuance Under Equity Compensation Plans

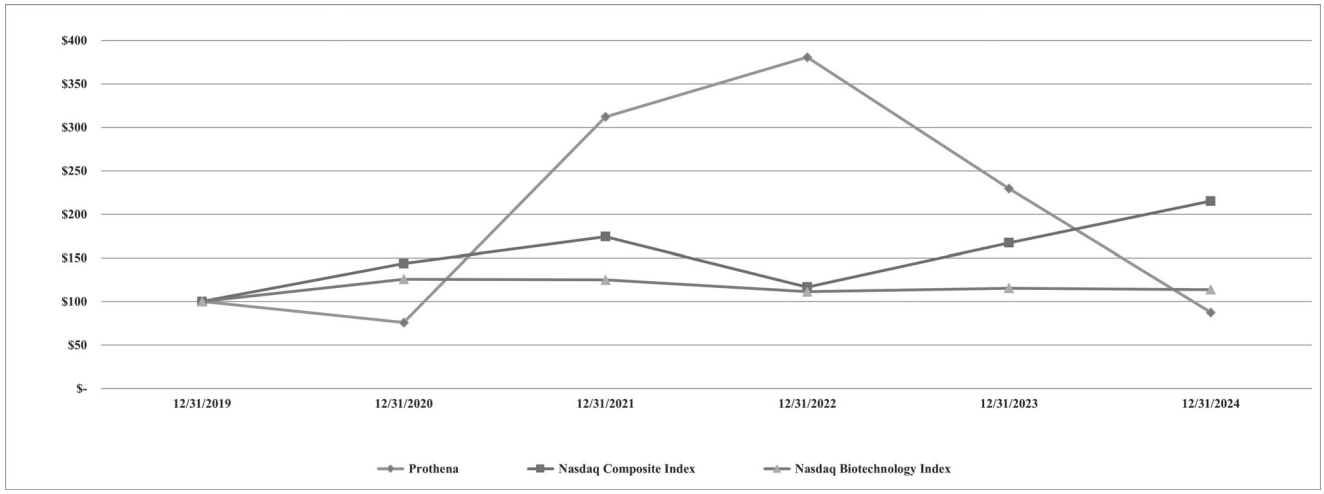
See Item 12 of Part III of this Form 10-K regarding information about securities authorized for issuance under our equity compensation plans.

Performance Graph[(1)]

The following graph shows a comparison from December 31, 2019, through December 31, 2024, of cumulative total return on assumed investment of $100.00 in cash in our ordinary shares, the Nasdaq Composite Index and the Nasdaq Biotechnology Index. Such returns are based on historical results and are not intended to suggest future performance. Points on the graph represent the performance as of end of each business day.

COMPARISON OF 5-YEAR CUMULATIVE TOTAL RETURN

Among Prothena Corporation plc, the Nasdaq Composite Index, and the Nasdaq Biotechnology Index



Cumulative Total Return as of	12/31/2019	12/31/2020	12/31/2021	12/31/2022	12/31/2023	12/31/2024
Prothena Corporation plc	$ 100	$ 76	$ 312	$ 381	$ 230	$ 87
Nasdaq Composite Index	$ 100	$ 144	$ 174	$ 117	$ 167	$ 215
Nasdaq Biotechnology Index	$ 100	$ 126	$ 125	$ 111	$ 115	$ 114

(1) *The information under the heading "Performance Graph" shall not be deemed "soliciting material" or to be "filed" with the SEC for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities under that Section, and shall not be deemed incorporated by reference into any filing of Prothena Corporation plc under the Securities Act of 1933, as amended.*

Recent Sales of Unregistered Securities

None.

Use of Proceeds

None.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

Irish Law Matters

As we are an Irish public limited company, the following matters of Irish law are relevant to the holders of our ordinary shares.

Irish Restrictions on Import and Export of Capital

Except as indicated below, there are no restrictions on non-residents of Ireland dealing in Irish domestic securities, which includes ordinary shares of Irish companies. Dividends and redemption proceeds also continue to be freely transferable to non-resident holders of such securities. The Irish Financial Transfers Act, 1992 (the "Transfers Act") gives power to the Minister for Finance of Ireland to restrict financial transfers between Ireland and other countries and persons. Financial transfers are broadly defined and include all transfers that would be movements of capital or payments within the meaning of the treaties governing the member states of the European Union. The acquisition or disposal of interests in shares issued by an Irish incorporated company and associated payments falls within this definition. In addition, dividends or payments on redemption or purchase of shares and payments on a liquidation of an Irish incorporated company would fall within this definition. At present, the Transfers Act prohibits financial transfers involving the late Slobodan Milosevic and associated persons, certain persons indicted by the International Criminal Tribunal for the former Yugoslavia, the late Osama bin Laden, Al-Qaida, the Taliban of

Afghanistan, certain persons, entities, and activities in Burma (Myanmar), Belarus, Democratic Republic of Congo, Democratic People's Republic of Korea (North Korea), Iran, Iraq, Côte d'Ivoire, Lebanon, Liberia, Zimbabwe, Sudan, Somalia, Republic of Guinea, Afghanistan, Egypt, Eritrea, Libya, Syria, Tunisia, Ukraine, Russia, certain known terrorists and terrorist groups, and countries that harbor certain terrorist groups, without the prior permission of the Central Bank of Ireland.

Irish Taxes Applicable to U.S. Holders

Withholding Tax on Dividends

While we have no current plans to pay dividends, dividends on our ordinary shares would generally be subject to Irish Dividend Withholding Tax ("DWT") at 25%, unless an exemption applies.

Dividends on our ordinary shares that are owned by residents of the U.S. and held beneficially through the Depository Trust Company ("DTC") will not be subject to DWT provided that the address of the beneficial owner of the ordinary shares in the records of the broker is in the U.S.

Dividends on our ordinary shares that are owned by residents of the U.S. and held directly (outside of DTC) will not be subject to DWT provided that the shareholder has completed the appropriate Irish DWT form and this form remains valid. Such shareholders must provide the appropriate Irish DWT form to our transfer agent at least seven business days before the record date for the first dividend payment to which they are entitled.

If any shareholder who is resident in the U.S. receives a dividend subject to DWT, he or she should generally be able to make an application for a refund from the Irish Revenue Commissioners on the prescribed form.

While the U.S./Ireland Double Tax Treaty contains provisions regarding withholding, due to the wide scope of the exemptions from DWT available under Irish domestic law, it would generally be unnecessary for a U.S. resident shareholder to rely on the treaty provisions.

Income Tax on Dividends

A shareholder who is neither resident nor ordinarily resident in Ireland and who is entitled to an exemption from DWT generally has no additional liability to Irish income tax or to the universal social charge on a dividend from us unless that shareholder holds their ordinary shares in connection with a trade or business carried on by such shareholder in Ireland through a branch or agency.

A shareholder who is neither resident nor ordinarily resident in Ireland and who is not entitled to an exemption from DWT generally has no additional liability to Irish income tax or to the universal social charge on a dividend from us. The DWT deducted by us discharges the liability to Irish income tax and to the universal social charge. This however is not the case where the shareholder holds their ordinary shares in connection with a trade or business carried on by such shareholder in Ireland through a branch or agency.

Irish Tax on Capital Gains

A shareholder who is neither resident nor ordinarily resident in Ireland and does not hold their shares in connection with a trade or business carried on by such shareholder in Ireland through a branch or agency should not be within the charge to Irish Capital Gains Tax on a disposal of our shares.

Capital Acquisitions Tax

Irish Capital Acquisitions Tax ("CAT") is comprised principally of gift tax and inheritance tax. CAT could apply to a gift or inheritance of our ordinary shares irrespective of the place of residence, ordinary residence or domicile of the parties. This is because our ordinary shares are regarded as property situated in Ireland as our share register must be held in Ireland. The person who receives the gift or inheritance has primary liability for CAT.

CAT is currently levied at a rate of 33% above certain tax-free thresholds. The appropriate tax-free threshold is dependent upon (i) the relationship between the donor and the donee and (ii) the aggregation of the values of previous gifts and inheritances received by the donee from persons within the same category of relationship for CAT purposes. Gifts and inheritances passing between spouses are exempt from CAT. Our shareholders should consult their own tax advisers as to whether CAT is creditable or deductible in computing any domestic tax liabilities.

Stamp Duty

Irish stamp duty may be payable in respect of transfers of our ordinary shares (currently at the rate of 1% of the price paid or the market value of the shares acquired, if greater). Payment of any Irish stamp duty is generally a legal obligation of the transferee.

A transfer of our ordinary shares from a seller who holds shares through DTC to a buyer who holds the acquired shares through DTC will not be subject to Irish stamp duty. A transfer of our ordinary shares (i) by a seller who holds shares outside of DTC to any buyer, or (ii) by a seller who holds the shares through DTC to a buyer who holds the acquired shares outside of DTC, may be subject to Irish stamp duty. Shareholders wishing to transfer their shares into or out of DTC may do so without giving rise to Irish stamp duty provided that there is no change in the beneficial ownership of such shares and the transfer into or out of DTC is not effected in contemplation of a subsequent sale of such shares to a third party. In order to benefit from this exemption from Irish stamp duty, the seller must confirm to us that there is no change in the ultimate beneficial ownership of the shares as a result of the transfer and there is no agreement for the sale of the shares by the beneficial owner to a third party being contemplated.

ITEM 6. [RESERVED]

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

In addition to historical information, this Form 10-K contains forward-looking statements which may cause our actual results to differ materially from expectations, plans and anticipated results discussed in forward-looking statements. Factors that could cause our actual results to differ materially include, but are not limited to, the risks and uncertainties set forth in the "Summary of Risks Affecting Our Business" at the beginning of this Form 10-K, Item 1A "Risk Factors" of this Form 10-K, and in our other filings with the SEC.

This discussion should be read in conjunction with the Consolidated Financial Statements and Notes to the Consolidated Financial Statements presented in Item 8 of this Form 10-K.

Overview

Prothena is 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 neurodegenerative and rare peripheral amyloid diseases.

Fueled by our deep scientific expertise built over decades of research, we are advancing a pipeline of therapeutic candidates for a number of indications and novel targets for which our ability to integrate scientific insights around neurological dysfunction and the biology of misfolded proteins can be leveraged. Our wholly-owned programs include birtamimab for the potential treatment of AL amyloidosis, and a portfolio of programs for the potential treatment of Alzheimer's disease including PRX012, which targets amyloid beta (Aβ), and PRX123, a novel dual Aβ-tau vaccine. Our partnered programs include prasinezumab for the potential treatment of Parkinson's disease and other related synucleinopathies that targets alpha-synuclein in collaboration with Roche. In addition, we have partnered BMS-986446 (formerly PRX005) for the potential treatment for Alzheimer's disease that targets tau and PRX019 for the potential treatment of neurodegenerative diseases with an undisclosed target in two separate license agreements with Bristol Myers Squibb (BMS). We are also entitled to certain potential milestone payments pursuant to our share purchase agreement with Novo Nordisk pertaining to our ATTR amyloidosis business (inclusive of coramitug, formerly PRX004).

We were formed on September 26, 2012, under the laws of Ireland and re-registered as an Irish public limited company on October 25, 2012. Our ordinary shares began trading on The Nasdaq Global Market under the symbol "PRTA" on December 21, 2012, and currently trade on The Nasdaq Global Select Market.

Critical Accounting Policies and Estimates

Management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with the accounting principles generally accepted in the U.S. ("GAAP"). The preparation of these consolidated financial statements requires us to make estimates and assumptions for the reported amounts of assets, liabilities, revenues, expenses and related disclosures. We believe the following policies to be critical to the judgments and estimates used in the preparation of our financial statements.

Revenue Recognition

Our collaboration revenue includes revenue recognized for milestone payments and reimbursements under our License Agreement with Roche as well as revenue recognized under our Collaboration Agreement with BMS. Our license and intellectual property revenue includes revenue from Novo Nordisk for the sale of intellectual property and related rights to the Company's ATTR amyloidosis business and pipeline and milestones payments.

Revenue is recognized only when we satisfy an identified performance obligation by transferring a promised good or service to a customer. We recognize revenue associated with our collaboration arrangements, which may require us to exercise considerable judgment in estimating revenue to be recognized, including judgments made on day one accounting and judgments associated with the amount of revenue to be recognized over time as performance obligations are satisfied.

Contracts with Multiple Performance Obligations

Significant judgment is required to apply the authoritative accounting guidance at the outset of a collaboration arrangement, and over time. Our Collaboration Agreement with BMS and our License Agreement with Roche contain multiple performance obligations. In the identification of performance obligations, there is judgment involved in identifying the promised goods or services in the collaboration agreement, determining whether these are distinct in the context of the contract, and determining if these represent a performance obligation to a customer. These determinations are highly subjective and can differ between arrangement based on specific contractual terms. The identified performance obligations will impact most significantly the timing of revenue recognition, and is a point-in-time assessment performed at the outset of a collaboration arrangement. We account for the individual performance obligations separately if they are distinct. Factors considered in the determination of whether the license performance obligations are distinct included, among other things, the research and development capabilities of each of BMS and Roche and their respective sublicense rights, and for the remaining performance obligations the fact that they are not proprietary and can be and have been provided by other vendors. The transaction price is allocated to the separate performance obligation on a relative standalone selling price basis.

Milestone Revenue

We generally classify each of our milestones into one of three categories: (i) clinical milestones; (ii) regulatory and development milestones; and (iii) commercial milestones. Clinical milestones are typically achieved when a product candidate advances into or completes a defined phase of clinical research. For example, a milestone payment may be due to us upon the initiation of a clinical trial for a new indication. Regulatory and development milestones are typically achieved upon acceptance of the submission for marketing approval of a product candidate or upon approval to market the product candidate by the FDA or other regulatory authorities. For example, a milestone payment may be due to us upon submission for marketing approval of a product candidate by the FDA. Commercial milestones are typically achieved when an approved product reaches certain defined levels of net royalty sales by the licensee of a specified amount within a specified period.

At the inception of each arrangement that includes developmental, regulatory or commercial milestone payments, we evaluate whether achieving the milestones is considered probable and estimate the amount to be included in the transaction price using the most likely amount method, which includes judgment. If it is probable that a significant revenue reversal would not occur, the value of the associated milestone (such as a regulatory submission by Prothena) is included in the transaction price. Milestone payments that are not within our control, such as approvals from regulators or where attainment of the specified event is dependent on the development activities of a third party, are not considered probable of being achieved until those approvals are received or the specified event occurs. In general, we consider such milestone payments as variable consideration with constraint and therefore we recognize the revenue from such milestone payments as collaboration revenue at point in time when we can conclude it is probable that a significant revenue reversal will not occur in future periods.

Research and Development

We expense R&D costs as incurred. R&D expenses include, but are not limited to, salary and benefits, share-based compensation, clinical trial activities, drug development and manufacturing prior to FDA approval and third-party service fees, including clinical research organizations, investigative sites and contract manufacturing organizations. A significant portion of our research and development expenses in the Consolidated Statements of Operations are external costs, which we track on a program-specific basis when the applicable program was separately tracked in preclinical development. These research and development expenses include the conduct of preclinical studies and clinical trials, contract manufacturing activities and consulting services. The measurement of these research and development costs and/or effort can impact the research and development expenses in the Consolidated Statements of Operations and of prepaid assets and accrued liabilities on the

Consolidated Balance Sheets. The level of judgment required to estimate research and development expenses varies based on the nature of the services being performed and the underlying support obtained. We recognize costs for certain development activities, such as clinical trials, based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, or information provided to us by our vendors on their actual costs incurred. We recognize costs for contract manufacturing based on evaluation of the progress to completion of specific tasks. As such, expense accruals related to clinical trials and contract manufacturing are recognized based on our estimate of the degree of completion of the events specified in the specific clinical study or trial contract or drug development and manufacturing contract, respectively. We estimate the amount of work completed through discussions with internal personnel and external service providers as to the progress or stage of completion of the services and the agreed-upon fee to be paid for such services. As actual costs become known, we adjust our accrued estimates. These estimates are based on certain assumptions and inputs that can be challenging to assess, including the evaluation of the status of and costs incurred for manufacturing activities, outsourced research and development programs and project milestones achieved. Although we do not expect our estimates to be materially different from amounts actually incurred, incomplete or inaccurate data from vendors could impact our understanding of the status and timing of services performed which could result in us reporting expenses that are too high or too low in any particular period.

We do not need to make significant estimates where costs incurred are supported by invoices or reports of costs incurred are obtained from a vendor that is directly performing the underlying services, such as a consultant, contract research organization or contract manufacturing organization. In some cases, however, expense is recorded using an underlying assumption of the progress to completion of specific activities. For example, costs may be recognized based on the passage of time for activities that span reporting periods. If the provision of services is not linear then this assumption could impact the amount of expense recognized. For other activities, such as for certain clinical trials, expense is recorded based on information obtained from vendors as an intermediary to those performing the underlying services, such as contract research organizations. These estimates are inherently more judgmental since the quality and availability of the underlying data may vary. We expect that the level of judgment in estimating research and development expenses may increase over time as we are entering later stage, more extensive, clinical trials.

The information contained in Note 2 to the Consolidated Financial Statements under the headings “Recently Issued Accounting Pronouncements Not Yet Adopted” and “Recently Adopted Accounting Pronouncement - Segment Reporting” are hereby incorporated by reference into this Part II, Item 7.

Results of Operations

Comparison of Years Ended December 31, 2024 and 2023

Revenue

	Year Ended December 31,		Change	
	2024	2023	$	%
	(Dollars in thousands)			
Collaboration revenue	$ 135,107	$ 91,320	$ 43,787	48 %
Revenue from license and intellectual property	50	50	—	— %
Total revenue	$ 135,157	$ 91,370	$ 43,787	48 %

Total revenue was $135.2 million and $91.4 million for the years ended December 31, 2024, and 2023, respectively.

Collaboration revenue from BMS increased $43.8 million for the year ended December 31, 2024, compared to the year ended December 31, 2023. Collaboration revenue from BMS for 2024 included recognition of $110.1 million from the PRX019 Global License Agreement and related development services and $25.0 million was related to BMS’s material rights for the US Rights and Global Rights for the TDP-43 Collaboration Target that expired unexercised as a result of the expiration of the research term of the Collaboration Agreement. Collaboration revenue from BMS for 2023 included recognition of $91.3 million from the Tau Global License Agreement and related development services. See Note 7, “Significant Agreements” to the Consolidated Financial Statements regarding the Collaboration Agreement with BMS for more information.

License and intellectual property revenue for the year ended December 31, 2024 was $50,000 compared to $50,000 for the year ended December 31, 2023. See Note 7, “Significant Agreements” to the Consolidated Financial Statements regarding the Novo Nordisk Share Purchase Agreement for more information.

Assuming no significant change in our business, we expect our 2025 revenue to decline over the prior year as our 2024 revenue was primarily comprised of nonrecurring revenue.

Operating Expenses

	Year Ended December 31,		Change	
	2024	2023	$	%
	(Dollars in thousands)			
Research and development	$ 222,519	$ 220,571	$ 1,948	1 %
General and administrative	67,199	61,835	5,364	9 %
Total operating expenses	$ 289,718	$ 282,406	$ 7,312	3 %

Total operating expenses consist of R&D expenses, general and administrative ("G&A") expenses. Our operating expenses were $289.7 million and $282.4 million for the years ended December 31, 2024, and 2023, respectively.

Our research activities are aimed at developing new drug products. Our development activities involve the translation of our research into potential new drugs. Our R&D expenses primarily consist of personnel costs and related expenses, including share-based compensation and external costs associated with clinical activities and drug development related to our drug programs, including birtamimab, BMS-986446 (PRX005), PRX012, PRX123, PRX019 and preclinical activities related to our discovery programs.

Our G&A expenses primarily consist of personnel costs and related expenses, including share-based compensation and consulting expenses.

Research and Development Expenses

Our R&D expense increased by $1.9 million for the year ended December 31, 2024, compared to the prior year. The increase for the year ended December 31, 2024, was primarily due to higher clinical trial expenses primarily related to the PRX012 and birtamimab programs, higher personnel expenses; offset in part by lower manufacturing expense and lower other R&D expenses.

The following table sets forth the R&D expenses for our major programs (specifically, any active program with successful first dosing in a Phase 1 clinical trial), which were birtamimab, prasinezumab, coramitug, BMS-986446 (PRX005), PRX012, PRX019 and other R&D expenses for the years ended December 31, 2024, and 2023 (in thousands):

	Year Ended December 31,	
	2024	2023
Birtamimab (NEOD001)	$ 85,649	$ 68,831
Prasinezumab (PRX002/RG7935)	49	34
Coramitug (NNC6019/PRX004)[1]	4	91
BMS-986446 (PRX005)	264	10,063
PRX012	116,359	102,767
PRX019[2]	5,035	7,703
Other R&D[3]	15,159	31,082
Total research and development	$ 222,519	$ 220,571

(1) *On July 8, 2021, we sold shares of one of our wholly-owned subsidiaries to Novo Nordisk. In connection with the transaction, Novo Nordisk acquired our ATTR amyloidosis business, including the clinical stage antibody coramitug (PRX004). Expenses incurred relate to certain close out activities and transition services provided to Novo Nordisk.*

(2) *R&D costs include the costs incurred from the date when PRX019 was separately tracked in preclinical development.*

(3) *Other R&D is comprised primarily of preclinical development and discovery programs that have not progressed to first patient dosing in a Phase 1 clinical trial and close out costs for programs that we are no longer advancing.*

General and Administrative Expenses

Our G&A expenses increased by $5.4 million, for the year ended December 31, 2024, compared to the prior year primarily due to higher personnel expense.

Other Income (Expense)

	Year Ended December 31,		Change	
	2024	2023	$	%
	(Dollars in thousands)			
Interest income	$ 25,816	$ 31,014	$ (5,198)	(17)%
Other income (expense), net	(185)	(458)	273	(60)%
Total other income (expense), net	$ 25,631	$ 30,556	$ (4,925)	(16)%

Interest income decreased by $5.2 million for the year ended December 31, 2024, compared to the prior year, primarily due to lower interest income from our cash and money market accounts resulting from lower interest rates and lower cash and money market balances.

Other income (expense), net for the year ended December 31, 2024, was primarily foreign exchange losses from transactions with vendors denominated in euros.

Provision for (benefit from) Income Taxes

	Year Ended December 31,		Change	
	2024	2023	$	%
	(Dollars in thousands)			
Benefit from income taxes	$ (6,620)	$ (13,452)	$ 6,832	(51)%

The benefit from income taxes decreased by $6.8 million for the year ended December 31, 2024, compared to the same period in the prior year. The decline in benefit from income taxes for the year ended December 31, 2024, compared to the prior year, was primarily due to a lower increase in deferred tax assets related to Section 174 R&D Capitalization.

The tax provisions for all periods presented primarily reflect U.S. federal taxes associated with recurring profits attributable to intercompany services that our U.S. subsidiary performs for the Company. No tax benefit has been recorded related to tax losses recognized in Ireland and any deferred tax assets for those losses are offset by a valuation allowance.

Comparison of the years ended December 31, 2023 and 2022

Refer to "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations—Results of Operations" in our 2023 Annual Report on Form 10-K for a discussion of the results of operations for the year ended December 31, 2023 compared to the year ended December 31, 2022.

Liquidity and Capital Resources

Overview

	December 31,	
	2024	2023
	(Dollars in thousands)	
Working capital	$ 436,911	$ 582,391
Cash and cash equivalents	$ 471,388	$ 618,830
Total assets	$ 547,108	$ 696,382
Total liabilities	$ 60,182	$ 135,017
Total shareholders' equity	$ 486,926	$ 561,365

Working capital was $436.9 million as of December 31, 2024, a decrease of $145.5 million from working capital of $582.4 million as of December 31, 2023. This decrease in working capital during the year ended December 31, 2024, was

primarily attributable to cash use of $289.7 million for operating expenses (adjusted to exclude non-cash charges) offset in part by $80.0 million option exercise payment from BMS, interest income on investments of $25.8 million, and net proceeds received from stock option exercises of approximately $1.9 million.

As of December 31, 2024, we had $471.4 million in cash and cash equivalents. Based on our current business plans, we believe that our existing cash and cash equivalents at December 31, 2024 are sufficient to meet our obligations for at least the next twelve months. To operate beyond such period, or if we elect to increase our spending on research and development programs significantly above current long-term plans or enter into potential licenses and/or other acquisitions of complementary technologies, products or companies, we may need additional capital. Additionally, in order to develop and obtain regulatory approval for our potential products we will need to raise substantial additional capital. We expect to continue to finance future capital needs that exceed our existing cash and cash equivalents, payments pursuant to our agreements with Roche, BMS, and Novo Nordisk, and, to the extent necessary, other collaboration agreements with corporate partners, or other arrangements, and through proceeds from public or private equity or debt financings, and loans, including pursuant to the Amended Distribution Agreement (See Note 8, "Shareholders' Equity" to the Consolidated Financial Statements for more information). We cannot assume that such additional financings will be available on acceptable terms, if at all, and such financings may only be available on terms dilutive to our shareholders.

In managing our liquidity needs in Ireland, we do not rely on unrepatriated earnings as a source of funds. As of December 31, 2024, $265.3 million of our outstanding cash and cash equivalents related to U.S. operations are considered permanently reinvested. We do not intend to repatriate these funds. However, if these funds were repatriated back to Ireland, we would incur a withholding tax from the dividend distribution.

The adequacy of our cash resources depends on many assumptions, including assumptions with respect to our expenses. These assumptions may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with completing the development of our product candidates. 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 nonclinical 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; the costs of any in-licensing transactions; and the timing, receipt, and amount of revenues or royalties, if any, from any approved drug candidates.

Our cash and cash equivalents may also be potentially supplemented in the future by proceeds from our collaboration partners BMS (formerly Celgene), Roche and milestone payments from Novo Nordisk. Pursuant to the Collaboration Agreement with Roche, we are eligible to receive payments for commercial and regulatory milestones and royalties on net sales of Collaboration Products. See Note 7, "Significant Agreements" to our Consolidated Financial Statements regarding the Roche License Agreement for more information. Pursuant to the Collaboration Agreement with BMS, we are eligible to receive payments for commercial and regulatory milestones and royalties on net sales of Collaboration Products. See Note 7, "Significant Agreements" to our Consolidated Financial Statements regarding the Collaboration Agreement with BMS for more information. Pursuant to the share purchase agreement with Novo Nordisk, we are eligible to receive development and sales milestone payments. See Note 7, "Significant Agreements" to our Consolidated Financial Statements regarding the Novo Nordisk Share Purchase Agreement for more information.

Cash Flows

The following table summarizes, for the periods indicated, selected items in our Consolidated Statements of Cash Flows (in thousands):

	Year Ended December 31,		
	2024	**2023**	**2022**
Net cash used in operating activities	$ (150,050)	$ (133,906)	$ (108,821)
Net cash used in investing activities	(298)	(2,773)	(464)
Net cash provided by financing activities	1,554	45,103	241,457
Net increase (decrease) in cash, cash equivalents and restricted cash	$ (148,794)	$ (91,576)	$ 132,172

Cash Used in Operating Activities

Net cash used in operating activities was $150.1 million for the year ended December 31, 2024, which was primarily due to ongoing research and development activities and general and administrative expenses to support those activities for a total of $289.7 million in operating expenses (adjusted to exclude non-cash charges of approximately $40.2 million) partially offset by $80.0 million option exercise payment from BMS, interest income on investments of $25.8 million, and cash from collection of accounts receivable of $5.2 million.

Cash Used in Investing Activities

Net cash used in investing activities was $0.3 million for the year ended December 31, 2024, which primarily consisted of expenditures to purchase property and equipment.

Cash Provided by Financing Activities

Net cash provided by financing activities was $1.6 million for the year ended December 31, 2024, primarily from proceeds from issuances of ordinary shares upon exercises of stock options of $1.9 million.

Years ended December 31, 2023 and 2022

Refer to "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations — Liquidity and Capital Resources" in our 2023 Annual Report on Form 10-K for a discussion of the cash flows for the years ended December 31, 2023 and 2022.

Off-Balance Sheet Arrangements

At December 31, 2024, we were not a party to any off-balance sheet arrangements that have, or are reasonably likely to have, a current or future effect on our financial condition, changes in financial condition, revenue or expenses, results of operations, liquidity, capital expenditures or capital resources.

Contractual Obligations

Our contractual obligations as of December 31, 2024, consisted of minimum cash payments under operating leases of $12.1 million, purchase obligations of $12.7 million (of which $1.8 million is included in current liabilities), and contractual obligations under license agreements of $0.3 million (of which nil is included in current liabilities). Purchase obligations consist of non-cancelable purchase commitments to suppliers. Operating leases represent our future minimum rental commitments under our non-cancelable operating leases. For additional information regarding the timing for our contractual obligations see Note 6, "Commitments and Contingencies" to Consolidated Financial Statements.

In June 2021, we entered into a lease agreement for office space in Dublin, Ireland, which commenced in August 2021 and had an initial term of one year. In addition, we entered into a lease agreement for additional office space in Dublin, Ireland, which commenced in August 2023 and had an initial term of one year. In April 2024, we renewed both leases, each for another one year term with termination dates in July 2025. Both leases have an automatic renewal clause, pursuant to which each agreement will be extended automatically for successive periods equal to their current terms, unless each agreement is cancelled by us. We do not consider the renewals in the lease term as we do not believe it to be reasonably certain that we will renew these leases, as our real estate needs are subject to change based on our business needs.

In October 2022, we entered into a noncancelable operating sublease to lease approximately 31,157 square feet of office and laboratory space in Brisbane, California. We are obligated to make lease payments totaling approximately $14.9 million over the lease term, which expires on September 30, 2028, unless terminated earlier. Of this obligation, approximately $12.0 million remains outstanding as of December 31, 2024.

The following is a summary of our contractual obligations as of December 31, 2024 (in thousands):

	Total	2025	2026	2027	2028	Thereafter
Operating leases [1]	$ 12,129	$ 3,179	$ 3,158	$ 3,269	$ 2,523	$ —
Purchase obligations [2]	12,729	12,633	96	—	—	—
Contractual obligations under license agreements	274	64	60	60	45	45
Total	$ 25,132	$ 15,876	$ 3,314	$ 3,329	$ 2,568	$ 45

[1] *See Note 6, "Commitments and Contingencies" to our Consolidated Financial Statements.*

[2] *Purchase obligations as of the filing date includes additional $2.1 million purchase commitments to our contract manufacturers.*

In addition to the contractual obligations above, we also expect to have future material cash requirements related to our clinical trials, discovery and pre-clinical programs, human capital and intellectual property. Assuming no significant change in our business, we expect the full year 2025 net cash used in operating and investing activities to be approximately $168 million to $175 million.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are exposed to market risks in the ordinary course of our business including the effect of changes in foreign currency exchange rates and interest rates. Market risk represents the risk of loss that may impact our financial position due to adverse changes in financial market prices and rates.

Foreign Currency Risk

Our business is primarily conducted in U.S. dollars except for our agreements with contract manufacturers for drug supplies which are primarily denominated in euros. We recorded losses on foreign currency exchange rate differences of approximately $185,000, $458,000 and $397,000 during the years ended December 31, 2024, 2023 and 2022, respectively. If we increase our business activities that require the use of foreign currencies, we may be exposed to losses if the euro and other such currencies strengthen against the U.S. dollar.

Interest Rate Risk

Our exposure to interest rate risk is limited to our cash equivalents, which consist of accounts maintained in money market funds. We have assessed that there is no material exposure to interest rate risk given the nature of money market funds. In general, money market funds are not subject to interest rate risk because the interest paid on such funds fluctuates with the prevailing interest rate. Accordingly, our interest income fluctuates with short-term market conditions.

In the future, we anticipate that our exposure to interest rate risk will primarily be related to our investment portfolio, which is currently invested in money market accounts. We may invest any surplus funds in accordance with a policy approved by our board of directors which will specify the categories, allocations, and ratings of securities we may consider for investment. The primary objectives of our investment policy are to preserve principal and maintain proper liquidity to meet our operating requirements. Our investment policy also specifies credit quality standards for our investments and limits the amount of credit exposure to any single issue, issuer or type of investment.

Credit Risk

Financial instruments that potentially subject us to concentration of credit risk consist of cash and cash equivalents and accounts receivable. We place our cash and cash equivalents with high credit quality financial institutions and pursuant to our investment policy, we limit the amount of credit exposure with any one financial institution. Deposits held with banks have exceeded, and will continue to exceed, federally insured limits on such deposits. We are exposed to credit risk in the event of a default by the financial institutions holding our cash and cash equivalents. We have not experienced any losses on our deposits of cash and cash equivalents. Our credit risk exposure is up to the extent recorded on the Company's Consolidated Balance Sheets.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Shareholders and Board of Directors
Prothena Corporation plc:

Opinions on the Consolidated Financial Statements and Internal Control Over Financial Reporting

We have audited the accompanying consolidated balance sheets of Prothena Corporation plc and subsidiaries (the Company) as of December 31, 2024 and 2023, the related consolidated statements of operations, cash flows, and shareholders' equity for each of the years in the three-year period ended December 31, 2024, and the related notes (collectively, the consolidated financial statements). We also have audited the Company's internal control over financial reporting as of December 31, 2024, based on criteria established in *Internal Control – Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2024 and 2023, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2024, in conformity with U.S. generally accepted accounting principles. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2024 based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's consolidated financial statements and an opinion on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made

only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of a critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Evaluation of accrued research and development costs and related prepaid expenses

As discussed in Notes 2 and 4 to the consolidated financial statements, research and development costs are expensed by the Company as incurred. As of December 31, 2024, the Company recognized accrued research and development costs of $13.4 million and prepaid research and development expenses of $12.0 million. Costs for certain development activities, such as clinical trials, are recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, or information provided to the Company by its vendors, including contract research organizations, on their actual costs incurred. Expense accruals related to clinical trials are recognized based on the Company's estimate of the degree of completion of the events specified in the specific clinical study or trial contract. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the consolidated financial statements as prepaid or accrued research and development.

We identified the evaluation of certain prepaid and accrued research and development costs relating to contract research organizations and investigative sites as a critical audit matter. Complex and subjective auditor judgment was involved in evaluating the estimated degree of completion of the events specified in the specific clinical study or trial contract used to determine certain prepaid and accrued research and development costs due to the nature and extent of evidence available.

The following are the primary procedures we performed to address this critical audit matter. We evaluated the design and tested the operating effectiveness of certain internal controls related to prepaid and accrued research and development costs. This included a control related to the estimated degree of completion of the events specified in the specific clinical study or trial contract. For a sample of certain prepaid and accrued research and development costs, we agreed the amount, duration and any key terms to the underlying contract. We examined underlying documentation and third-party evidence from contract research organizations and compared them to the inputs used in developing the estimated degree of completion of the events specified in the specific clinical study or trial contract. In addition, we inquired of the individuals who are responsible for monitoring and tracking the status of the clinical trials to understand the degree of completion of the reported activities.

/s/ KPMG LLP

We have served as the Company's auditor since 2012.

San Francisco, California
February 27, 2025

Prothena Corporation plc and Subsidiaries
Consolidated Balance Sheets
(in thousands, except share and per share data)

	December 31,	
	2024	2023
Assets		
Current assets:		
Cash and cash equivalents	$ 471,388	$ 618,830
Accounts receivable	—	5,159
Prepaid expenses and other current assets	14,024	13,941
Restricted cash, current	—	1,352
Total current assets	485,412	639,282
Non-current assets:		
Property and equipment, net	3,081	3,836
Operating lease right-of-use assets	10,708	12,162
Deferred tax assets	43,239	33,893
Restricted cash, non-current	860	860
Other non-current assets	3,808	6,349
Total non-current assets	61,696	57,100
Total assets	$ 547,108	$ 696,382
Liabilities and Shareholders' Equity		
Current liabilities:		
Accounts payable	$ 7,770	$ 25,391
Accrued research and development	13,428	14,724
Deferred revenue, current	8,850	—
Lease liability, current	2,610	1,114
Other current liabilities	15,843	15,662
Total current liabilities	48,501	56,891
Non-current liabilities:		
Deferred revenue, non-current	3,448	67,405
Lease liability, non-current	8,233	10,721
Total non-current liabilities	11,681	78,126
Total liabilities	60,182	135,017
Commitments and contingencies (Note 6)		
Shareholders' equity:		
Euro deferred shares, €22 nominal value:	—	—
Authorized shares — 10,000 at December 31, 2024 and 2023		
Issued and outstanding shares — none at December 31, 2024 and 2023		
Ordinary shares, $0.01 par value:	538	537
Authorized shares — 100,000,000 at December 31, 2024 and 2023		
Issued and outstanding shares — 53,826,982 and 53,682,117 at December 31, 2024 and 2023, respectively		
Additional paid-in capital	1,588,729	1,540,859
Accumulated deficit	(1,102,341)	(980,031)
Total shareholders' equity	486,926	561,365
Total liabilities and shareholders' equity	$ 547,108	$ 696,382

See accompanying Notes to Consolidated Financial Statements.

Prothena Corporation plc and Subsidiaries
Consolidated Statements of Operations
(in thousands, except per share data)

	Year Ended December 31,		
	2024	**2023**	**2022**
Collaboration revenue	$ 135,107	$ 91,320	$ 13,855
Revenue from license and intellectual property	50	50	40,050
Total revenue	135,157	91,370	53,905
Operating expenses:			
Research and development	222,519	220,571	135,562
General and administrative	67,199	61,835	49,900
Total operating expenses	289,718	282,406	185,462
Loss from operations	(154,561)	(191,036)	(131,557)
Other income (expense):			
Interest income	25,816	31,014	6,349
Other expense, net	(185)	(458)	(397)
Total other income, net	25,631	30,556	5,952
Loss before income taxes	(128,930)	(160,480)	(125,605)
Benefit from income taxes	(6,620)	(13,452)	(8,656)
Net loss	$ (122,310)	$ (147,028)	$ (116,949)
Basic and diluted net loss per ordinary share	$ (2.27)	$ (2.76)	$ (2.47)
Shares used to compute basic and diluted net loss per share	53,772	53,216	47,369

See accompanying Notes to Consolidated Financial Statements.

Prothena Corporation plc and Subsidiaries
Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,		
	2024	2023	2022
Operating activities			
Net loss	$ (122,310)	$ (147,028)	$ (116,949)
Adjustments to reconcile net loss to cash used in operating activities:			
Depreciation and amortization	893	928	744
Share-based compensation	45,964	40,914	31,322
Deferred income taxes	(9,346)	(15,689)	(11,133)
Reduction in the carrying amount of right-of-use assets	2,692	7,484	5,997
Loss on disposal of fixed assets	—	15	1
Changes in operating assets and liabilities:			
Accounts receivable	5,159	(5,159)	—
Prepaid expenses and other assets	2,539	(2,537)	(10,809)
Deferred revenue	(55,107)	(29,330)	(13,855)
Accounts payable, accruals and other liabilities	(18,298)	22,855	11,865
Operating lease liabilities	(2,236)	(6,359)	(6,004)
Net cash used in operating activities	(150,050)	(133,906)	(108,821)
Investing activities			
Purchases of property and equipment	(298)	(2,810)	(464)
Proceeds from disposal of fixed assets	—	37	—
Net cash used in investing activities	(298)	(2,773)	(464)
Financing activities			
Proceeds from issuance of ordinary shares in public offering, net	—	20,689	172,583
Proceeds from issuance of ordinary shares in at-the market offering, net	(353)	2,894	51,033
Proceeds from issuance of ordinary shares upon exercise of stock options	1,907	21,520	17,841
Net cash provided by financing activities	1,554	45,103	241,457
Net increase (decrease) in cash, cash equivalents and restricted cash	(148,794)	(91,576)	132,172
Cash, cash equivalents and restricted cash, beginning of the year	621,042	712,618	580,446
Cash, cash equivalents and restricted cash, end of the year	$ 472,248	$ 621,042	$ 712,618
Supplemental disclosures of cash flow information			
Cash paid for income taxes, net	$ 3,172	$ 1,554	$ 2,659
Supplemental disclosures of non-cash investing and financing activities			
Receivable from option exercises	$ —	$ —	$ 62
Acquisition of property and equipment included in accounts payable and accrued liabilities	$ 75	$ 237	$ —
Right-of-use assets obtained in exchange for lease obligations	$ 217	$ 3,810	$ 151
Reclassification of prepaid lease payments to right-of-use assets upon lease commencement	$ —	$ 7,763	$ —
At-the market offering costs included in accounts payable and accrued liabilities	$ —	$ 6	$ 13
Public offering costs included in accounts payable and accrued liabilities	$ —	$ —	$ 220

See accompanying Notes to Consolidated Financial Statements.

The following table provides a reconciliation of cash, cash equivalents and restricted cash reported within the statement of financial position that sum to the total of the same such amounts shown in the Consolidated Statements of Cash Flows.

	Year Ended December 31,		
	2024	2023	2022
Cash and cash equivalents	$ 471,388	$ 618,830	$ 710,406
Restricted cash, current	—	1,352	—
Restricted cash, non-current	860	860	2,212
Total cash, cash equivalents and restricted cash, end of the year	$ 472,248	$ 621,042	$ 712,618

Prothena Corporation plc and Subsidiaries
Consolidated Statements of Shareholders' Equity
(in thousands, except share data)

	Ordinary Shares		Additional Paid-in Capital	Accumulated Deficit	Total Shareholders' Equity
	Shares	Amount			
Balances at December 31, 2021	**46,660,294**	**$ 466**	**$ 1,181,630**	**$ (716,054)**	**$ 466,042**
Share-based compensation	—	—	31,322	—	31,322
Issuance of ordinary shares upon exercise of stock options	1,282,086	14	17,876	—	17,890
Issuance of ordinary shares in public offering, net of issuance costs of $11.3 million	3,250,000	32	172,331	—	172,363
Issuance of ordinary shares under the at-the-market offering program, net of issuance costs of $1.7 million	911,228	9	51,365	—	51,374
Net loss	—	—	—	(116,949)	(116,949)
Balances at December 31, 2022	**52,103,608**	**521**	**1,454,524**	**(833,003)**	**622,042**
Share-based compensation			40,914		40,914
Issuance of ordinary shares upon exercise of stock options	1,135,302	12	21,445	—	21,457
Issuance of ordinary shares upon vesting of restricted stock units	5,750	—	—	—	—
Issuance of ordinary shares in public offering, net of issuance costs of $1.4 million	395,096	4	20,905	—	20,909
Issuance of ordinary shares under the at-the-market offering program, net of issuance costs of $153 thousand	42,361	—	3,071	—	3,071
Net loss	—	—	—	(147,028)	(147,028)
Balances at December 31, 2023	**53,682,117**	**537**	**1,540,859**	**(980,031)**	**561,365**
Share-based compensation			45,964		45,964
Issuance of ordinary shares upon exercise of stock options	125,615	1	1,906		1,907
Issuance of ordinary shares upon vesting of restricted stock units	19,250	—	—		—
Net loss				(122,310)	(122,310)
Balances at December 31, 2024	**53,826,982**	**$ 538**	**$ 1,588,729**	**$ (1,102,341)**	**$ 486,926**

See accompanying Notes to Consolidated Financial Statements.

Notes to the Consolidated Financial Statements

1. Organization

Description of Business

Prothena Corporation plc ("Prothena" or the "Company") is 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 neurodegenerative and rare peripheral amyloid diseases.

Fueled by its deep scientific expertise built over decades of research, the Company is advancing a pipeline of therapeutic candidates for a number of indications and novel targets for which its ability to integrate scientific insights around neurological dysfunction and the biology of misfolded proteins can be leveraged. The Company's wholly-owned programs include birtamimab for the potential treatment of AL amyloidosis, and a portfolio of programs for the potential treatment of Alzheimer's disease including PRX012, which targets amyloid beta (Aβ), and PRX123, a novel dual Aβ-tau vaccine. The Company's partnered programs include prasinezumab for the potential treatment of Parkinson's disease and other related synucleinopathies that targets alpha-synuclein in collaboration with Roche. In addition, we have partnered BMS-986446 (formerly PRX005) for the potential treatment of Alzheimer's disease that targets tau and PRX019 for the potential treatment of neurodegenerative diseases with an undisclosed target in two separate license agreements with Bristol Myers Squibb ("BMS"). The Company is also entitled to certain potential milestone payments pursuant to the Company's share purchase agreement with Novo Nordisk pertaining to the Company's ATTR amyloidosis business (inclusive of coramitug, formerly PRX004).

The Company was formed on September 26, 2012, under the laws of Ireland and re-registered as an Irish public limited company on October 25, 2012. The Company's ordinary shares began trading on The Nasdaq Global Market under the symbol "PRTA" on December 21, 2012, and currently trade on The Nasdaq Global Select Market.

Liquidity and Business Risks

As of December 31, 2024, the Company had an accumulated deficit of $1.1 billion and cash and cash equivalents of $471.4 million.

Based on the Company's business plans, management believes that the Company's cash and cash equivalents at December 31, 2024, are sufficient to meet its obligations for at least the next twelve months. To operate beyond such period, or if the Company elects to increase its spending on research and development programs significantly above current long-term plans or enters into potential licenses and/or other acquisitions of complementary technologies, products or companies, the Company may need additional capital. Additionally, in order to develop and obtain regulatory approval for our potential products the Company will need to raise substantial additional capital. The Company expects to continue to finance future capital needs that exceed its existing cash and cash equivalents from payments pursuant to its agreements with Roche, BMS, and Novo Nordisk, and, to the extent necessary, other collaborative agreements with corporate partners, or other arrangements, and through proceeds from public or private equity or debt financings, and loans including pursuant to the Amended Distribution Agreement (See Note 8, "Shareholders' Equity" for more information). The Company cannot assume that such additional financings will be available on acceptable terms, if at all, and such financings may only be available on terms dilutive to its shareholders.

2. Summary of Significant Accounting Policies

Basis of Preparation and Presentation of Financial Information

These Consolidated Financial Statements have been prepared in accordance with the accounting principles generally accepted in the U.S. ("U.S. GAAP") and pursuant to the rules and regulations of the Securities and Exchange Commission ("SEC"). These Consolidated Financial Statements include the accounts of the Company and its wholly-owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation. The Consolidated Financial Statements of Prothena Corporation plc are presented in U.S. dollars, which is the functional currency of the Company and its consolidated subsidiaries. Monetary assets and liabilities denominated in foreign currency are remeasured at period-end exchange rates. Foreign currency gains and losses resulting from remeasurement are recognized in other expense, net in the Consolidated Statements of Operations.

Use of Estimates

The preparation of the Consolidated Financial Statements in conformity with U.S. GAAP requires the Company to make judgments, estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosures. On an ongoing basis, management evaluates its estimates, including critical accounting policies or estimates related to revenue recognition and research and development expenses. The Company bases its estimates on historical experience and on various other market specific and other relevant assumptions that management believes to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Because of the uncertainties inherent in such estimates, actual results may differ materially from these estimates.

Significant Accounting Policies

Cash, Cash Equivalents, and Restricted Cash

The Company considers all highly liquid investments held at financial institutions, such as commercial paper, money market funds, and other money market securities with original maturities of three months or less at date of purchase to be cash equivalents.

Cash accounts that are restricted to withdrawal or usage are presented as restricted cash. As of December 31, 2024, the Company had $0.9 million of restricted cash held by a bank in certificates of deposit as collateral to standby letters of credit under certain operating leases. See Note 6, "Commitments and Contingencies" for additional information regarding the Company’s operating leases.

Accounts Receivable

The accounts receivable balance on the Consolidated Balance Sheets represents amounts receivable from the Company's collaboration partners. The Company monitors the financial performance and creditworthiness of customers so that it can properly assess and respond to changes in their credit profiles. The Company makes judgments as to its ability to collect outstanding receivables and provides an allowance for credit losses against the trade account receivables, when appropriate.

Property and Equipment, net

Property and equipment, net are stated at cost less accumulated depreciation and amortization. Depreciation and amortization is computed using the straight-line method over the estimated useful lives of the related assets. Maintenance and repairs are charged to expense as incurred, and leasehold improvements where the Company is deemed the accounting owner are capitalized. When assets are retired or otherwise disposed of, the cost and accumulated depreciation are removed from the balance sheet and any resulting gain or loss is reflected in operations in the period realized. Depreciation and amortization periods for the Company’s property and equipment are as follows:

Asset	Estimated Useful Life
Machinery and equipment	4-7 years
Leasehold improvements	Shorter of expected useful life or lease term
Purchased computer software	4 years

Impairment of Long-lived Assets

The Company periodically evaluates its property and equipment and right-of-use assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable or the estimated useful life is no longer appropriate. If such events or changes in circumstances arise, the Company compares the carrying amount of the asset to the estimated undiscounted future cash flows expected to be generated by the asset. If the carrying amount of the long-lived asset is not recoverable on an undiscounted cash flow basis, an impairment charge is recognized to the extent that the carrying amount exceeds its fair value. The Company determines fair value using the income approach based on the present value of expected future cash flows. The Company’s cash flow assumptions consider historical and forecasted revenue and operating costs and other relevant factors.

There were no impairment charges recorded during the years ended December 31, 2024, 2023 and 2022. See Note 4, "Composition of Certain Balance Sheet Items" for discussion on disposals.

Leases

The Company leases both real property and certain equipment for use in its operations. A determination is made as to whether an arrangement is a lease at inception. If so, the Company evaluates the lease agreement to determine whether the lease is an operating or finance lease using the criteria in ASC 842. The Company does not recognize right-of-use assets and lease liabilities that arise from short-term leases for any class of underlying assets.

When lease agreements also require the Company to make additional payments for taxes, insurance and other operating expenses incurred during the lease period, such payments are expensed as incurred. See Note 6, "Commitments and Contingencies," which provides additional details on the Company's current lease arrangements. As of December 31, 2024 and 2023, the Company had no financing leases.

Operating leases are included in the operating lease right-of-use ("ROU") assets, lease liability, current and lease liability, non-current in the Company's Consolidated Balance Sheets. Operating lease ROU assets represent the Company's right to use an underlying asset for the lease term and lease liabilities represent the Company's obligation to make lease payments arising from the lease. Operating lease ROU assets and liabilities are recognized at the lease commencement date based on the present value of all lease payments over the lease term. In determining the present value of lease payments, the Company uses its incremental borrowing rate based on information available at the lease commencement date. The operating lease ROU assets also include any lease prepayments made and exclude lease incentives such as rent abatements and/or concessions and rent holidays. The Company does not assume renewals in its determination of the lease term unless the renewals are deemed by management to be reasonably certain at lease inception. Tenant improvements made by the Company as a lessee in which they are deemed to be owned by the lessor are viewed as lease prepayments by the Company and included in the operating lease ROU assets upon commencement of the lease prior to which they are recorded as prepaid assets. Lease expense for operating leases is recognized on a straight-line basis over the expected lease term as an operating expense. For lease agreements that include lease and non-lease components, such components are generally accounted for separately.

Revenue Recognition

The Company's collaboration revenue includes revenue recognized under the Company's Collaboration Agreement with BMS as well as revenue recognized for milestone payments and reimbursements under the Company's License Agreement with Roche. The Company's license and intellectual property revenue includes revenue from Novo Nordisk for the sale of intellectual property and related rights to the Company's ATTR amyloidosis business and pipeline and milestones payments.

The Company analyzes its collaboration arrangements to assess whether they are financing arrangements within the scope of ASC 730 or as a collaboration arrangement pursuant to ASC 808, or whether such arrangements are reflective of a vendor-customer relationship and therefore within the scope of Topic 606. As of December 31, 2024, the Company has not had any arrangements outside the scope of Topic 606. The following describes the Company's accounting treatment pursuant to Topic 606:

License, Option and Collaboration Revenue

The terms of license, option and collaboration agreements entered into typically include payment of one or more of the following: non-refundable, up-front license fees; option exercise fees; development, regulatory and commercial milestone payments; payments for manufacturing supply and research and development services and royalties on net sales of licensed products.

In determining the appropriate amount of revenue to be recognized as the Company fulfills its obligations under each of its agreements, the Company performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations based on estimated selling prices; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation.

Amounts received prior to satisfying the revenue recognition criteria are recorded as contract liabilities recorded as deferred revenue in the Company's Consolidated Balance Sheets.

At contract inception, for contracts that contain multiple performance obligations, such as the Company's Collaboration Agreement with BMS and the License Agreement with Roche, the Company accounts for the individual performance obligations separately if they are distinct. Factors considered in the determination of whether the license performance obligations are distinct included, among other things, the research and development capabilities of each of BMS and Roche and their respective sublicense rights, and for the remaining performance obligations the fact that they are not proprietary and can be and have been provided by other vendors. The transaction price is allocated to the separate performance obligation on a relative standalone selling price basis.

Revenue is recognized only when the Company satisfies an identified performance obligation by transferring a promised good or service to a customer (in the Company's case, BMS and Roche). An asset is transferred when, or as, the customer obtains control of that asset, which for a service is considered to be as the services are received and used. The Company recognizes revenue over time by measuring the progress toward complete satisfaction of the relevant performance obligation using an appropriate input or output method based on the nature of the service promised to the customer.

Milestone Revenue

The Company generally classifies each of its milestones into one of three categories: (i) clinical milestones; (ii) regulatory and development milestones; and (iii) commercial milestones. Clinical milestones are typically achieved when a product candidate advances into or completes a defined phase of clinical research. For example, a milestone payment may be due to the Company upon the initiation of a clinical trial for a new indication. Regulatory and development milestones are typically achieved upon acceptance of the submission for marketing approval of a product candidate or upon approval to market the product candidate by the FDA or other regulatory authorities. For example, a milestone payment may be due to the Company upon submission for marketing approval of a product candidate by the FDA. Commercial milestones are typically achieved when an approved product reaches certain defined levels of net royalty sales by the licensee of a specified amount within a specified period.

At the inception of each arrangement that includes developmental, regulatory or commercial milestone payments, the Company evaluates whether achieving the milestones is considered probable and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the value of the associated milestone (such as a regulatory submission by the Company) is included in the transaction price. Milestone payments that are not within the control of the Company, such as approvals from regulators or where attainment of the specified event is dependent on the development activities of a third party, are not considered probable of being achieved until those approvals are received or the specified event occurs. The Company considers such milestone payments as variable consideration with constraint and therefore recognizes the revenue from such milestone payments as collaboration revenue at point in time when the Company can conclude it is probable that a significant revenue reversal will not occur in future periods.

Taxes, Shipping and Handling

The Company excludes from the measurement of the transaction price all taxes assessed by a governmental authority that are both imposed on and concurrent with a specific revenue-producing transaction and collected by the Company from a customer (e.g., sales, use, value added, some excise taxes). In addition, the Company accounts for shipping and handling as activities that are performed after its customers obtain control of the goods as activities to fulfill our performance obligation to transfer the goods.

Research and Development

Research and development costs are expensed as incurred. Such costs include, but are not limited to, salaries and benefits, share-based compensation, costs related to preclinical and clinical trial activities including fees paid to clinical research organizations and investigative sites, costs related to drug development and manufacturing prior to regulatory approval for commercial sale, and consulting fees.

There can be judgment involved in measuring the research and development expenses to be recognized in a particular period. The level of judgment varies based on the nature of the services being performed and the underlying support obtained. The Company recognizes costs for certain development activities, such as clinical trials, based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, or information provided to the Company by our vendors on their actual costs incurred. For certain clinical trials, expense is recorded based on information obtained from vendors as an intermediary to those performing the underlying services, such as contract research organizations. These estimates are inherently more judgmental because the quality and availability of the underlying data may vary. The Company recognizes costs for contract manufacturing based on evaluation of the progress to completion of specific tasks. The

objective of the Company's accrual policy is to match the recording of the expenses in the Consolidated Financial Statements to the actual services the Company has received and efforts expended by our vendors. As such, expense accruals related to clinical trials and contract manufacturing are recognized based on the Company's estimate of the degree of completion of the events specified in the specific clinical study or trial contract or drug development and manufacturing contract, respectively. The Company does not make significant estimates where costs incurred are supported by invoices or reports of costs incurred are obtained from a vendor that is directly performing the underlying services, such as a consultant or contract manufacturing organization. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the Consolidated Financial Statements as prepaid or accrued research and development. Amounts due may be fixed fee, fee for service, and may include upfront payments, monthly payments, and payments upon the completion of milestones or receipt of deliverables. Nonrefundable advance payments for goods and services that will be used or received in future research and development activities are deferred and recognized as expense in the period in which the related goods are delivered or services are performed.

The Company has acquired and may continue to acquire the rights to develop and commercialize new drug candidates from third parties. The upfront payments to acquire license, product or rights, as well as any future milestone payments, are immediately recognized as research and development expense provided that the drug has not achieved regulatory approval for marketing and, absent obtaining such approval, has no alternative future use.

Share-based Compensation

The Company's share-based compensation programs include options for the purchase of shares and restricted share units (RSUs). Such awards may be granted to employees, directors, and non-employee service providers.

The Company measures compensation expense for all share-based awards at the grant date based on the fair value measurement of the award. Share-based compensation expense is recognized on a straight-line basis over the requisite service period, which is generally the vesting period, for each award. The fair value of RSUs is based on the closing market price of the Company's ordinary shares on the date of grant. To determine the fair value of options for the purchase of shares, the Company uses the Black-Scholes option-pricing model. The determination of fair value using the Black-Scholes option-pricing model is affected by the Company's share price as well as assumptions regarding a number of complex and subjective variables. Judgment is required in determining the assumptions used in these models which include the risk-free interest rate, expected term, expected volatility and expected dividend yield. The Company uses its historical volatility for the Company's shares to estimate expected volatility. The simplified method has been used to estimate the expected term of all options in previous years. Beginning January 1, 2023, expected term is estimated based on historical experience.

Share-based compensation expense recognized in the Consolidated Statements of Operations is based on awards expected to vest and therefore the amount of expense has been reduced for estimated forfeitures which are based on historical experience. Share-based compensation expense is adjusted in subsequent periods for actual forfeitures.

The Company records any excess tax benefits or tax shortfalls from its equity awards in its Consolidated Statements of Operations in the reporting periods in which options for the purchase of shares are exercised or RSUs vest.

Income Taxes

The Company files its own U.S. and foreign income tax returns and income taxes are presented in the Consolidated Financial Statements using the asset and liability method prescribed by the accounting guidance for income taxes. Deferred tax assets ("DTAs") and liabilities are determined based on the difference between the financial statement and tax basis of assets and liabilities using the enacted tax rates projected to be in effect for the year in which the differences are expected to reverse. Net deferred tax assets are recorded to the extent the Company believes that these assets will more likely than not be realized. In making such determination, all available positive and negative evidence is considered, including scheduled reversals of deferred tax liabilities, recent cumulative earnings/losses by taxing jurisdiction, projected future taxable income, tax planning strategies and recent financial operations. Actual operating results in future years could differ from our current assumptions, judgments and estimates.

The Company's significant tax jurisdictions are Ireland and the United States. Estimates are required in determining the Company's provision for income taxes. Some of these estimates are based on management's interpretations of jurisdiction-specific tax laws or regulations. Various internal and external factors may have favorable or unfavorable effects on the future effective income tax rate of the business. These factors include, but are not limited to, changes in tax laws, regulations and/or rates, changing interpretations of existing tax laws or regulations, changes in estimates of prior years' items, past and future

levels of R&D spending, the impact of accounting for share-based compensation, and changes in overall levels of income before taxes.

The Company did not recognize certain tax benefits from uncertain tax positions within the provision for income taxes. The tax benefit from an uncertain tax position is recognized only if it is more likely than not the tax position will be sustained on examination by the taxing authorities, based on the technical merits of the position. The tax benefits recognized in the financial statements from such positions are then measured based on the largest benefit that has a greater than 50% likelihood of being realized upon settlement. Changes in recognition or measurement are reflected in the period in which the change in judgment occurs. Interest and penalties related to unrecognized tax benefits are accounted for in income tax expense.

Net Income (Loss) per Ordinary Share

Basic net income (loss) per ordinary share is calculated by dividing net income (loss) by the weighted-average number of ordinary shares outstanding during the period. Diluted net income per ordinary share is computed based on the treasury stock method by dividing net income by the weighted-average number of ordinary shares outstanding, plus potentially dilutive ordinary equivalent shares outstanding. However, where there is a net loss, no adjustment is made for potentially issuable ordinary shares because their effect would be anti-dilutive and therefore diluted net loss per share is equal to basic net loss per share.

Comprehensive Loss

Comprehensive income (loss) is comprised of net income (loss) and other comprehensive income (loss). The Company has no components of other comprehensive income (loss). Therefore, net income (loss) equals comprehensive income (loss) for all periods presented and, accordingly, the Consolidated Statements of Comprehensive Income (Loss) is not presented in a separate statement.

Concentration of Risks

Financial instruments that potentially subject the Company to concentration of credit risk consist of cash and cash equivalents and accounts receivable. The Company places its cash equivalents with high credit quality financial institutions and, by policy, limits the amount of credit exposure with any one financial institution. Deposits held with banks have exceeded, and will continue to exceed, federally insured limits. The Company is exposed to credit risk in the event of a default by the financial institutions holding its cash and cash equivalents. The Company has not experienced any losses on its deposits of cash and cash equivalents and its credit risk exposure is up to the extent recorded on the Company's Consolidated Balance Sheet.

The Company’s business is primarily conducted in U.S. dollars except for its agreements with contract manufacturers for drug supplies which are primarily denominated in euros. The Company recorded losses on foreign currency exchange rate differences of approximately $185,000, $458,000 and $397,000 during the years ended December 31, 2024, 2023 and 2022, respectively. If the Company increases its business activities that require the use of foreign currencies, it may be exposed to losses if the euro and other such currencies continue to strengthen against the U.S. dollar.

As of December 31, 2024, and 2023, $3.1 million and $3.8 million, respectively, of the Company’s property and equipment, net were held in the U.S. and a nominal amount were in Ireland.

The Company does not own or operate facilities for the manufacture, packaging, labeling, storage, testing or distribution of nonclinical or clinical supplies of any of its drug candidates. The Company instead contracts with and relies on third-parties to manufacture, package, label, store, test and distribute all preclinical development and clinical supplies of our drug candidates, and it plans to continue to do so for the foreseeable future. The Company also relies on third-party consultants to assist in managing these third-parties and assist with its manufacturing strategy.

Recently Issued Accounting Pronouncements Not Yet Adopted

On November 4, 2024, the Financial Accounting Standards Board (“FASB”) issued Accounting Standards Update (ASU) 2024-03, Income Statement — Reporting Comprehensive Income — Expense Disaggregation Disclosures, which requires public business entities to disclose, on an annual and interim basis, disaggregated information about certain income statement line items in a tabular format in the notes to the financial statements. This guidance will be effective for the Company’s annual period ending December 31, 2027, and interim periods beginning January 1, 2028. Early adoption is permitted. Entities may apply the guidance prospectively or retrospectively. The Company is currently evaluating the impact of this new standard on its financial statement disclosures.

On March 6, 2024, the SEC issued final rule, “The Enhancement and Standardization of Climate-Related Disclosures for Investors”, which requires registrants to disclose material climate-related risks, including descriptions of board oversight and risk management activities, the material impacts of these risks on a registrants strategy, business model and outlook and any material climate-related targets or goals. The rule requires these climate-related information to be disclosed in registration statements and annual reports. Registrants will also need to quantify certain effects of severe weather events and other natural conditions in a note to their audited financial statements. In addition, accelerated and large accelerated filers will need to disclose Scope 1 and Scope 2 greenhouse gas (GHG) emissions, if material, which will be subject to third-party assurance. The Company would be required to comply with the rule in fiscal year beginning January 1, 2025 for all disclosures other than the compliance with quantitative and qualitative disclosure requirements of material expenditures and material impacts on financial estimates that directly result from (1) activities to mitigate or adapt to the climate-related risks, (2) targets or goals and (3) transition plans will be required beginning fiscal year 2026. The Company’s other compliance dates are the following: 1) Scope 1 and Scope 2 GHG emissions - fiscal year beginning January 1, 2026; Limited assurance - fiscal year beginning January 1, 2029; Reasonable assurance - fiscal year beginning January 1, 2033; and Electronic tagging - fiscal year beginning January 1, 2026. The Company is currently evaluating the impact of the new standard on its consolidated financial statements and related disclosures. On April 4, 2024, the Securities and Exchange Commission (SEC) voluntarily stayed implementation of its recently adopted Climate Disclosure Rules.

In December 2023, the FASB issued ASU 2023-09, Improvements to Income Tax Disclosures, which requires public business entities to disclose a tabular reconciliation using both percentages and amounts, broken out into specific categories with certain reconciling items at or above 5% of the expected tax further broken out by nature and/or jurisdiction. The guidance also requires all entities to disclose income taxes paid, net of refunds, disaggregated by federal (national), state and foreign taxes for annual periods and to disaggregate the information by jurisdiction based on a quantitative threshold. All entities are required to apply the guidance prospectively, with the option to apply it retrospectively. The guidance will be effective for the Company’s annual period ending December 31, 2025. Early adoption is permitted. The Company is currently evaluating the impact of the new standard on its income tax disclosures.

Recently Adopted Accounting Pronouncement - Segment Reporting

On November 27, 2023, FASB issued Accounting Standards Update 2023-07 ("ASU 2023-07"), Segment Reporting - Improvements to Reportable Segment Disclosures, which requires public entities to provide disclosures on significant segment expenses that are regularly provided to the chief operating decision maker (“CODM”) and included within each reported measure of segment profit or loss and other segment items on an annual and interim basis. The guidance also requires public entities to provide all disclosures about reportable segment’s profit or loss and assets in interim periods that are currently required annually. Public entities with a single reportable segment have to provide all disclosures required by Accounting Standards Codification (ASC) 280, Segment Reporting including the significant segment expense disclosures. The guidance is applied retrospectively to all periods presented in financial statements and is effective for fiscal years beginning after December 15, 2023, and for interim periods beginning after December 15, 2024. Early adoption is permitted. The Company adopted ASU 2023-07 during its fiscal year ended December 31, 2024. For the purpose of the adoption of ASU 2023-07, the Company performed an evaluation of financial information regularly reviewed by the Company’s CODM for purposes of evaluating performance, allocating resources, setting incentive compensation targets, and planning and forecasting future periods. Financial information provided to and used by the CODM is consistent with the Company’s consolidated GAAP financial statements including its Consolidated Statements of Operations that includes the Company’s consolidated profit and loss.

Segment Information

The Company currently manages its operations as a single segment focused on the discovery and development of novel therapies to treat diseases caused by protein dysregulation. A single management team reports to the chief operating decision maker who comprehensively manages the entire business. All clinical programs are included in one operating segment because the majority of the Company’s clinical programs have similar economic and other characteristics, including the nature of the clinical programs and production processes, and regulatory environment.

Consistent with the Company’s operational structure, the chief executive officer, as the CODM, manages and allocates resources at the global corporate level using consolidated, single-segment GAAP financial statement reported profit and loss and consolidated budget and forecast information for purpose of evaluating performance, allocating resources, setting incentive targets, and planning and forecasting future periods. Managing and allocating resources at the global corporate level enables the CODM to assess both the overall level of resources available and how to best deploy these resources across functions, therapeutic areas and research and development projects in line with our overarching long-term corporate-wide strategic goals, rather than on a clinical program basis. The Company is not organized by market and is managed and operated as one business.

As a single reportable segment entity the determined measure of profit or loss is the Company's consolidated net income (loss). Consolidated asset information for the Company's single-segment is presented in the Company's consolidated Balance Sheet.

The following table sets forth significant research and development ("R&D") expenses by program as regularly provided to the CODM (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Birtamimab (NEOD001)	$ 85,649	$ 68,831	$ 49,312
BMS-986446 (PRX005)	264	10,063	14,444
PRX012	116,359	102,767	41,990
PRX019	5,035	7,703	9,117
Other R&D	15,212	31,207	20,699
Total research and development	$ 222,519	$ 220,571	$ 135,562

3. Fair Value Measurements

The Company measures certain financial assets and liabilities at fair value on a recurring basis, including cash equivalents. Fair value is an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or a liability. A three-tier fair value hierarchy is established as a basis for considering such assumptions and for inputs used in the valuation methodologies in measuring fair value:

Level 1 — inputs are quoted prices (unadjusted) for identical assets or liabilities in active markets.

Level 2 — inputs are other than quoted prices included in Level 1 that are observable for the asset or liability, either directly or indirectly.

Level 3 — inputs are unobservable inputs that are supported by little or no market activities, which would require the Company to develop its own assumptions.

The fair value hierarchy also requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value. The carrying amounts reflected in the Consolidated Balance Sheets for cash equivalents, prepaid expenses and other current assets, accounts receivable, accounts payable and accrued liabilities, approximate their fair value due to their short-term nature.

Based on the fair value hierarchy, the Company classifies its cash equivalents within Level 1. This is because the Company values its cash equivalents using quoted market prices. The Company's Level 1 securities consisted of $440.3 million and $589.9 million in money market funds included in cash and cash equivalents at December 31, 2024, and 2023, respectively.

4. Composition of Certain Balance Sheet Items

Prepaid Expenses and Other Current Assets

Prepaid and other current assets consisted of the following (in thousands):

	December 31,	
	2024	2023
Prepaid R&D expenses	$ 12,029	$ 10,998
Prepaid G&A expenses	830	803
Other	1,165	2,140
Prepaid and other current assets	$ 14,024	$ 13,941

Property and Equipment, net

Property and equipment, net consisted of the following (in thousands):

	December 31,	
	2024	2023
Machinery and equipment	$ 9,137	$ 9,019
Purchased computer software	2,252	2,232
	11,389	11,251
Less: accumulated depreciation and amortization	(8,308)	(7,415)
Property and equipment, net	$ 3,081	$ 3,836

Depreciation expense was $0.9 million, $0.9 million, and $0.7 million for the years ended December 31, 2024, 2023 and 2022, respectively.

Other Current Liabilities

Other current liabilities consisted of the following (in thousands):

	December 31,	
	2024	2023
Payroll and related expenses	$ 14,468	$ 13,245
Professional services	445	288
Other	930	2,129
Other current liabilities	$ 15,843	$ 15,662

5. Net Loss Per Ordinary Share

Net loss per ordinary share was determined as follows (in thousands, except per share amounts):

	Year Ended December 31,		
	2024	2023	2022
Numerator:			
Net loss	$ (122,310)	$ (147,028)	$ (116,949)
Denominator:			
Weighted-average ordinary shares outstanding used in per share calculations	53,772	53,216	47,369
Net loss per share:			
Basic and diluted net loss per ordinary share	$ (2.27)	$ (2.76)	$ (2.47)

Potentially issuable ordinary shares were not used in computing diluted net loss per ordinary share as their effect would be anti-dilutive due to the loss recorded during the years ended December 31, 2024, 2023 and 2022, and therefore diluted net loss per share is equal to basic net loss per share.

The equivalent ordinary shares not included in diluted net loss per share because their effect would be anti-dilutive are as follows (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Stock options to purchase ordinary shares	11,107	9,866	9,480
Restricted Stock Units (RSU)	6	25	23
Total	11,113	9,891	9,503

6. Commitments and Contingencies

Lease Commitments

As of December 31, 2024, the Company currently has four leases relating to its facilities in the United States and Dublin, Ireland.

South San Francisco Facility

The Company had a noncancelable operating sublease (the “SSF Lease”) covering 128,751 square feet of office and laboratory space in South San Francisco, California, U.S. (the “SSF Facility”), which expired on December 31, 2023.

Total operating lease cost was nil, $6.3 million and $6.3 million for the years ended December 31, 2024, 2023 and 2022, respectively. Total cash paid against the operating lease liability was nil, $6.5 million, and $6.3 million for the years ended December 31, 2024, 2023 and 2022, respectively. The Company obtained a standby letter of credit which could be drawn down by the sublandlord in the event the Company failed to fully and faithfully perform all of its obligations under the SSF Lease and to compensate the sublandlord for all losses and damages the sublandlord may have suffered as a result of the occurrence of any default on the part of Company not cured within the applicable cure period. This standby letter of credit was collateralized by a certificate of deposit of the same amount which was classified as restricted cash as of December 31, 2023. The remaining standby letter of credit amount of $1.4 million was released to the Company in May 2024.

Sub-Sublease of South San Francisco Facility

The Company had a Sub-Sublease Agreement (the “Sub-Sublease”) with Assembly Biosciences, Inc. covering approximately 46,641 square feet of office and laboratory space of the SSF Facility. The Sub-Sublease expired on December 15, 2023, in connection with the expiration of the SSF Lease. The Sub-Sublease was considered an operating lease under ASC 842. For the years ended December 31, 2024, 2023 and 2022, the Company recorded nil, $2.8 million, and $2.9 million respectively, of sub-lease rental income as an offset to its operating expenses.

Dublin

In June 2021, the Company entered into a lease agreement for office space in Dublin, Ireland, which commenced in August 2021 and had an initial term of one year. In addition, the Company entered into a lease agreement for additional office space in Dublin, Ireland, which commenced in August 2023 and had an initial term of one year. Both leases have an automatic renewal clause, pursuant to which each agreement will be extended automatically for successive periods equal to their current terms, unless each agreement is cancelled by the Company. In April 2024, the Company renewed both leases, each for another one year term with termination dates in July 2025.

Brisbane Facility

On October 28, 2022, the Company entered into a noncancelable operating sublease (the "Brisbane Sublease") to sublease approximately 31,157 square feet of office and laboratory space located in Brisbane, California (the “Brisbane Facility”) with Arcus Biosciences, Inc., (the "Sublandlord"). The Brisbane Sublease became effective on October 28, 2022. The Brisbane Sublease provides that the Company's obligation to pay rent commenced on July 1, 2023, which is subject to abatement for the first six months following such date, with the exception of the seventh rent payment that was due upon execution of the Brisbane Sublease. The Company is obligated to make lease payments totaling approximately $14.9 million over the lease term, which expires on September 30, 2028, unless terminated earlier. The Brisbane Sublease further provides that the Company is obligated to pay the Sublandlord certain costs, including taxes and operating expenses. The Company has the option to extend the sublease by providing written notice at least nine months prior to the expiration of the sublease term. As of December 31, 2024, the Brisbane Sublease has a remaining lease term of 3.8 years.

The Brisbane Sublease is considered an operating lease and the accounting lease commencement date was on July 31, 2023 when the Company gained control over the Brisbane Facility. The Company recorded a right-of-use asset of approximately $11.4 million and lease liability of approximately $3.6 million relating to the Brisbane Sublease on the lease commencement date. The discount rate used to determine the lease liability was 5.76%. The initial measurement of the right-of-use asset for the Brisbane Sublease includes the tenant improvement added by the Company wherein the lessor was deemed the accounting owner.

The Company was entitled to an improvement allowance of up to $9.3 million, to be used for costs incurred by the Company to construct certain improvements to the Brisbane Facility and to prepare for the Company's occupancy of the Brisbane Facility. As of December 31, 2024, all of the $9.3 million improvement allowance has been received from the Sublandlord and the Company is obligated to fund construction costs incurred in excess of the improvement allowance.

Total operating lease cost for the Brisbane Sublease was $3.2 million and $1.3 million for the year ended December 31, 2024 and 2023, respectively. Total cash paid against the operating lease liability was $2.7 million and $0.4 million for the year ended December 31, 2024 and 2023, respectively.

In conjunction with the Brisbane Sublease, the Company obtained a standby letter of credit in the initial amount of $0.9 million, which may be drawn down by the Sublandlord in the event the Company fails to fully and faithfully perform all of its obligations under the Brisbane Sublease and to compensate the Sublandlord for all losses and damages the Sublandlord may suffer as a result of the occurrence of any default on the part of the Company not cured within the applicable cure period. As of December 31, 2024, none of the standby letter of credit amount of $0.9 million has been used.

The following table sets out a maturity analysis of payments under the Company’s operating leases, including a reconciliation to the lease liabilities recognized in the Consolidated Balance Sheets as of December 31, 2024 (in thousands):

Year Ended December 31,	Operating Leases
2025	3,179
2026	3,158
2027	3,269
2028	2,523
Thereafter	—
Total	$ 12,129
Less: Present value adjustment	(1,286)
Total lease liability	$ 10,843
Less: Lease liability, current	(2,610)
Lease liability, non-current	$ 8,233

Indemnity Obligations

The Company has entered into indemnification agreements with its current and former directors and officers and certain key employees. These agreements contain provisions that may require the Company, among other things, to indemnify such persons against certain liabilities that may arise because of their status or service and advance their expenses incurred as a result of any indemnifiable proceedings brought against them. The obligations of the Company pursuant to the indemnification agreements continue during such time as the indemnified person serves the Company and continues thereafter until such time as a claim can be brought. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is unlimited; however, the Company has a director and officer liability insurance policy that limits its exposure and enables the Company to recover a portion of any future amounts paid. As a result of its insurance policy coverage, the Company believes the estimated fair value of these indemnification agreements is minimal. Accordingly, the Company had no liabilities recorded for these agreements as of December 31, 2024, and 2023.

Other Commitments

In the normal course of business, the Company enters into various firm purchase commitments primarily related to research and development activities. As of December 31, 2024, the Company had non-cancelable purchase commitments to suppliers for $12.7 million of which $1.8 million is included in current liabilities, and contractual obligations under license agreements of $0.3 million of which nil is included in current liabilities. The following is a summary of the Company's non-cancelable purchase commitments and contractual obligations as of December 31, 2024 (in thousands):

	Total	2025	2026	2027	2028	Thereafter
Purchase Obligations [1]	$ 12,729	$ 12,633	$ 96	$ —	$ —	$ —
Contractual obligations under license agreements	274	64	60	60	45	45
Total	$ 13,003	$ 12,697	$ 156	$ 60	$ 45	$ 45

[1] *Purchase obligations consist of non-cancelable purchase commitments to suppliers and contract research organizations.*

Legal Proceedings

We are not currently a party to any material legal proceedings. We may at times be party to ordinary routine litigation incidental to our business. When appropriate in management's estimation, we may record reserves in our financial statements for pending legal proceedings.

7. Significant Agreements

Roche License Agreement

In December 2013, the Company through its wholly owned subsidiary Prothena Biosciences Limited and Prothena Biosciences Inc entered into a License, Development, and Commercialization Agreement (the "License Agreement") with F. Hoffmann-La Roche Ltd. and Hoffmann-La Roche Inc. (together, "Roche") to develop and commercialize certain antibodies that target α-synuclein, including prasinezumab, which are referred to collectively as "Licensed Products." Upon the effectiveness of the License Agreement in January 2014, the Company granted to Roche an exclusive, worldwide license to develop, make, have made, use, sell, offer to sell, import and export the Licensed Products. The Company retained certain rights to conduct development of the Licensed Products and an option to co-promote prasinezumab in the U.S. During the term of the License Agreement, the Company and Roche will work exclusively with each other to research and develop antibody products targeting alpha-synuclein (or α-synuclein) potentially including incorporation of Roche's proprietary Brain Shuttle™ technology to potentially increase delivery of therapeutic antibodies to the brain. The License Agreement provided for Roche making an upfront payment to the Company of $30.0 million, which was received in February 2014; making a clinical milestone payment of $15.0 million upon initiation of the Phase 1 clinical trial for prasinezumab, which was received in May 2014; making a clinical milestone payment of $30.0 million upon dosing of the first patient in the Phase 2 clinical trial for prasinezumab, which was achieved in June 2017; and making a clinical milestone payment of $60.0 million upon dosing of the first patient in the global Phase 2b PADOVA study for prasinezumab, which was achieved in May 2021.

For prasinezumab, Roche is obligated to pay:

- up to $290.0 million upon the achievement of development, regulatory, and various first commercial sales milestones;
- up to $155.0 million upon achievement of U.S. commercial sales milestones;
- up to $175.0 million upon achievement of ex-U.S. commercial sales milestones; and
- tiered, high single-digit to high double-digit royalties in the teens based on U.S. and ex-U.S. annual net sales, subject to certain adjustments, with respect to the applicable Licensed Product.

Roche bore 100% of the cost of conducting the research collaboration under the License Agreement during the research term, which expired December 31, 2017. In May 2021, the Company exercised its rights under the terms of License Agreement to receive potential U.S. commercial sales milestone and royalties, in lieu of a U.S. profit and loss share for prasinezumab in Parkinson's disease. Thus, in the U.S., through May 28, 2021, the parties shared all development costs, all of which were allocated 70% to Roche and 30% to the Company, for prasinezumab in the Parkinson's disease indication. If the Company opts in to participate in co-development and co-funding for any other Licensed Products and/or indications, the parties will share all development and commercialization costs, as well as profits, all of which will be allocated 70% to Roche and 30% to the Company.

The Company initiated a Phase 1 clinical trial for prasinezumab in 2014. Following the Phase 1 clinical trial, Roche became primarily responsible for developing, obtaining and maintaining regulatory approval for and commercializing Licensed Products. Roche also became responsible for the clinical and commercial manufacture and supply of Licensed Products.

In addition, the Company has an option under the License Agreement to co-promote prasinezumab in the U.S. in the Parkinson's disease indication. If the Company exercises such option, it may also elect to co-promote additional Licensed Products in the U.S. approved for Parkinson's disease. Outside the U.S., Roche will have responsibility for developing and commercializing the Licensed Products. Roche bears all costs that are specifically related to obtaining or maintaining regulatory approval outside the U.S. and will pay the Company a variable royalty based on annual net sales of the Licensed Products outside the U.S.

The License Agreement continues on a country-by-country basis until the expiration of all payment obligations under the License Agreement. The License Agreement may also be terminated (i) by Roche at will after the first anniversary of the effective date of the License Agreement, either in its entirety or on a Licensed Product-by-Licensed Product basis, upon 90 days' prior written notice to the Company prior to first commercial sale and 180 days' prior written notice to Prothena after first commercial sale, (ii) by either party, either in its entirety or on a Licensed Product-by-Licensed Product or region-by-region basis, upon written notice in connection with a material breach uncured 90 days after initial written notice, and (iii) by either party, in its entirety, upon insolvency of the other party. The License Agreement may be terminated by either party on a patent-by-patent and country-by-country basis if the other party challenges a given patent in a given country. The Company's rights to co-develop Licensed Products under the License Agreement will terminate if the Company commences certain studies for certain types of competitive products. The Company's rights to co-promote Licensed Products under the License Agreement will terminate if the Company commences a Phase 3 study for such competitive products.

The License Agreement cannot be assigned by either party without the prior written consent of the other party, except to an affiliate of such party or in the event of a merger or acquisition of such party, subject to certain conditions. The License Agreement also includes customary provisions regarding, among other things, confidentiality, intellectual property ownership, patent prosecution, enforcement and defense, representations and warranties, indemnification, insurance, and arbitration and dispute resolution.

Performance Obligations

As of December 31, 2024, and December 31, 2023, there were no remaining performance obligations under the License Agreement since the obligations related to research and development activities were only for the Phase 1 clinical trial and the remaining obligations were delivered or performed.

Milestone Accounting

Under the License Agreement, the Company is eligible to receive certain milestone payments upon the achievement of development, regulatory and various first commercial sales milestones. Milestone payments are evaluated under ASC Topic 606. Factors considered in this determination included scientific and regulatory risk that must be overcome to achieve each milestone, the level of effort and investment required to achieve the milestone, and the monetary value attributed to the milestone. Accordingly, the Company estimates payments in the transaction price based on the most likely approach, which considers the single most likely amount in a range of possible amounts related to the achievement of these milestones. Additionally, milestone payments are included in the transaction price only when the Company can conclude it is probable that a significant revenue reversal will not occur in future periods when the milestone is achieved.

The Company excludes the milestone payments and royalties in the initial transaction price calculation because such payments are considered to be variable considerations with constraint. Such milestone payments and royalties will be recognized as revenue once the Company can conclude it is probable that a significant revenue reversal will not occur in future periods.

The clinical and regulatory milestones under the License Agreement after the point at which the Company could opt out are considered to be variable considerations with constraint due to the fact that active participation in the development activities that generate the milestones is not required under the License Agreement, and the Company can opt out of these activities. There are no refunds or claw-back provisions and the milestones are uncertain of occurrence even after the Company has opted out. Based on this determination, these milestones will be recognized when the Company can conclude it is probable that a significant revenue reversal will not occur in future periods.

Collaboration Agreement with Bristol Myers Squibb

Overview

On March 20, 2018, the Company, through its wholly owned subsidiary Prothena Biosciences Limited ("PBL"), entered into a Master Collaboration Agreement (the "Collaboration Agreement") with Celgene Switzerland LLC ("Celgene"), a subsidiary of Celgene Corporation (which was acquired by Bristol Myers Squibb ("BMS") in November 2019), pursuant to which Prothena granted to Celgene a right to elect in its sole discretion to exclusively license rights both in the U.S. (the "US Rights") and on a global basis (the "Global Rights"), with respect to the Company's programs to develop and commercialize antibodies targeting tau, TDP-43 and an undisclosed target (the "Collaboration Targets").

The Collaboration Agreement provided for Celgene making an upfront payment to the Company of $100.0 million, plus future potential license exercise payments and regulatory and commercial milestones for each program under the Collaboration Agreement, as well as royalties on net sales of any resulting marketed products. In connection with the Collaboration Agreement, the Company and Celgene entered into a Share Subscription Agreement on March 20, 2018, under which Celgene subscribed to 1,174,536 of the Company's ordinary shares for a price of $42.57 per share, for a total of approximately $50.0 million.

BMS US and Global Rights and Licenses

On a program-by-program basis, beginning on the effective date of the Collaboration Agreement and ending on the date that the IND Option term expires for such program (which generally occurs sixty days after the date on which the Company delivers to BMS the first complete data package for an IND that was filed for a lead candidate from the relevant program), BMS may elect in its sole discretion to exercise its US Rights to receive an exclusive license to develop, manufacture and commercialize antibodies targeting the applicable Collaboration Target in the U.S. (the "US License"). If BMS exercises its US Rights for a collaboration program, it is obligated to pay the Company an exercise fee of approximately $80.0 million per program. Thereafter, following the first to occur of (a) completion by the Company, in its discretion and at its cost, of Phase 1 clinical trials for such program or (b) BMS' election to assume responsibility to complete such Phase 1 clinical trials (at its cost), BMS would have the sole right to develop, manufacture and commercialize antibody products targeting the relevant Collaboration Target for such program (the "Collaboration Products") in the U.S.

On a program-by-program basis, following completion of a Phase 1 clinical trial for a collaboration program for which BMS has previously exercised its US Rights, BMS may elect in its sole discretion to exercise its Global Rights with respect to such collaboration program to receive a worldwide, exclusive license to develop, manufacture and commercialize antibodies targeting the applicable Collaboration Target (the "Global License"). If BMS exercises its Global Rights, BMS would be obligated to pay the Company an additional exercise fee of $55.0 million for such collaboration program. The Global Rights would then replace the US Rights for that collaboration program, and BMS would have decision making authority over developing, obtaining and maintaining regulatory approval for, manufacturing and commercializing the Collaboration Products worldwide.

After BMS' exercise of Global Rights for a collaboration program, the Company is eligible to receive up to $562.5 million in regulatory and commercial milestones per program. Following an exercise by BMS of either US Rights or Global Rights for such collaboration program, the Company will also be eligible to receive tiered royalties on net sales of Collaboration Products ranging from high single digit to high teen percentages, on a weighted average basis depending on the achievement of certain net sales thresholds. Such exercise fees, milestones and royalty payments are subject to certain reductions as specified in the Collaboration Agreement, the agreement for US Rights and the agreement for Global Rights.

BMS will continue to pay royalties on a Collaboration Product-by-Collaboration Product and country-by-country basis, until the latest of (i) expiration of certain patents covering the Collaboration Product, (ii) expiration of all regulatory exclusivity for the Collaboration Product, and (iii) an agreed period of time after the first commercial sale of the Collaboration Product in the applicable country (the "Royalty Term").

Term and Termination

The term of the Collaboration Agreement expired on May 24, 2024.

The term of any US License or Global License would continue on a Licensed Product-by-Licensed Product and country-by-country basis until the expiration of all Royalty Terms under such agreement.

Performance Obligations

The Company assessed the Collaboration Agreement and concluded that it represented a contract with a customer within the scope of ASC 606. Per ASC 606, a performance obligation is defined as a promise to transfer a good or service or a series of distinct goods or services. At inception of the Collaboration Agreement, the Company is not obligated to transfer any US License or Global License to BMS unless BMS exercises its US Rights or Global Rights, respectively, and the Company is not obligated to perform development activities under the development plan during preclinical and Phase 1 clinical trials including the regulatory filing of the IND.

The discovery, preclinical and clinical development activities performed by the Company are to be performed at the Company's discretion and are not promised goods or services and therefore are not considered performance obligations under ASC 606, unless and until the Company agrees to perform the Phase 1 clinical trials (after the IND option exercise) that are determined to be performance obligations at the time the option is exercised. Per the terms of the Collaboration Agreement, the Company may conduct discovery activities to characterize, identify and generate antibodies to become collaboration candidates that target such Collaboration Target, and thereafter may pre-clinically develop collaboration candidates to identify lead candidates that target such Collaboration Target and file an IND with the U.S. Food and Drug Administration (the "FDA") for a Phase 1 clinical trial for such lead candidates. In the event the Company agrees to be involved in a Phase 1 clinical trial, the Company will further evaluate whether any such promise represents a performance obligation at the time the option is exercised. If it is concluded that the Company has obligated itself to an additional performance obligation besides the license granted at IND option exercise, then the effects of the changes in the arrangement will be evaluated under the modification guidance of ASC 606.

The Company is not obligated to perform manufacturing activities. Per the terms of the Collaboration Agreement, to the extent that the Company, at its discretion, conducts a program, the Company shall be responsible for the manufacture of collaboration candidates and collaboration products for use in such program, as well as the associated costs. Delivery of manufactured compound (clinical product supply) is not deemed a performance obligation under ASC 606 as the Company is not obligated to transfer supply of collaboration product to BMS unless BMS exercises its right to participate in the Phase 1 development.

Compensation for the Company's provision of inventory supply, to the extent requested by BMS would be paid to the Company by BMS at a reasonable stand-alone selling price for such supply. Given that (i) there is substantial uncertainty about the development of the programs, (ii) the pricing for the inventory is at its standalone selling price and (iii) the manufacturing services require the entity to transfer additional goods or services that are incremental to the goods and services provided prior to the resolution of the contingency, the Company's supply of product is not a material right. Therefore, the inventory supply is not considered a performance obligation unless and until, requested by BMS.

In addition to the grant of the Global License after BMS exercises the Global Rights for a program, BMS is entitled to receive certain ancillary development services from the Company, such as ongoing clinical trial support upon request by BMS, transition supply, if requested by BMS, and regulatory support for coordination of pharmacovigilance matters.

The Company evaluated the potential obligations to transfer the US Licenses and Global Licenses and performance of the ancillary development services subsequent to exercise of the US Rights and Global Rights, if the options are exercised by BMS, under ASC 606-10-55-42 and 55-43 to determine whether the US Rights or the Global Rights provided BMS a "material right" and concluded that BMS' options to exercise its US Rights and Global Rights represented "material rights" to BMS that it would not have received without entering into the Collaboration Agreement.

At inception of the Collaboration Agreement, there were a total of six options, including US Rights and Global Rights to acquire a US License and a Global License, respectively, and rights to request certain development services (following exercise of the US Rights and Global Rights, respectively) for each of the three programs. None of which were remaining as of May 24, 2024. The deferred revenue balance as of December 31, 2024 of $12.3 million is related to the outstanding PRX019 Phase 1 Clinical Trial Obligation ("PRX019 Phase 1 Clinical Trial Obligation").

US License Agreement for the Tau/BMS-986446 Collaboration Target

BMS exercised its US Rights for the tau/BMS-986446 (formerly PRX005) Collaboration Target and on July 30, 2021, PBL entered into a U.S. License Agreement granting BMS an exclusive license to develop, manufacture and commercialize tau Collaboration Products in the United States targeting tau (the "Tau US License Agreement"). The Company received an associated option exercise fee of $80.0 million.

The Tau US License Agreement included the following distinct performance obligations: (1) the delivery of the US License for tau/BMS-986446 Collaboration Target ("Tau US License Obligation"); and (2) the Company's obligation to provide development activities under the development plan during any Phase 1 clinical trials (the "Tau US Development Services Obligation"). Revenue allocated to the Tau US License Obligation was recognized when the Company satisfied its obligation at a point in time, while the revenue allocated to the Tau US Development Services Obligation was recognized over time using an input-based model. All performance obligations have been delivered.

Global License Agreement for the Tau/BMS-986446 Collaboration Target

Subsequently, BMS exercised its Global Rights for the tau/BMS-986446 Collaboration Target and on July 5, 2023, PBL entered into a Global License Agreement granting BMS an exclusive license to develop, manufacture and commercialize tau Collaboration Products globally for any and all uses or purposes with respect to any human or animal disease, disorder or condition (the "Tau Global License Agreement"). The Tau Global License Agreement supersedes and replaces the Tau US License Agreement in its entirety. The Company received an associated option exercise fee of $55.0 million in August 2023 and it is eligible to receive regulatory and sales milestones up to $562.5 million upon achievement of certain events, including regulatory approval of a tau Collaboration Product, and on BMS achieving certain annual, worldwide net sales thresholds. The Company also is eligible to receive tiered royalties on net sales of tau Collaboration Products, ranging from high single digit to high teen percentages, on a weighted average basis depending on the achievement of certain net sales thresholds.

The Company's distinct performance obligation under the Tau Global License Agreement was limited to the delivery of the Global License for tau/BMS-986446 Collaboration Target ("Tau Global License Obligation"). Revenue allocated to the Tau Global License Obligation was recognized by the Company at the time that the license was delivered in July 2023.

Global License Agreement for the undisclosed/PRX019 Collaboration Target

On May 24, 2024, PBL entered into a Global License Agreement granting BMS an exclusive license to develop, manufacture and commercialize Collaboration Products targeting an undisclosed target (including PRX019) globally for any and all uses or purposes with respect to any human or animal disease, disorder or condition (the "PRX019 Global License Agreement"). The Company received an associated option exercise fee of $80.0 million in June 2024 and is eligible to receive further development and regulatory milestones of up to $242.5 million upon achievement of certain development and regulatory milestones, including regulatory approval, of a Collaboration Product, and up to $375.0 million upon BMS achieving certain annual, worldwide net sales thresholds. The Company also is eligible to receive tiered royalties on annual, worldwide net sales of Collaboration Products, ranging from high single digit to high teen percentages, on a weighted average basis depending on the achievement of certain net sales thresholds. Such milestones and royalty payments (i) could be reduced in the case where BMS is successful in developing a modified version of PRX019 that achieves certain specified improved metrics, and (ii) are subject to certain reductions as specified in the PRX019 Global License Agreement.

The PRX019 Global License Agreement included the following distinct performance obligations: (1) the delivery of the Global License for the undisclosed Collaboration Target ("PRX019 Global License Obligation"); and (2) the Company's obligation to run a Phase 1 clinical trial for PRX019. Pursuant to the terms of the PRX019 Global License Agreement, BMS may elect to assume responsibility for completing such Phase 1 clinical trial (at its cost). Revenue allocated to the PRX019 Global License Obligation was recognized when the Company satisfied its obligation at a point in time, while the revenue allocated to the PRX019 Phase 1 Clinical Trial Obligation is recognized over time using an input-based model.

Transaction Price

At inception of the Collaboration Agreement, the Company did not transfer any goods or services to BMS that were material. Accordingly, the Company concluded that the initial transaction price would be recognized as a contract liability and would be deferred until the Company transfers control of goods or services to BMS (which would be when BMS exercises the US Right or Global Right and receives control of the US License or Global License for at least one of the programs), or when the IND Option term expires if BMS had not yet exercised the US Right, or when the Phase 1 Option term expires if BMS had not yet exercised the Global Right, or at the termination of the Collaboration Agreement, whichever occurs first. At such point that the Company transfers control of goods or services to BMS, or when the option expires, the Company would recognize revenue as a continuation of the original contract. Under this approach, the Company would treat the consideration allocated to the material right as an addition to the consideration for the goods or services underlying the contract option.

At inception of the Collaboration Agreement, the Company estimated the standalone selling price for each performance obligation (i.e., the US Rights and Global Rights by program). The estimate of standalone selling price for the US Rights and Global Rights by program was based on the adjusted market assessment approach using a discounted cash flow model. The key assumptions used in the discounted cash flow model included the market opportunity for commercialization of each program in

the U.S. or globally depending on the license, the probability of successfully developing and commercializing a given program target, the estimated remaining development costs for the respective program, the estimated time to commercialization of the drug for that program, and a discount rate.

The initial transaction price under the Collaboration Agreement, pursuant to ASC 606, was $110.2 million, including the $100.0 million upfront payment and $10.2 million premium on the ordinary shares purchased under the SSA. The Company allocated the initial transaction price across the US Rights and Global Rights for each program in a range of approximately $15-$25 million and $10-$18 million, respectively.

The Company did not include the option fees in the initial transaction price because such fees are contingent on the options to the US Rights and the Global Rights being exercised. Upon the exercise of the US Rights and the Global Rights for a program, the Company would have the obligation to deliver the US License and Global License and provide certain ancillary development services if requested by BMS, subsequent to its exercise of the US Rights and Global Rights, respectively, for such program. The Company would include the option fees in the transaction price at the point in time a material right is exercised and the Company transfers control of the goods and services to BMS. In addition, the Company did not include in the initial transaction price certain clinical and regulatory milestone payments since they relate to licenses for which BMS had not yet exercised its option to obtain and these variable considerations are constrained due to the likelihood of a significant revenue reversal.

Upon entering into the Tau Global License Agreement, the Company granted BMS a Global License for the tau/BMS-986446 Collaboration Target, which transferred control of such underlying Global License to BMS. Following execution of the Tau Global License Agreement, BMS paid the Company a $55.0 million option exercise fee. Under the continuation of the original contract method, the Company computed the relative sales price after the Company transferred control of the Global License for tau/BMS-986446. The Company used the original allocated consideration for the Global Right for tau/BMS-986446 of $17.9 million (computed at the inception of the contract) plus the $55.0 million option exercise fee to arrive at the total transaction price of approximately $72.9 million. Given that the Company's distinct performance obligation under the Tau Global License Agreement was limited to the Tau Global License Obligation no further allocation was required.

Upon entering into the PRX019 Global License Agreement, the Company granted BMS a Global License for the undisclosed/PRX019 Collaboration Target, which transferred control of such underlying Global License to BMS. Following execution of the PRX019 Global License Agreement, BMS paid the Company an $80.0 million option exercise fee. As the original contract contemplated a US and Global payment for $80.0 million and $55.0 million, respectively, and a new payment structure and only one license was agreed to, accordingly, the payment was accounted for under modification accounting. The Company concluded that the modification would be accounted for on a prospective basis as a termination of the existing contract and creation of a new contract. The Company computed the relative sales price for the identified remaining performance obligations consisting of the Global License for PRX019 and the PRX019 Phase 1 Clinical Trial Obligation. The transaction price consisted of the original allocated consideration for the US Right for PRX019 of $24.9 million, and original allocated consideration for the Global Right for PRX019 of $17.4 million (both computed at the inception of the Collaboration Agreement) plus the $80.0 million option exercise fee to arrive at the total transaction price of approximately $122.4 million. This total transaction price was allocated using the relative sales price method between the PRX019 Global License Obligation and the PRX019 Phase 1 Clinical Trial Obligation.

The best estimate of selling price for the Global License for PRX019 was based on a discounted cash flow model. The key assumptions used in the discounted cash flow model used to determine the best estimate of selling price for the license included the market opportunity for commercialization of PRX019, the probability of successfully developing/commercializing PRX019, the remaining development costs for PRX019, and the estimated time to commercialization of PRX019 using a discount rate of 13%. Based on the relative selling price method, the amount that the Company allocated to the performance obligations was as follows: $106.3 million to the license to be recognized concurrent with the delivery of the license; and $16.1 million as development services for the Phase 1 clinical trial to be recognized based on input-based model over the service period.

Significant Payment Terms

The upfront payment of $100.0 million was received in April 2018, while all option fees and milestone payments are due within 30 days after the achievement of the relevant milestone by BMS or receipt by BMS of an invoice for such an amount from the Company.

The Collaboration Agreement does not have a significant financing component since a substantial amount of consideration promised by BMS to the Company is variable and the amount of such variable consideration varies based upon

the occurrence or non-occurrence of future events that are not within the control of either BMS or the Company. Variable considerations related to clinical and regulatory milestone payments and option fees are constrained due to the likelihood of a significant revenue reversal.

Revenue and Expense Recognition

Collaboration revenue from BMS was $135.1 million, $91.3 million and $13.9 million for the year ended December 31, 2024, 2023 and 2022, respectively. For the year ended December 31, 2024, collaboration revenue included recognition of $110.1 million for the transfer of the PRX019 Global License and partial performance of the PRX019 Phase 1 Clinical Trial Obligation. In addition, the material rights for the US Rights and Global Rights for the TDP-43 Collaboration Target of $14.6 million and $10.4 million, respectively, expired unexercised on May 24, 2024 as a result of the expiration of the research term of the Collaboration Agreement. Accordingly, $25.0 million of deferred revenue was recognized as revenue on May 24, 2024.

Collaboration revenue for the year ended December 31, 2023 included recognition of $72.9 million for the Tau Global License Obligation ($55.0 million tau global option exercise fee and $17.9 million of deferred revenue recognized for the Global Right for the tau Collaboration Product), $4.7 million under a supply agreement with BMS and the remainder was primarily recognized for Tau US Development Services Obligation. Collaboration revenue for the year ended December 31, 2022, included recognition of $13.9 million for Tau US Development Services Obligation.

As of December 31, 2024, the aggregate amount of the transaction price allocated to the performance obligations that are unsatisfied was $12.3 million. The Company had nil and $5.2 million accounts receivable from BMS at December 31, 2024, and December 31, 2023, respectively.

Deferred Revenue

The deferred revenue balance at the beginning of the fiscal year was $67.4 million and the $80.0 million global exercise fee was added during 2024. During the year ended December 31, 2024, $110.1 million of deferred revenue was recognized as collaboration revenue related to the PRX019 Global License and Phase 1 Clinical Trial Obligation performed, and $25.0 million was recognized for TDP-43 Collaboration Target which expired unexercised. As of December 31, 2024, the total deferred revenue balance of $12.3 million relates to outstanding performance obligations related to the PRX019 Phase 1 Clinical Trial Obligation of which $8.9 million, and $3.4 million remained in current and non-current deferred revenue, respectively. The deferred revenue balance will be recognized as revenue over the remaining service period.

Milestone and Royalties Accounting

Under the Tau Global License Agreement, the Company is eligible to receive milestone payments of up to $187.5 million upon the achievement of certain specified regulatory milestones and milestone payments of up $375.0 million upon the achievement of certain specified commercial sale milestones. Under the PRX019 Global License Agreement, the Company is eligible to receive milestone payments of up to $242.5 million upon the achievement of certain specified development and regulatory milestones and milestone payments of up $375.0 million upon the achievement of certain specified commercial sale milestones. Milestone payments are evaluated under ASC Topic 606. Factors considered in this determination included scientific and regulatory risk that must be overcome to achieve each milestone, the level of effort and investment required to achieve the milestone, and the monetary value attributed to the milestone. Accordingly, the Company estimates payments in the transaction price based on the most likely approach, which considers the single most likely amount in a range of possible amounts related to the achievement of these milestones. Additionally, milestone payments are included in the transaction price only when the Company can conclude it is probable that a significant revenue reversal will not occur in future periods.

The Company excluded the milestone payments and royalties in the initial transaction price because such payments are considered to be variable considerations with constraint. Such milestone payments and royalties will be recognized as revenue at a point in time when the Company can conclude it is probable that a significant revenue reversal will not occur in future periods.

The Company did not achieve any clinical and regulatory milestones under the Collaboration Agreement during the years ended December 31, 2024, 2023 and 2022, respectively.

Novo Nordisk Share Purchase Agreement

On July 8, 2021, the Company together with its wholly owned subsidiary, PBL, entered into a definitive share purchase agreement with Novo Nordisk A/S and Novo Nordisk Region Europe A/S (each an unrelated party). Under the terms of such agreement, Novo Nordisk acquired PBL's wholly-owned subsidiary, Neotope Neuroscience Limited ("NNL") and gained full worldwide rights to the intellectual property and related rights to the Company's ATTR amyloidosis business and pipeline. Upon consummation of the transaction, NNL ceased to be a related party of PBL. The aggregate purchase price consisted of an upfront payment of $60.0 million in cash, subject to customary purchase price adjustments.

Should Novo Nordisk achieve certain stages of development or commercialization for products or product candidates containing coramitug (formerly PRX004) or a derivative thereof in ATTR amyloidosis, PBL is entitled to receive certain milestone payments based on specified development and commercial milestones. The development and commercialization milestone payments will be discounted if the milestone events are achieved with respect to other indications. Should Novo Nordisk achieve specified thresholds of worldwide, annual net sales of the milestone products, regardless of indication, PBL will also be entitled to receive specified one-time net sales milestone payments. All milestone payments attributable to an achieved milestone will be paid to PBL, subject to Novo Nordisk's offset right for indemnity claims or unpaid amounts in respect of any purchase price adjustment.

The upfront payment of $60.0 million was accounted for as revenue in 2021. In addition to the upfront payment, Novo Nordisk agreed to pay for certain out of pocket expenses under the Transition Services Agreement, which netted to $0.7 million after closing adjustments related to the sale of the ATTR amyloidosis business and pipeline.

Contingent Consideration/Milestone Accounting

In December 2022, the Company received a $40.0 million development milestone payment related to the continued advancement of coramitug in a Phase 2 clinical trial for the treatment of ATTR cardiomyopathy. This amount was accounted for as revenue from license and intellectual property in 2022.

The Company is eligible to receive additional development and sales milestone payments from Novo Nordisk totaling up to $1.13 billion upon achievement of certain specified development and commercial sales milestones under the share purchase agreement.

The Company excluded the milestone payments in the initial transaction price because such payments are considered to be variable considerations with constraint. Such milestone payments will be recognized as revenue at a point in time when the Company can conclude it is probable that a significant revenue reversal will not occur in future periods.

Revenue Recognition

Total revenue recognized related to the transaction during the years ended December 31, 2024, 2023 and 2022 was nil, nil and $40.0 million, respectively. The Company had no accounts receivable from Novo Nordisk as of December 31, 2024, and 2023, respectively.

8. Shareholders' Equity

Ordinary Shares

As of December 31, 2024, the Company had 100,000,000 ordinary shares authorized for issuance with a par value of $0.01 per ordinary share and 53,826,982 ordinary shares issued and outstanding. Each ordinary share is entitled to one vote and, on a pro rata basis, to dividends when declared and the remaining assets of the Company in the event of a winding up. As of December 31, 2024, 15,332,174 ordinary shares are reserved for issuance pursuant to outstanding and future equity awards under the Company's equity incentive plans.

Euro Deferred Shares

As of December 31, 2024, the Company had 10,000 Euro Deferred Shares authorized for issuance with a nominal value of €22 per share. No Euro Deferred Shares are outstanding at December 31, 2024. The rights and restrictions attaching to the Euro Deferred Shares rank *pari passu* with the ordinary shares and are treated as a single class in all respects.

December 2022 Offering

In December 2022, the Company completed an underwritten public offering of an aggregate of 3,250,000 of its ordinary shares at a public offering price of $56.50 per ordinary share. The Company received aggregate net proceeds of approximately $172.4 million, after deducting the underwriting discount and offering costs.

In January 2023, the Company issued an additional 395,096 ordinary shares resulting from the underwriters' partial exercise of their 30-day option to purchase up to an additional 487,500 ordinary shares of as part of the December 2022 underwritten public offering. The Company received approximately $20.9 million proceeds from the exercise, net of underwriting discount but before deducting any offering costs.

At-the-Market Offerings

In December 2021, the Company entered into an Equity Distribution Agreement (the "December 2021 Distribution Agreement"), pursuant to which the Company could issue and sell, from time to time, the Company's ordinary shares. In connection with entering into the December 2021 Distribution Agreement, on December 23, 2021, the Company filed with the SEC a prospectus supplement relating to the offer, issuance and sale of up to $250.0 million of the Company's ordinary shares (the "December 2021 Prospectus") pursuant to the December 2021 Distribution Agreement.

For the years ended December 31, 2023, and 2022 the Company sold and issued 42,361 and 911,228 ordinary shares, respectively, pursuant to the December 2021 Distribution Agreement under the December 2021 Prospectus. For the years ended December 31, 2023, and 2022, total gross proceeds were approximately $3.2 million and $53.1 million, respectively, before deducting underwriting discounts, commissions, and other offering expenses payable by the Company of $0.1 million and $1.7 million, respectively.

The December 2021 Prospectus was no longer effective as of March 23, 2024. As of March 23, 2024, the Company had sold and issued 953,589 ordinary shares pursuant to the December 2021 Distribution Agreement under the December 2021 Prospectus for total gross proceeds of approximately $56.3 million before deducting underwriting discounts, commissions, and other offering expenses paid by the Company of $1.8 million.

In February 2024, the Company amended the Equity Distribution Agreement that it entered into in December 2021 (the "Amended Distribution Agreement"), pursuant to which the Company may issue and sell, from time to time, the Company's ordinary shares. In connection with amending the Amended Distribution Agreement, on February 22, 2024, the Company filed with the SEC a prospectus relating to the offer, issuance, and sale of up to $250.0 million of the Company's ordinary shares (the "February 2024 Prospectus") pursuant to the Amended Distribution Agreement. For the year ended December 31, 2024, the Company sold and issued no ordinary shares pursuant to the Amended Distribution Agreement under the February 2024 Prospectus.

The issuance and sale of the Company's ordinary shares pursuant to the December 2021 Distribution Agreement and the Amended Distribution Agreement is deemed an "at-the-market" offering and is registered under the Securities Act of 1933, as amended.

9. Share-Based Compensation

Equity Incentive Plans

The Company's equity incentive plans, the 2018 Long Term Incentive Plan, as amended (the "2018 LTIP"), 2020 Employment Inducement Incentive Plan, as amended (the "2020 EIIP"), and previously, the Amended and Restated 2012 Long Term Incentive Plan (the "2012 LTIP"), reserve ordinary shares for the issuance of stock options, stock appreciation rights, restricted shares, RSUs, performance bonus awards, performance share units awards, dividend equivalents and other share or cash-based awards to eligible individuals. Options granted under each of the 2018 LTIP, 2020 EIIP, and 2012 LTIP expire no later than ten years from the date of grant.

In May 2024, the Company's shareholders approved an amendment to the 2018 LTIP to increase the number of ordinary shares available for issuance under the 2018 LTIP by 2,000,000 ordinary shares. As of December 31, 2024, the number of ordinary shares authorized under the 2018 LTIP was 16,620,433. Upon adoption of the 2018 LTIP, no new awards are permitted under the 2012 LTIP.

As of December 31, 2024, the number of ordinary shares authorized under the 2020 EIIP was 1,485,000 and 341,584 ordinary shares remained available for future awards under the 2020 EIIP. The Company's Board of Directors has adopted a

series of amendments to increase the ordinary shares available for issuance under the 2020 EIIP and it reserves the right to both amend the 2020 EIIP to increase the number of ordinary shares available and make additional awards to key new hires.

The Company's option awards generally vest over four years, while RSUs vest over two years. As of December 31, 2024, 4,218,801 ordinary shares remained available for grant under its equity plans.

Share-based Compensation Expense

Share-based compensation expense recorded in these Consolidated Financial Statements for the years ended December 31, 2024, 2023 and 2022, was based on awards granted under the 2012 LTIP, the 2018 LTIP, and the 2020 EIIP. The estimated forfeiture rate as of December 31, 2024 was 7%. Changes in our estimates and assumptions relating to forfeitures may cause us to realize changes in stock-based compensation expense in the future.

The amount of unearned share-based compensation related to unvested stock options at December 31, 2024, is $74.5 million. The weighted-average period over which this unearned share-based compensation is expected to be recognized is 2.54 years.

The following table summarizes share-based compensation expense for the periods presented (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Research and development	$ 20,931	$ 19,211	$ 14,805
General and administrative	25,033	21,703	16,517
Total share-based compensation expense	$ 45,964	$ 40,914	$ 31,322

The Company recognized tax benefits from share-based awards of $8.3 million, $7.2 million, and $5.8 million, for the years ended December 31, 2024, 2023 and 2022, respectively.

The fair value of the options granted to employees and non-employee directors during the years ended December 31, 2024, 2023 and 2022 was estimated as of the grant date using the Black-Scholes option-pricing model using the key assumptions listed in the following table.

	Year Ended December 31,		
	2024	2023	2022
Expected volatility*	74.5% - 78.6%	76.4% - 90.1%	82.1% - 86.0%
Risk-free interest rate*	3.5% - 4.7%	3.5% - 4.8%	1.5% - 4.2%
Expected dividend yield	—%	—%	—%
Expected life (in years)*	4.6 - 5.7	4.4 - 5.4	6.0 - 6.0
Weighted average grant date fair value	$18.69	$37.32	$23.43

**The presentation of the expected volatility, risk-free interest rate, and expected life for 2023 and 2022 has been revised to present as range of values to conform to the current year presentation.*

The fair value of employee stock options is amortized on a straight-line basis over the requisite service period for each award. Each of the inputs discussed above is subjective and generally requires management judgment to determine.

The following table summarizes the Company's stock option activity during the year ended December 31, 2024:

	Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2023	9,866,337	$ 29.06	6.60	$ 118,447
Granted	2,288,450	28.69		
Exercised	(125,615)	15.19		
Forfeited	(524,505)	36.44		
Expired	(397,294)	31.70		
Outstanding at December 31, 2024	11,107,373	$ 28.70	6.16	$ 3,401
Vested and expected to vest at December 31, 2024	10,827,212	$ 28.52	6.09	$ 3,401
Exercisable at December 31, 2024	7,546,069	$ 25.17	4.99	$ 3,397

The total intrinsic value of options exercised was $1.3 million, $52.1 million, and $49.2 million during the years ended December 31, 2024, 2023 and 2022, respectively, determined as of the date of exercise.

The following table summarizes the activity and related information for RSUs during the year ended December 31, 2024:

	Number of Units	Weighted Average Grant-Date Fair Value	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Unvested at December 31, 2023	25,250	$ 58.01	1.09	$ 918
Units Granted	—	—		
Units Vested	(19,250)	59.95		
Units Forfeited	—	—		
Unvested at December 31, 2024	6,000	$ 51.80	0.71	$ 83
Unvested and expected to vest at December 31, 2024	5,699	$ 52.06	0.71	$ 79

The fair value of RSUs was determined on the date of grant based on the market price of the Company's ordinary shares as of that date. The fair value of the RSUs is recognized as an expense on a straight-line basis over the vesting period of each RSU. Upon the vesting of the RSUs, a portion of the shares vested are sold by the employee to satisfy employee withholding tax requirements (sell-to-cover). As of December 31, 2024, total compensation cost not yet recognized related to unvested RSUs was $0.1 million, which is expected to be recognized over a weighted-average period of 0.71 years. RSUs settle into ordinary shares upon vesting.

10. Income Taxes

The Company files its U.S. and Irish income tax returns and income taxes are presented in the Consolidated Financial Statements using the asset and liability method prescribed by the accounting guidance for income taxes.

Income (loss) before provision for income taxes by country for each of the fiscal periods presented is summarized as follows (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Ireland	$ (129,602)	$ (153,920)	$ (119,571)
U.S.	672	(6,560)	(6,034)
Loss before provision for income taxes	$ (128,930)	$ (160,480)	$ (125,605)

Components of the provision for income taxes for each of the fiscal periods presented consisted of the following (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Current:			
U.S. Federal	$ 2,676	$ 2,200	$ 2,422
U.S. State	50	37	55
Ireland	—	—	—
Total current provision	$ 2,726	$ 2,237	$ 2,477
Deferred:			
U.S. Federal	$ (9,298)	$ (15,647)	$ (11,039)
U.S. State	(48)	(42)	(94)
Ireland	—	—	—
Total deferred benefit	$ (9,346)	$ (15,689)	$ (11,133)
Benefit from income taxes	$ (6,620)	$ (13,452)	$ (8,656)

The Company recorded a net tax shortfall (windfall) from stock option exercises of $1.0 million, $(3.5) million, and $(3.2) million for the years ended December 31, 2024, 2023 and 2022 respectively, all of which were recorded as part of its income tax provision in the Consolidated Statements of Operations.

The provision for income taxes differs from the statutory tax rate of 12.5% applicable to Ireland primarily due to Irish net operating losses for which a tax provision benefit is not recognized, U.S. income taxed at different rates, adjustments to deferred tax assets for the deductibility of stock compensation and capitalization of research and development costs. Following is a reconciliation between income taxes computed at the Irish statutory tax rate and the provision for income taxes for each of the fiscal periods presented (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Taxes at the Irish statutory tax rate of 12.5%	$ (16,116)	$ (20,060)	$ (15,700)
Income tax at rates other than applicable statutory rate	(5,594)	(7,072)	(2,338)
Change in valuation allowance	18,760	22,406	22,681
Share-based payments	7,533	615	518
Tax credits	(8,769)	(9,382)	(8,949)
Income not subject to tax	(2,560)	—	(5,000)
Other	126	41	132
Benefit from income taxes	$ (6,620)	$ (13,452)	$ (8,656)

Deferred income taxes reflect the net tax effect of temporary differences between the carrying amount of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes.

Significant components of the Company's net deferred tax assets as of December 31, 2024, and 2023 are as follows (in thousands):

	December 31,	
	2024	2023
Deferred tax assets:		
Net operating loss carryforwards	$ 171,191	$ 156,046
Tax credits	23,968	23,728
Lease liabilities	2,424	2,686
Accruals and other	1,521	1,887
Capitalized R&D	33,951	25,067
Share-based compensation	11,810	9,364
Gross deferred tax assets	244,865	218,778
Valuation allowance	(198,869)	(181,713)
Net deferred tax assets	45,996	37,065
Deferred tax liability:		
Operating lease right-of-use assets	(2,393)	(2,706)
Fixed Assets	(364)	(466)
Net deferred tax assets	$ 43,239	$ 33,893

The Company's deferred tax assets ("DTA") are composed primarily of its Irish subsidiaries' net operating loss carryforwards, state net operating loss carryforwards available to reduce future taxable income of the Company's U.S. subsidiaries, federal and California tax credit carryforwards, share-based compensation, capitalized R&D, and other temporary differences. The Company maintains a valuation allowance against certain U.S. federal and state and Irish deferred tax assets. Each reporting period, the Company evaluates the need for a valuation allowance on its deferred tax assets by jurisdiction.

For the year ended December 31, 2024, the Company recorded an increase in DTA of $9.3 million, primarily due to Section 174 R&D Capitalization requirements of $8.9 million. For the year ended December 31, 2023, the Company recorded an increase in DTA of $15.7 million, primarily due to Section 174 R&D Capitalization requirements of $14.5 million, which became effective in 2022.

Recognition of deferred tax assets is appropriate when realization of such assets is more likely than not. Based upon the weight of available evidence, especially the uncertainties surrounding the realization of deferred tax assets through future taxable income, the Company believes it is not yet more likely than not that certain deferred tax assets will be fully realizable. Accordingly, the Company has provided a valuation allowance of $198.9 million against its deferred tax assets as of December 31, 2024, primarily in relation to deferred tax assets arising from Irish net operating losses and Federal and California tax credits. The deferred tax assets recognized net of the valuation allowance, $43.2 million as of December 31, 2024, consisted predominantly of U.S. federal temporary differences. Due to expected future U.S. operating income, the Company expects to realize such deferred tax assets. The net increase of $17.2 million in the valuation allowance during the year ended December 31, 2024, was primarily due to Irish net operating losses.

As of December 31, 2024, certain of the Company's Irish entities had trading loss carryovers of $1.2 billion and non-trading loss carryovers of $20.9 million, each of which can be carried forward indefinitely. Trading losses are available against income from the same trade/trades while non-trading losses (excess management expenses) are available against future investment income in the company in which they arise. In addition, as of December 31, 2024, the Company had state net operating loss carryforwards of approximately $128.9 million, which are available to reduce future taxable income, if any, for the Company's U.S. subsidiary. If not utilized, the state net operating loss carryforward begins expiring in 2032.

The Company also has federal and California research and development credit carryforwards of $17.3 million and $22.1 million, respectively, at December 31, 2024. The Tax Reform Act of 1986 and similar California legislation impose substantial restrictions on the utilization of net operating losses and tax credit carryforwards in the event that there is a change in ownership as provided by Section 382 of the Internal Revenue Code and similar state provisions. Such a limitation could result in the expiration of the net operating loss carryforwards and tax credits before utilization, which could result in increased future tax

liabilities. The federal research and development credit carryforwards will expire starting in 2042 if not utilized. The California tax credits can be carried forward indefinitely.

Cumulative unremitted earnings of the Company's U.S. subsidiaries total approximately $247.4 million at December 31, 2024. The Company's U.S. subsidiaries' cash balances at December 31, 2024, are committed for its working capital needs and are considered to be indefinitely invested. As such, no provision for income tax has been recognized on undistributed earnings of the Company's U.S. subsidiaries. The determination of a hypothetical unrecognized deferred tax liability as of December 31, 2024 is not practicable because of the complexity and variety of assumptions necessary to compute the tax.

A reconciliation of the beginning and ending amounts of unrecognized tax benefits is as follows (in thousands):

	2024	2023
Gross Unrecognized Tax Benefits at January 1	$ 13,354	$ 11,564
Additions for tax positions taken in the current year	2,201	2,355
Additions for tax positions taken in the prior year	—	—
Reductions for tax positions taken in the prior year	(128)	(565)
Gross Unrecognized Tax Benefits at December 31	$ 15,427	$ 13,354

If recognized, none of the Company's unrecognized tax benefits as of December 31, 2024, would reduce its annual effective tax rate, primarily due to corresponding adjustments to its deferred tax valuation allowance. As of December 31, 2024, the Company has not recorded a liability for potential interest or penalties. The Company also does not expect its unrecognized tax benefits to change significantly over the next 12 months.

The Company is subject to reviews and audits by the U.S. Internal Revenue Service ("IRS"), the Irish Revenue Commissioners, and other taxing authorities from time to time. The Company's U.S. subsidiaries are currently under examination by the IRS for tax year 2021. The Company periodically reviews its uncertain tax positions. The Company's assessment is based on many factors, including any ongoing IRS audits. For the year ended December 31, 2024, the Company's assessment did not result in a material change in unrecognized tax benefits. The tax years 2013 to 2024 remain subject to examination by the U.S taxing authorities and the tax years 2019 to 2024 remain subject to examination by the Irish taxing authorities as of December 31, 2024.

11. Employee Retirement Plan

In the U.S., the Company provides a qualified retirement plan under section 401(k) of the Internal Revenue Code (the "IRC") under which participants may contribute up to 100% of their eligible compensation, subject to maximum deferral limits specified by the IRC. In addition, the Company contributes 3% of each participating employee's eligible compensation, subject to limits specified by the IRC, on a quarterly basis. Further, the Company may make an annual discretionary matching and/or profit-sharing contribution as determined solely by the Company. The Company recorded total expense for matching contributions in the U.S. of $1.9 million, $1.7 million and $1.3 million for the years ended December 31, 2024, 2023 and 2022, respectively.

In Ireland, the Company operates a defined contribution plan in which it contributes up to 7.5% of an employee's eligible earnings. The Company recorded total expense for employer contribution in Ireland of $181,000, $152,000, and $133,000 in the years ended December 31, 2024, 2023 and 2022, respectively.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our chief executive officer ("CEO") and chief financial officer ("CFO") evaluated the effectiveness of our disclosure controls and procedures pursuant to Rule 13a-15 under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), as of the end of the period covered by this Form 10-K. Based on this

evaluation, our CEO and CFO concluded that, as of December 31, 2024, our disclosure controls and procedures are designed and are effective to provide reasonable assurance that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our CEO and CFO, as appropriate, to allow timely decisions regarding required disclosure.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rule 13a-15(f) of the Exchange Act. Internal control over financial reporting is a process designed by, or under the supervision of, our CEO and CFO, and effected by our Board of Directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- Pertain to the maintenance of records that accurately and fairly reflect in reasonable detail the transactions and dispositions of the assets of our company;
- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and
- Provide reasonable assurances regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material adverse effect on our financial statements.

Our management assessed our internal control over financial reporting as of December 31, 2024, the end of our fiscal year. Management based its assessment on criteria established in "Internal Control-Integrated Framework (2013)" issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on management's assessment of our internal control over financial reporting, management concluded that, as of December 31, 2024, our internal control over financial reporting was effective. The effectiveness of our internal control over financial reporting as of December 31, 2024, has been audited by KPMG LLP, an independent registered public accounting firm, as stated in its report which is included in Item 8 of this Form 10-K.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting identified in management's evaluation pursuant to Rules 13a-15(d) or 15d-15(d) of the Exchange Act during our fourth fiscal quarter ended December 31, 2024, that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Limitations on Effectiveness of Controls and Procedures

Internal control over financial reporting has inherent limitations. Internal control over financial reporting is a process that involves human diligence and compliance and is subject to lapses in judgment and breakdowns resulting from human failures. Internal control over financial reporting also can be circumvented by collusion or improper management override. Because of such limitations, there is a risk that material misstatements will not be prevented or detected on a timely basis by internal control over financial reporting. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk.

Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management necessarily applies its judgment in evaluating the benefits of possible controls and procedures relative to their costs.

ITEM 9B. OTHER INFORMATION

On December 11, 2024, Tran B. Nguyen, Chief Strategy Officer and Chief Financial Officer, adopted a Rule 10b5-1 trading arrangement that is intended to satisfy the affirmative defense of Rule 10b5-1(c) for the sale of up to 423,837 shares of the Company's ordinary shares until March 23, 2026.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

None.

PART III

Certain information required by Part III is incorporated herein by reference from our definitive proxy statement relating to our Annual General Meeting of Shareholders to be held on May 13, 2025 (our "Proxy Statement").

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

Except for the information about our executive officers, Code of Conduct, and Insider Trading Compliance Policy shown below, the information appearing in our Proxy Statement under the following headings is incorporated herein by reference:

- Proposal No. 1 - Election of Directors
- Corporate Governance and Board Matters
- Delinquent Section 16(a) Reports

Information about Our Executive Officers

Following is certain information regarding our executive officers.

Name	Age	Position(s)	Since
Gene G. Kinney	56	President and Chief Executive Officer, Director	2016
David A. Ford	56	Chief People Officer	2024
Carol D. Karp	72	Chief Regulatory Officer	2016
Michael J. Malecek	59	Chief Legal Officer and Company Secretary	2019
Tran B. Nguyen	51	Chief Financial Officer	2013
		Chief Strategy Officer	2021
Brandon S. Smith	50	Chief Operating Officer	2021
Chad J. Swanson	53	Chief Development Officer	2024
Karin L. Walker	61	Chief Accounting Officer	2013
Wagner M. Zago	52	Chief Scientific Officer	2017

Gene G. Kinney, Ph.D., has served as our President and Chief Executive Officer as well as a member of our Board of Directors 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 held various positions with Elan Pharmaceuticals, Inc.: Vice President, Pharmacology (from 2009 to 2011) and Senior Vice President of Pharmacological Sciences (from 2011 to 2012); and 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 BA from Bloomsburg University and his MA and PhD from Florida Atlantic University.

David A. Ford has served as our Chief People Officer since March 2024. He brings over 25 years of experience in a variety of human resources roles across the United States, Europe, Latin America and New Zealand. Prior to joining Prothena, he was the Chief Human Resources Officer at Intercept Pharmaceuticals from May 2017 through December 2023. Prior to that, he spent nearly 15 years at Sanofi, where he last served as Vice President Human Resources for the Sanofi Genzyme global business unit from January 2016 to May 2017. Prior to that, from November 2011 through December 2015, Mr. Ford served as Vice President Human Resources for the Sanofi North American businesses. Mr. Ford joined the pharmaceutical industry in 2002 as the HR Director - United Kingdom and Republic of Ireland for Sanofi-Synthelabo. He earned his master's degree in business administration from INSEAD, Fontainebleau (France).

Carol D. Karp has served as our Chief Regulatory Officer since 2016. Prior to joining Prothena, she was an independent regulatory consultant to biotechnology and pharmaceutical companies. From 2013 to 2014, Ms. Karp was Senior Vice President, Regulatory Affairs and Compliance at Esperion Therapeutics, Inc., and from 2010 to 2013, she was Vice President,

Head of Global Regulatory Affairs, Pharmacovigilance & Risk Management at Janssen Alzheimer Immunotherapy, a Johnson & Johnson Company. Previously, Ms. Karp held senior regulatory positions at CV Therapeutics, Inc., PowderJect Technologies, VIVUS, Inc., Cygnus, Inc., and Janssen Pharmaceutica. She earned her BA in Biology from the University of Rochester, where she is Vice Chair of the Board of Trustees.

Michael J. Malecek has served as our Chief Legal Officer since 2019. Prior to joining Prothena in 2019, he was Vice President, Deputy General Counsel, Intellectual Property and Litigation of Snowflake (a data warehouse company) from 2018. From 2010 to 2018, he was a Partner at Arnold & Porter Kaye Scholer LLP. From 2008 to 2010, Mr. Malecek was Partner at Dewey & LeBoeuf, LLP. From 2002 to 2008, he was Vice President and Chief Advocacy Counsel at Affymetrix. Mr. Malecek earned his BA in American Studies from Yale University and his JD from the University of Virginia School of Law.

Tran B. Nguyen has served as our Chief Strategy Officer since September 2021 and as our Chief Financial Officer since 2013. He served as our Chief Operating Officer from June 2018 to September 2021. He has over 25 years of finance experience in the biotechnology, banking, and private equity industries. Prior to joining Prothena in 2013, Mr. Nguyen was the Chief Financial Officer at Somaxon Pharmaceuticals, Inc. from 2010 until its sale in 2013. He was Chief Financial Officer at Metabasis Therapeutics, Inc. from 2009 until its sale in 2010. From 2007 to 2009, he was a Vice President in the Healthcare Investment Banking group at Citi Global Markets, Inc., and from 2004 to 2007 he served in various capacities as a healthcare investment banker at Lehman Brothers, Inc. He earned his BA in Economics and Psychology from Claremont McKenna College and his MBA from the Anderson School of Management at the University of California, Los Angeles.

Brandon S. Smith has served as our Chief Operating Officer since September 2021. He served as our Chief Business Officer from March 2020 to September 2021. Prior to joining Prothena in 2020, he was Chief Operating Officer at Iconic Therapeutics, Inc. (a biopharmaceutical company) from 2017 to 2020. From 2012 to 2017, Mr. Smith held senior positions at Impax Laboratories, LLC (a specialty pharmaceutical company), including Senior Vice President, and Vice President of Corporate Development and Strategy. Mr. Smith also held several positions of increasing responsibility at Amgen Inc. between 2005 and 2012, including Executive Director, Biosimilars Strategy, Director, Strategy and Corporate Development and Director, Operations Strategy. Mr. Smith was also a Consultant and Project Leader at The Boston Consulting Group between 2002 and 2005. Mr. Smith earned his BS in Chemical Engineering at the University of Michigan and his MBA at The University of Texas at Austin McCombs Graduate School of Business.

Chad J. Swanson, Ph.D., has served as Chief Development Officer since September 2024. He served as SVP, Head of Clinical Development from January 2023 to September 2024. Prior to joining Prothena, he held several positions of increasing responsibility at Eisai, Inc. from 2011 to December 2022, including as the International Project Team Leader for the lecanemab program, leading clinical development for the first Alzheimer's disease therapy targeting amyloid beta to receive full approval from the U.S. Food and Drug Administration. Prior to that role, Dr. Swanson held clinical research roles at Schering Plough and Merck Research Laboratories, and discovery research roles culminating as the US Head of Neurochemistry at Lundbeck Research US, Inc. Dr. Swanson earned his BS from the University of Wisconsin-Madison and his PhD from Medical University of South Carolina, while completing postdoctoral training at Eli Lilly and Co.

Karin L. Walker has served as our Chief Accounting Officer since 2013. Prior to joining Prothena in 2013, she was Vice President, Finance and Chief Accounting Officer of Affymax, Inc., a position she held from 2012 to 2013. From 2009 to 2012, Ms. Walker was Vice President, Finance and Corporate Controller at Amyris Inc. From 2006 to 2009, she was Vice President, Finance and Corporate Controller for CV Therapeutics, Inc. Ms. Walker also held senior financial leadership positions at Knight Ridder Digital, Accellion, Niku Corporation, Financial Engines, Inc. and NeoMagic Corporation. Ms. Walker served on the boards of Cyclacel Pharmaceutical Inc. (a publicly traded clinical-stage oncology company) from 2020 to January 2025 and LifeSci Acquisition Corp. (a publicly traded special purpose acquisition company) in 2020. She earned her BS in business from the California State Polytechnic University, San Luis Obispo, and is a certified public accountant.

Wagner M. Zago, Ph.D., has served as our Chief Scientific Officer since 2017. Prior to that, from 2015 to 2017, he was our Vice President, Head of Research. From 2012 to 2015, Dr. Zago was our Head of Pharmacology and Neuropathology. From 2006 to 2012, he held various scientific positions at Elan Pharmaceuticals, Inc, performing research aimed at developing new therapeutics for central nervous system disorders and inflammation. While in these positions, from 2009 to 2013, Dr. Zago also served as a scientist at Janssen Alzheimer Immunotherapy, a Johnson & Johnson Company. He earned his BS in Biomedicine from the Universidade Federal de Sao Paulo (Escola Paulista de Medicina), Brazil, and his MS and PhD (both in Pharmacology) from the Universidade de Sao Paulo, Brazil, and was a Post-Doctoral Researcher at the University of California, San Diego and the Burnham Institute.

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 the Company's website at *https://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, 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 to our website at *https://ir.prothena.com/corporate-governance*. The contents of our websites are not intended to be incorporated by reference into this Form 10-K 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.

Insider Trading Compliance Policy

We have an Insider Trading Compliance Policy governing the purchase, sale, and other dispositions of Prothena's securities that applies to all personnel of Prothena and its subsidiaries, including directors, officers, and employees and other covered persons. We believe that our Insider Trading Compliance Policy is reasonably designed to promote compliance with insider trading laws, rules and regulations, as well as applicable listing standards. A copy of our Insider Trading Compliance Policy is filed as Exhibit 19.1 to this Form 10-K.

ITEM 11. EXECUTIVE COMPENSATION

The information appearing in our Proxy Statement under the following headings is incorporated herein by reference, provided that the Report of the Compensation Committee of the Board of Directors shall not be deemed filed in this Form 10-K:

- Compensation Discussion and Analysis
- Report of the Compensation Committee of the Board of Directors
- Executive Compensation
- Director Compensation
- Corporate Governance and Board Matters - Other Corporate Governance Matters

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information appearing in our Proxy Statement under the following headings is incorporated herein by reference:

- Equity Compensation Plan Information
- Security Ownership of Certain Beneficial Owners and Management

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information appearing in our Proxy Statement under the following headings is incorporated herein by reference:

- Transactions with Related Persons and Indemnification
- Proposal No. 1 - Election of Directors
- Corporate Governance and Board Matters - Independent Directors

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The Company's independent registered public accounting firm is KPMG LLP, San Francisco, CA, Auditor Firm ID: 185.

The information appearing in our Proxy Statement under the following headings is incorporated herein by reference:

- Proposal No. 2 - Ratification of Appointment of Independent Registered Public Accounting Firm

With the exception of the information specifically incorporated by reference in Part III to this Form 10-K from our Proxy Statement, our Proxy Statement shall not be deemed to be filed as part of this Form 10-K.

PART IV

ITEM 15. EXHIBIT AND FINANCIAL STATEMENT SCHEDULES

(a) The following documents are filed as part of this report on Form 10-K:

(1) *Financial Statements.* Reference is made to the Index to the registrant's Financial Statements under Item 8 in Part II of this Form 10-K.

(2) *Financial Statement Schedules.* Financial statement schedules have been omitted because the required information is not present or not present in the amounts sufficient to require submission of the schedule or because the information is already included in the consolidated financial statements or notes thereto.

(3) *Exhibits.* The exhibits listed on the accompanying index to exhibits in Item 15(b) below are filed as part of, or hereby incorporated by reference into, this report on Form 10-K.

(b) Exhibits.

The exhibits listed in the Exhibit Index hereto are incorporated or filed herewith.

EXHIBIT INDEX

Exhibit No.	Description	Previously Filed				Filed Herewith
		Form	File No.	Filing Date	Exhibit	
2.1	Demerger Agreement, dated as of November 8, 2012, between Elan Corporation, plc and Prothena Corporation plc	10/A	001-35676	11/30/2012	2.1	
2.2(a)	Amended and Restated Intellectual Property License and Contribution Agreement, dated as of December 20, 2012, by and among Neotope Biosciences Limited, Elan Pharma International Limited, and Elan Pharmaceuticals, Inc.	8-K	001-35676	12/21/2012	2.1	
2.2(b)	Amendment Number One to the Amended and Restated Intellectual Property License and Contribution Agreement, effective as of December 20, 2012, among Neotope Biosciences Limited, Elan Pharma International Limited, Elan Pharmaceuticals, LLC, Elan Corporation, plc, and Crimagua Limited	S-1/A	333-191218	9/30/2013	2.2(b)	
2.3	Intellectual Property License and Conveyance Agreement, dated as of December 20, 2012, among Neotope Biosciences Limited, Elan Pharma International Limited and Elan Pharmaceuticals, Inc.	8-K	001-35676	12/21/2012	2.2	
3.1	Amended and Restated Memorandum and Articles of Association (Constitution) of Prothena Corporation plc	8-K	001-35676	5/25/2016	3.1	
4.1	Amended and Restated Memorandum and Articles of Association (Constitution) of Prothena Corporation plc	8-K	001-35676	5/25/2016	3.1	
4.2	Description of Registrant's Securities					X
10.1(a)	Tax Matters Agreement, dated as of December 20, 2012, between Elan Corporation, plc and Prothena Corporation plc	8-K	001-35676	12/21/2012	10.1	
10.1(b)	Amendment No. 1 to Tax Matters Agreement, dated as of June 25, 2013, between Elan Corporation, plc and Prothena Corporation plc	10-Q	001-35676	8/13/2013	10.2	
10.2	License Agreement, dated as of December 31, 2008, between the University of Tennessee Research Foundation and Elan Pharmaceuticals, Inc.	10/A	001-35676	11/30/2012	10.14	
10.3(a)†	License Agreement, dated as of November 4, 2013, between The Regents of the University of California and Neotope Biosciences Limited	10-Q/A	001-35676	8/17/2018	10.1(a)	
10.3(b)†	License Agreement Amendment Number One, dated as of January 15, 2014, to License Agreement dated as of November 4, 2013, between The Regents of the University of California and Neotope Biosciences Limited	10-Q/A	001-35676	8/17/2018	10.1(b)	
10.4(a)†	License, Development, and Commercialization Agreement, dated as of December 11, 2013, among Neotope Biosciences Limited and Prothena Biosciences Inc, F. Hoffmann-La Roche Ltd. and Hoffmann-La Roche Inc.	10-K/A	001-35676	6/6/2014	10.4	
10.4(b)+	Amendment to License, Development, and Commercialization Agreement, entered into on October 1, 2019, among Prothena Biosciences Limited, Prothena Biosciences Inc, F. Hoffman-La Roche Ltd and Hoffman-La Roche Inc.	10-K	001-35676	3/3/2020	10.6	

Exhibit No.	Description	Previously Filed				Filed Herewith
		Form	File No.	Filing Date	Exhibit	
10.4(c)+	Amendment No. 2 to License, Development, and Commercialization Agreement, entered into on August 26, 2021, among Prothena Biosciences Limited, Prothena Biosciences Inc, F. Hoffman-La Roche Ltd and Hoffman-La Roche Inc.	10-Q	001-35676	11/4/2021	10.3	
10.5(a)	Understanding Related to License, Development, and Commercialization Agreement, dated as of March 1, 2020, among Prothena Biosciences Limited, Prothena Biosciences Inc, F. Hoffman-La Roche Ltd and Hoffman-La Roche Inc.	10-Q	001-35676	5/6/2020	10.4(a)	
10.5(b)+	License Agreement, dated as of March 1, 2020, between Prothena Biosciences Limited and F. Hoffmann-La Roche Ltd.	10-Q	001-35676	5/6/2020	10.4(b)	
10.6+	Global License Agreement, dated as of July 5, 2023, by and between Prothena Biosciences Limited and Celgene Switzerland LLC	10-Q	001-35676	11/2/2023	10.2	
10.7+	Global License Agreement, dated as of May 24, 2024, by and between Prothena Biosciences Limited and Celgene Switzerland LLC	10-Q	001-35676	8/8/2024	10.3	
10.8+	Share Purchase Agreement, dated as of July 8, 2021, by and among Novo Nordisk A/S, Novo Nordisk Region Europe A/S, Prothena Corporation plc, and Prothena Biosciences Limited	10-Q	001-35676	11/4/2021	10.4	
10.9(a)	Sublease, dated as of October 28, 2022, by and between Arcus Biosciences, Inc. and Prothena Biosciences Inc.	10-K	001-35676	2/28/2023	10.15(a)	
10.9(b)	Consent to Sublease Agreement, dated as of October 28, 2022, by and among HCP LS Brisbane, LLC, Arcus Biosciences, Inc., and Prothena Biosciences Inc.	10-K	001-35676	2/28/2023	10.15(b)	
10.10#	Prothena Corporation plc Amended and Restated 2012 Long Term Incentive Plan	8-K	001-35676	5/23/2017	10.1	
10.11(a)#	Prothena Corporation plc 2018 Long Term Incentive Plan	8-K	001-35676	5/18/2018	10.1	
10.11(b)#	First through Fifth Amendments to the Prothena Corporation plc 2018 Long Term Incentive Plan					X
10.12(a)#	Prothena Corporation plc 2020 Employment Inducement Incentive Plan	10-Q	001-35676	5/6/2020	10.2	
10.12(b)#	First through Fourteenth Amendments to the Prothena Corporation plc 2020 Employment Inducement Incentive Plan	10-K	001-35676	2/22/2024	10.23	
10.13#	Prothena Corporation plc Amended and Restated Incentive Compensation Plan	10-Q	001-35676	5/9/2017	10.1	
10.14#	Prothena Biosciences Inc Amended and Restated Severance Plan	8-K	001-35676	12/15/2015	10.1	
10.15#	Form of Deed of Indemnification between Prothena Corporation plc and its Directors and Officers	8-K	001-35676	12/11/2014	10.1	
10.16#	Form of Option Award Agreement between Prothena Corporation plc and its Non-Employee Directors under the Prothena Corporation plc 2012 Long Term Incentive Plan (used beginning January 29, 2013)	S-8	333-196572	6/6/2014	99.2	

Exhibit No.	Description	Previously Filed				Filed Herewith
		Form	File No.	Filing Date	Exhibit	
10.17#	Form of Option Award Agreement between Prothena Corporation plc and its Non-Employee Directors under the Prothena Corporation plc 2018 Long Term Incentive Plan (used beginning May 16, 2018)	10-Q	001-35676	8/7/2018	10.2	
10.18#	Form of Option Award Agreement between Prothena Corporation plc and its Named Executive Officers under the Prothena Corporation plc 2012 Long Term Incentive Plan (used beginning January 29, 2013 until February 4, 2014)	S-8	333-196572	6/6/2014	99.3	
10.19#	Form of Option Award Agreement between Prothena Corporation plc and its Named Executive Officers under the Prothena Corporation plc 2012 Long Term Incentive Plan (used beginning February 4, 2014)	10-K	001-35676	3/13/2015	10.11	
10.20#	Form of Option Award Agreement between Prothena Corporation plc and its Named Executive Officers under the Prothena Corporation plc 2018 Long Term Incentive Plan (used beginning June 21, 2018)	10-Q	001-35676	8/7/2018	10.3	
10.22 #	Form of Option Award Agreement under the Prothena Corporation plc 2020 Employment Inducement Incentive Plan (used beginning March 2, 2020)	10-Q	001-35676	8/6/2020	10.3	
10.23#	Offer letter, dated March 20, 2013, between Prothena Biosciences Inc and Tran B. Nguyen	8-K	001-35676	3/28/2013	10.1	
10.24#	Employment Agreement, dated September 30, 2016, between Prothena Biosciences Inc and Gene G. Kinney	8-K	001-35676	11/4/2016	10.1	
10.25#	Offer letter, dated April 19, 2013, between Prothena Biosciences Inc and Karin L. Walker	8-K	001-35676	5/22/2013	10.1	
10.26#	Offer letter, dated December 5, 2016, between Prothena Biosciences Inc and Carol D. Karp	10-K	001-35676	2/27/2017	10.28	
10.27#	Promotion letter, dated June 9, 2017, between Prothena Biosciences Inc and Wagner M. Zago	10-Q	001-35676	8/9/2017	10.3	
10.28#	Offer letter, dated June 4, 2019, between Prothena Biosciences Inc and Michael J. Malecek	10-Q	001-35676	8/6/2019	10.1	
10.29#	Offer Letter, dated February 18, 2020, between Prothena Biosciences Inc and Brandon S. Smith	10-Q	001-35676	5/6/2020	10.1	
10.30#	Promotion letter, dated September 27, 2024, between Prothena Biosciences Inc and Chad J. Swanson	10-Q	001-35676	11/12/2024	10.2	
10.31#	Consulting Agreement, dated October 1, 2024, between Prothena Biosciences Inc and Dennis J. Selkoe	10-Q	001-35676	11/12/2024	10.1	
19.1	Prothena Corporation plc Insider Trading Compliance Policy					X

Exhibit No.	Description	Previously Filed				Filed Herewith
		Form	File No.	Filing Date	Exhibit	
21.1	List of Subsidiaries					X
23.1	Consent of KPMG LLP, independent registered public accounting firm					X
24.1	Power of Attorney (see signature page hereto)					X
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X
32.1*	Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
97#	Policy on Recoupment of Incentive Compensation	10-K	001-35676	2/22/2024	97	
101.INS	The instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document					X
101.SCH	Inline XBRL Taxonomy Extension Schema Document					X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document					X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document					X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document					X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document					X
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)					X

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* *Exhibit 32.1 is being furnished and shall not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liability of that section, nor shall such exhibit be deemed to be incorporated by reference in any registration statement or other document filed under the Securities Act of 1933, as amended, or the Exchange Act, except as otherwise specifically stated in such filing.*

\# *Indicates management contract or compensatory plan or arrangement.*

† *Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment and this exhibit has been filed separately with the Securities and Exchange Commission.*

\+ *Certain information in this exhibit (indicated by asterisks) has been excluded pursuant to Regulation S-K, Item 601(b)(10). Such information is both not material and the type of information that the registrant customarily and actually treats as private and confidential.*

ITEM 16. FORM 10-K SUMMARY

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

Dated: February 27, 2025

Prothena Corporation plc
(Registrant)

/s/ Gene G. Kinney

Gene G. Kinney
President and Chief Executive Officer

/s/ Tran B. Nguyen

Tran B. Nguyen
Chief Strategy Officer and Chief Financial Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose individual signature appears below hereby authorizes and appoints Gene G. Kinney and Tran B. Nguyen, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

Name	Title	Date
/s/ Gene G. Kinney Gene G. Kinney, Ph.D.	President and Chief Executive Officer (Principal Executive Officer) and Director	February 27, 2025
/s/ Tran B. Nguyen Tran B. Nguyen	Chief Strategy Officer and Chief Financial Officer (Principal Financial Officer)	February 27, 2025
/s/ Karin L. Walker Karin L. Walker	Chief Accounting Officer (Principal Accounting Officer)	February 27, 2025
/s/ Daniel G. Welch Daniel G. Welch	Chair of the Board	February 27, 2025
/s/ Paula K. Cobb Paula K. Cobb	Director	February 27, 2025
/s/ Richard T. Collier Richard T. Collier	Director	February 27, 2025
/s/ Shane M. Cooke Shane M. Cooke	Director	February 27, 2025
/s/ William H. Dunn, Jr. William H. Dunn, Jr., M.D.	Director	February 27, 2025
/s/ Lars G. Ekman Lars G. Ekman, M.D., Ph.D.	Director	February 27, 2025
/s/ Helen S. Kim Helen S. Kim	Director	February 27, 2025
/s/ Dennis J. Selkoe Dennis J. Selkoe, M.D.	Director	February 27, 2025