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, 2025

☐ **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, 2025, 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 $326.6 million based on the last reported sale of the registrant's ordinary shares on the Nasdaq Global Market on such date.

53,832,982 of the Registrant's ordinary shares, par value $0.01 per share, were outstanding as of February 20, 2026.

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 14, 2026, 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, 2025.

PROTHENA CORPORATION PLC
Annual Report on Form 10-K
For the Year Ended December 31, 2025

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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; 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 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 pipeline includes both wholly-owned and partnered programs being developed for the potential treatment of diseases including Parkinson's disease, ATTR amyloidosis with cardiomyopathy, Alzheimer's disease, Amyotrophic lateral sclerosis (ALS) and a number of other neurodegenerative diseases. Prothena is developing and applying its proprietary CYTOPE® technology to target a broad spectrum of intracellular disease pathways in the brain and periphery.

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.

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, 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) is a rare, progressive and fatal disease characterized by deposition of aggregated misfolded transthyretin proteins in vital organs such as the heart. It is believed two different proteins – Aβ (amyloid beta) and tau – are important contributors to Alzheimer's disease pathology. Misfolded Aβ builds up to form plaques between nerve cells in the brain. Tangles of twisted tau fibrils aggregate within neurons and spread from cell to cell and cause build up inside the neurons.

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 near-term plan is to continue to support our active clinical programs which are all partnered with large pharmaceutical companies, while investing in early-stage research programs and technology to create future partnership opportunities and collaborations. Our active clinical portfolio includes prasinezumab currently being evaluated in the Phase 3 PARAISO clinical trial for the treatment of early Parkinson's disease in partnership with Roche, coramitug currently being evaluated in the Phase 3 CLEOPATTRA clinical trial for the treatment of ATTR-CM by Novo Nordisk, BMS-986446 currently being evaluated in the Phase 2 TargetTau-1 clinical trial for the treatment of early Alzheimer's disease by Bristol Myers Squibb, and PRX019 currently being evaluated in a Phase 1 clinical trial by Prothena as part of a global partnership with Bristol Myers Squibb. Our early-stage research programs include development of a new technology, CYTOPE®, which enables precise targeting of intracellular disease pathways in the brain and periphery through an endosomal uptake and escape mechanism that preserves membrane and vesicle integrity following systemic administration. This technology potentially allows for targeting of previously undruggable intracellular disease targets. In addition, we are conducting further preclinical development of PRX012, our wholly-owned anti-Aβ antibody for the treatment of Alzheimer's disease in conjunction with a transferrin receptor (TfR) technology to potentially further enhance its clinical profile. Our near-term strategy is to develop these programs efficiently while evaluating potential strategic research collaborations and licensing deals with large pharmaceutical companies to further advance and elucidate their potential at the appropriate value inflection point. For example, we currently have and are focused

on developing additional research collaborations with large pharmaceutical companies to further develop and explore applications of our CYTOPE® technology.

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. 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 ATTR amyloidosis. In addition, our research team has developed a new technology, CYTOPE ®, which enables precise targeting of intracellular disease pathways in the brain and periphery through an endosomal uptake and escape mechanism that preserves membrane and vesicle integrity following systemic administration. This technology potentially allows for targeting of previously undruggable intracellular disease targets and was developed by our team since currently available alternate technologies do not efficiently accomplish these desired outcomes.

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;
- Disease driven antibody engineering for therapeutics engineered to optimally eliminate pathogenic proteins while preserving normal biology;
- Application of CYTOPE® technology to effectively and efficiently target previously undruggable intracellular disease targets.

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 alpha-synuclein, transthyretin, tau and Aβ to relevantly influence biology and achieve clinical benefit across a number of indications. In addition, we have applied our new CYTOPE® technology to target phosphorylated TDP-43, a key pathogenic feature of TDP-43 proteinopathies, including amyotrophic lateral sclerosis or ALS.

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 ATTR amyloidosis and Parkinson's disease where preclinical findings in our programs have translated to positive clinical data leading our partners to advance our programs into Phase 3 development.

- ***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 Parkinson's disease, ATTR amyloidosis, Alzheimer's disease, ALS 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.

ATTR amyloidosis is a disease caused by misfolded, pathogenic forms of 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 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 approach we are developing with coramitug (formerly PRX004) for ATTR amyloidosis is an investigational monoclonal antibody designed to clear the pathogenic amyloid deposits. Coramitug is 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 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 coramitug's differentiated depleter mechanism that targets the amyloid that causes organ dysfunction and failure and puts patients at risk for early mortality.

Amyotrophic Lateral Sclerosis (ALS) is a progressive, fatal neurodegenerative disease characterized by the selective loss of upper and lower motor neurons, and in the majority of cases by cytoplasmic aggregation and nuclear depletion of the RNA-binding protein TDP-43. Current approved therapies that broadly target ALS seek to affect disease progression by targeting broad mechanisms such as excitotoxicity and oxidative stress, rather than the core molecular pathology. These treatments do not stop or reverse motor neuron degeneration and, to date, provide limited clinical benefit. Consequently, there remains a major unmet need for disease-modifying therapies that directly address TDP-43-driven mechanisms. Using our internally discovered CYTOPE® technology, we have developed an anti-pTDP-43 CYTOPE® that is designed to address the core molecular pathology associated with ALS in in the majority of cases.

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 the acquisition of our ATTR amyloidosis business by Novo Nordisk are examples of this, as are our two global licensing deals with BMS focused on neurodegenerative diseases. 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. In addition, we will leverage research collaborations with large pharmaceuticals companies to explore applications of our CYTOPE® technology. These collaborations are designed to further investigate discovery programs which may lead to potential licensing deals or partnerships in the future.

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.

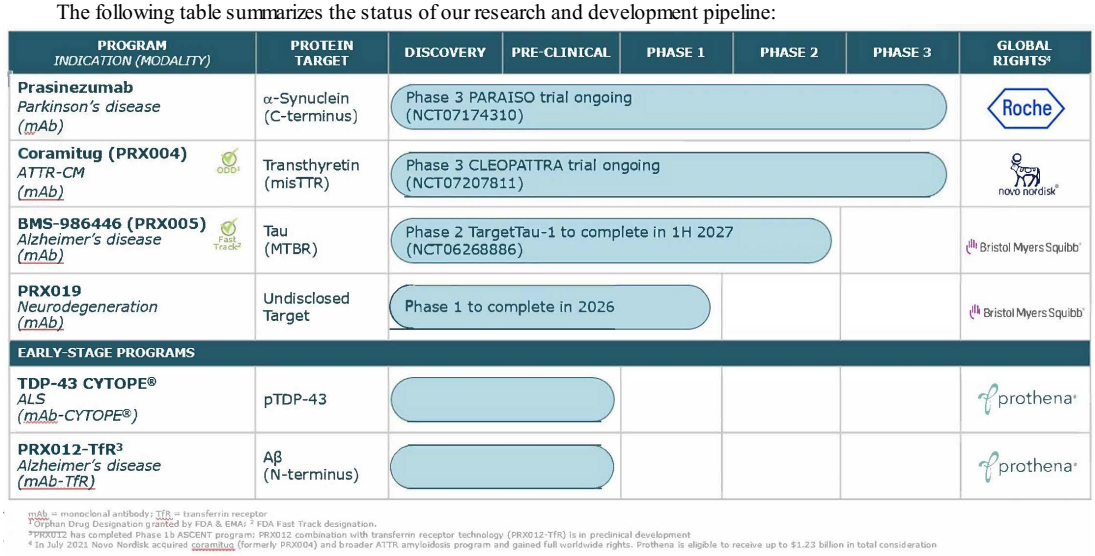
Our Research and Development Pipeline

Our active clinical research and development pipeline includes four therapeutic antibody programs currently in active clinical development: 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; 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 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. This includes our TDP-43 CYTOPE® program for the potential treatment of ALS and additional undisclosed discovery programs leveraging our novel CYTOPE® technology and our preclinical PRX012-TfR program for the potential treatment of Alzheimer's disease.

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:



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 3 PARAISO Clinical Trial

In the fourth quarter of 2025, Roche initiated the Phase 3 PARAISO clinical trial (NCT07174310) evaluating prasinezumab as a potential treatment for early Parkinson's disease. PARAISO is a Phase 3, randomized, double-blind, placebo-controlled, multicenter clinical trial to evaluate the efficacy and safety of prasinezumab in approximately 900 participants with early-stage Parkinson's disease on stable symptomatic monotherapy with levodopa. Primary endpoint of the trial is time to confirmed motor progression event on Movement Disorder Society - Unified Parkinson's Disease Rating Scale ("MDS-UPDRS") Part III score at a minimum of 104 weeks.

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.

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 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.

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.

Clinical Development Program for Coramitug

Phase 3 CLEOPATTRA Clinical Trial

In the fourth quarter of 2025, Novo Nordisk initiated the Phase 3 CLEOPATTRA clinical trial (NCT07207811) evaluating coramitug as a potential treatment for ATTR-CM. CLEOPATTRA is a randomized, double-blind, placebo-controlled, multicenter clinical trial in approximately 1,280 participants with ATTR-CM. Primary endpoint is the number of occurrences of composite endpoint of cardiovascular (CV) deaths and recurrent CV events (CV hospitalizations and urgent heart failure visits) in a timeframe to end of study up to approximately four years.

Phase 2 Clinical Trial

A Phase 2 clinical trial of coramitug in 105 patients with ATTR amyloidosis with cardiomyopathy was conducted by Novo Nordisk (NCT05442047). Top-line results were presented as a late-breaking session at the American Heart Association (AHA) Scientific Sessions in November 2025 and simultaneously published in the AHA journal, *Circulation*. Treatment with coramitug 60 mg/kg resulted in a statistically significant reduction in NT-proBNP levels compared with placebo (–48%; p=0.0017) over 52 weeks and notably with a reduction at in NT-proBNP levels at 12 months from baseline. This favorable reduction was achieved on top of background use of standard-of-care TTR stabilizers in most patients (80% in the coramitug 60 mg/kg group and 85.7% in the placebo group). Coramitug 60 mg/kg showed an estimated treatment difference of 13.45 meters in the six-minute walk test (6MWT) vs. placebo. Statistical significance was not achieved on the 6MWT endpoint, however this was potentially due to the small sample size and relatively short study duration. In addition, across a wide range of

echocardiographic parameters, including measures of left ventricle (LV) and right ventricle (RV) systolic function, diastolic function, and estimated pulmonary arterial pressures, coramitug 60 mg/kg was associated with improvements versus placebo, suggestive of favorable cardiac remodeling. Coramitug demonstrated an acceptable safety profile and was generally well tolerated.

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.

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.

Clinical Development Program for BMS-986446

In October 2025, Bristol Myers Squibb obtained Fast Track designation from the U.S. FDA for BMS-986446 for the treatment of Alzheimer's disease.

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 TargetTau-1 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 310 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 change from baseline to week 76 in brain tau deposition as measured by tau positron emission tomography (PET). Secondary endpoints include change from baseline to week 76 in Clinical Dementia Rating Scale Sum of Boxes (CDR-SB) score and in the integrated Alzheimer's Disease Rating Scale (iADRS) score.

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.

In 2025, BMS completed a Phase 1 clinical trial to assess drug levels, tolerability and absolute biological availability of single subcutaneous dose of BMS-986446 in healthy participants. This was a Phase 1, randomized, open-label, parallel, single-dose clinical trial to assess the pharmacokinetics, tolerability, and absolute bioavailability of subcutaneous administration of BMS-986446, an anti-MTBR tau monoclonal antibody, in approximately 46 healthy participants.

License, Development, and Commercialization Agreement with BMS

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 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. In October 2025, Bristol Myers Squibb obtained Fast Track designation from the U.S. FDA for BMS-986446 for the potential treatment of Alzheimer's disease.

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 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.

Early-Stage Programs

We are also advancing several early-stage programs for neurological diseases with significant unmet medical needs. If promising, we expect to advance our discovery and preclinical programs to clinical 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.

TDP-43 CYTOPE®

In November 2025, we presented a poster titled *Treatment with a Cell-Internalizing CYTOPE® Targeting pTDP-43 Reduces Intraneuronal Pathology in a Mouse Model of ALS* at Neuroscience 2025, hosted by the Society for Neuroscience (SfN) and subsequently presented an encore at the 36th International Symposium of ALS/MND. The scientific poster described our TDP-43 CYTOPE® developed using our new CYTOPE® technology. CYTOPE® enables precise targeting of intracellular disease pathways in the brain and periphery through an endosomal uptake and escape mechanism that preserves membrane and vesicle integrity following systemic administration. To demonstrate the potential of CYTOPE® we developed and investigated our TDP-43 CYTOPE® program in multiple preclinical models which was the basis of the scientific presentation.

Preclinical data from in vivo transgenic mouse model of ALS expressing human mutant TDP-43:

- Systemically-administered TDP-43 CYTOPE® rapidly and efficiently distributed to the brain, internalized into the cytosol and colocalized with intracellular pTDP-43 pathology in rNLS8 mice

- Systemically-administered TDP-43 CYTOPE® significantly reduced intracellular pTDP-43 pathology in rNLS8 mouse motor cortex and neuromuscular junction

Preclinical in vitro data from rat and human-derived neuronal cell lines and human iPSC motor neurons:

- TDP-43 CYTOPE rapidly and efficiently internalized into the cytosol and colocalized with pre-formed cytosolic pTDP-43 aggregates
- TDP-43 CYTOPE promoted significant clearance of cytosolic pTDP-43 aggregates and meaningfully reduced RNA dysregulation driven by cryptic exon inclusions, defining pathogenic features of ALS and other TDP-43 proteinopathies

These results demonstrate the potential of our CYTOPE® technology as a novel modality, enabling precise targeting of intracellular disease pathways.

CYTOPE®

We are developing a new technology, CYTOPE®, which enables precise targeting of intracellular disease pathways in the brain and periphery through an endosomal uptake and escape mechanism that preserves membrane and vesicle integrity following systemic administration. This technology potentially allows for targeting of previously undruggable intracellular disease targets.

Our strategy is to efficiently identify and develop programs leveraging CYTOPE® while evaluating potential strategic research collaborations and licensing deals with large pharmaceutical companies to further advance and elucidate their potential at the appropriate value inflection point.

PRX012 and PRX012-TfR 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.

PRX012 is a potential next-generation anti-Aβ antibody designed 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 August 2025, we announced topline Phase 1 data from our ongoing multiple dose trial.

We plan to explore potential partnership interest to advance PRX012 and our preclinical PRX012-TfR (transferrin receptor) antibody programs.

Phase 1 ASCENT Clinical Program

The Phase 1 ASCENT clinical program includes ASCENT-1: a randomized, double-blind, placebo-controlled single-ascending-dose trial; ASCENT-2: a randomized, double-blind, placebo-controlled six-month multiple-dose trial; and ASCENT-3: a twelve-month open-label extension trial. The objectives of the ASCENT clinical program were to determine the safety, tolerability, immunogenicity, and pharmacokinetics of PRX012. The ASCENT-2 and ASCENT-3 trials also evaluated the pharmacodynamics of PRX012, including amyloid plaque deposition as measured by positron emission tomography (PET), in participants with early symptomatic AD. The results summarize key data points from the five ASCENT-2 Group A cohorts in 228 participants with early symptomatic AD who are either APOε4 non-carriers or heterozygous carriers ranging in doses of PRX012 from 45 mg to 400 mg, randomized to PRX012 or placebo in a 3:1 ratio. Additional amyloid plaque reduction data from ASCENT-3, the open-label extension (OLE) trial, was available.

The Phase 1 ASCENT clinical program results demonstrated PRX012 as a potential once-monthly, subcutaneous anti-Aβ antibody with dose- and time-dependent reductions in amyloid plaque. At the 400 mg dose level, PRX012 demonstrated a mean reduction in amyloid PET to 27.47 centiloids (CL) at month 12. In clinical trials for FDA approved anti-Aβ antibodies, amyloid negativity defined as <30 CL or <24.1 CL. However, PRX012 was associated with higher overall ARIA-E rates relative to FDA approved anti-Aβ antibodies, making PRX012 less appropriate for the patients studied in the ASCENT clinical program. When ARIA-E did occur, the characteristics were similar to those reported following treatment with other anti-Aβ antibodies.

Additionally, preliminary data from the patients who were administered the 400 mg dose level of PRX012 for 18 months, mean CL value observed at 18 months was approximately 16.0 with 9 of 12 participants reaching amyloid negativity - amyloid levels below 24.1 CL.

PRX012-TfR Preclinical Program

Based on the profile observed in the ASCENT clinical program and feasibility work already completed on its preclinical Aβ-transferrin receptor antibody surrogate, we believe this approach may represent an opportunity to significantly lower the risk of ARIA and quickly reduce amyloid plaque with a once-monthly subcutaneous administration. Initial preclinical studies on our surrogate Aβ-TfR antibody have demonstrated substantially increased brain exposure and facilitated rapid targeting of Aβ plaques in an APP/PS1 transgenic mouse model.

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. We are exploring potential partnership interest to advance PRX123.

Discontinuation of Birtamimab Development

In May 2025, we announced the discontinuation of development of birtamimab, an investigational monoclonal antibody for the potential treatment of AL amyloidosis, based on the results from the Phase 3 AFFIRM-AL clinical trial for birtamimab, which did not meet its primary or secondary endpoints.

Workforce Reduction

In June 2025, we announced an approximate 63% reduction in our workforce to substantially reduce our operating costs to those necessary to support our remaining wholly-owned programs, obligations to partnered programs, and anticipated business development activities.

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 support 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).

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.

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.

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, know-how, and trademarks to protect our business. We may seek licenses from others as appropriate to enhance or maintain our competitive position.

Our patent portfolio is generally directed to composition of matter for programs, product candidates, and platform technologies, related methods of use, including treatment of diseases and related processes.

We own or hold exclusive licenses to issued patents and pending patent applications in the U.S. and other jurisdictions. As of December 31, 2025, our patent portfolio included approximately 59 patent families of patents or patent applications related to neurodegenerative disease programs, CYTOPE® platform technologies, and other assets. These include approximately 11 families related to the prasinezumab program.

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.

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

Prasinezumab - Boehringer Ingelheim Biopharmaceuticals GmbH ("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 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 Biopharma SE ("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 Solutions, LLC ("Catalent Pharma") was 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") 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 $134.9 million, $222.5 million, and $220.6 million in 2025, 2024, and 2023, 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, 2025, we had 67 employees, including 13 who held M.D. and/or Ph.D. degrees.Of our total employees, 36 were engaged in research and development (R&D) activities and the remainder were engaged in general and administrative (G&A) functions. In 2026, we expect to reduce our headcount by 17 employees, including 16 in R&D and the remainder in G&A roles. These anticipated reductions may change as we continue to assess and optimize our workforce to support our remaining wholly-owned programs, obligations to partnered programs, and anticipated business development activities.

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, 2025, we employed approximately 57% women and 43% men, and approximately 42% of our employees are racially or ethnically diverse. Our executive team, including employees at or above the vice president level, includes approximately 39% 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 $244.1 million $122.3 million and $147.0 million for the years ended December 31, 2025, 2024, and 2023, respectively. As of December 31, 2025, we had an accumulated deficit of $1.3 billion. We expect to continue to incur substantial losses for the foreseeable future as we:

- wind down the Phase 1 clinical trials for PRX012, and support the Phase 1 clinical trial for PRX019 and potential additional clinical trials for these and other programs;
- develop and possibly commercialize our drug candidates;
- 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, 2025, we had cash and cash equivalents of $307.5 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 prasinezumab being conducted by Roche, the Phase 3 clinical trial for coramitug (formerly PRX004) being conducted by Novo Nordisk, the Phase 2 clinical trial for BMS-986446 being conducted by BMS, 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.

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, trade policies or 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.

- Trade policies and geopolitical disputes and other international conflicts can result in tariffs, sanctions, and other measures that restrict international trade. Unfavorable government policies on international trade, such as export controls, capital controls or tariffs, new legislation or regulations, renegotiation of existing trade agreements, or any retaliatory trade actions due to recent or future trade tension, may impede, delay, limit, or increase the cost of manufacturing our drug candidates.

- 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, operations at 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, barriers to international trade, 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. 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"), among other things, imposes 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. 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. Although the CCPA 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, the Virginia Consumer Data Protection Act, the Colorado Privacy Act, and Connecticut Personal Data Privacy and Online Monitoring Act. 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 prasinezumab, the Phase 3 clinical trial for coramitug, the Phase 2 clinical trial for BMS-986446, 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 prasinezumab, the Phase 3 clinical trial for coramitug, the Phase 2 clinical trial for BMS-986446, 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 Phase 3 clinical trial 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 3 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 a Biologics License Application ("BLA") or a New Drug Application ("NDA") 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, complex 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-approval clinical

trials or other post-approval commitments or requirements, or may approve our 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.

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.

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. 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. 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.

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.

Coramitug has been granted Orphan Drug Designation by both the FDA and EMA for the treatment of transthyretin (or ATTR) 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.

BMS-986446, for the treatment of Alzheimer's disease, has 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.

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, 2025, are anticipated to expire on dates ranging from 2026 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, 2025, the resulting patents are projected to expire on dates ranging from 2028 to 2046. 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, 2025, the number of ordinary shares available for issuance pursuant to outstanding and future equity awards under our equity plans was 16,780,773.

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, 2025. 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. 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. 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, subject to the availability of a relief or exemption. Payment of any Irish stamp duty is generally a legal obligation of the transferee.

Ireland's Finance Act 2025 introduced a new exemption from Irish stamp duty (the "Market Capitalization Exemption") under section 86B of the Stamp Duties Act for transfers of shares in certain Irish incorporated companies where: (i) those shares are admitted to trading on a regulated market or multilateral trading facility (within the meaning of Directive 2014/65/EU of the European Parliament and of the Council of 15 May 2014 on markets in financial instruments and amending Directive 2002/92/EC and Directive 2011/61/EU) or a market located outside the European Union that is equivalent to a regulated market or multilateral trading facility; (ii) the closing market capitalization of the issuer is below the specified threshold of €1 billion on December 1 of the preceding year; and (iii) a valid notification has been made to the Irish Revenue Commissioners for the relevant year. Future transfers of our ordinary shares may be eligible for this exemption, subject to compliance with applicable notification requirements and other conditions under the Stamp Duties Act. There can be no assurance that we will qualify for this exemption in any particular year, or that the exemption will continue to be available, as eligibility depends on market capitalization thresholds, timely notification to the Irish Revenue Commissioners and other relevant conditions.

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, 2026.

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 5,106 shareholders of record of our ordinary shares as of February 20, 2026. 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

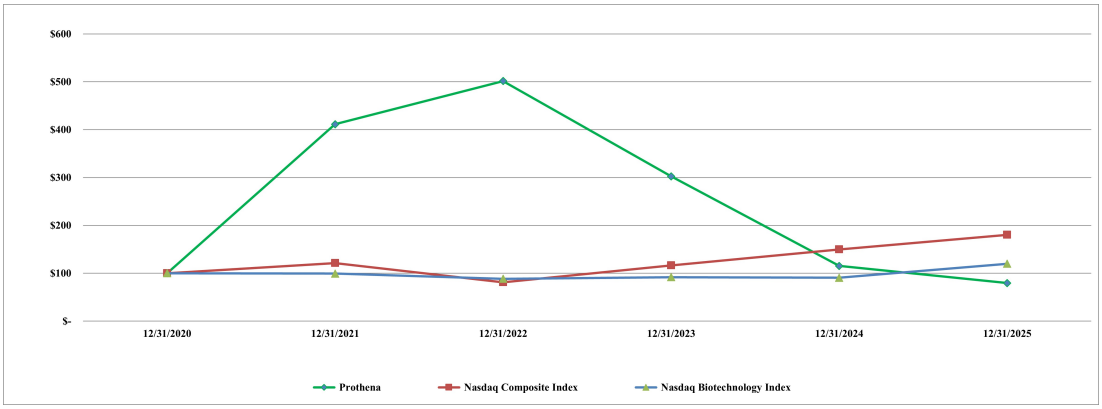
See Item 12 of Part III of this Form 10-K regarding information about securities authorized for issuance under our equity compensation plans.

Performance Graph[(1)]

The following graph shows a comparison from December 31, 2020, through December 31, 2025, 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	12/31/2020	12/31/2021	12/31/2022	12/31/2023	12/31/2024	12/31/2025
Prothena Corporation plc	$ 100	$ 411	$ 502	$ 303	$ 115	$ 80
Nasdaq Composite Index	$ 100	$ 121	$ 81	$ 116	$ 150	$ 180
Nasdaq Biotechnology Index	$ 100	$ 99	$ 89	$ 92	$ 91	$ 120

(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 tax on dividends, 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, subject to the availability of relief or exemption. 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. These 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). Our wholly-owned and unpartnered portfolio includes clinical and preclinical-stage programs that we are exploring strategic interest to further develop.

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 contained 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 the 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, 2025 and 2024

Revenue

	Year Ended December 31,		Change	
	2025	2024	$	%
	(Dollars in thousands)			
Collaboration revenue	$ 9,634	$ 135,107	$ (125,473)	(93)%
Revenue from license and intellectual property	50	50	—	—%
Total revenue	$ 9,684	$ 135,157	$ (125,473)	(93)%

Total revenue was $9.7 million and $135.2 million for the years ended December 31, 2025, and 2024, respectively.

Collaboration revenue from BMS was $9.6 million for the year ended December 31, 2025, compared to $135.1 million for the year ended December 31, 2024, a decrease of $125.5 million compared to the prior year. Collaboration revenue for the year ended December 31, 2025 was related to the partial performance of our PRX019 Phase 1 Clinical Trial Obligation. 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. 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 years ended December 31, 2025 and 2024, included $50,000 in each period, respectively, in license fees recognized under the License Agreement entered into on March 1, 2020, between the Company's wholly owned subsidiary, Prothena Biosciences Limited, and F. Hoffmann-La Roche Ltd.

Operating Expenses

	Year Ended December 31,		Change	
	2025	2024	$	%
	(Dollars in thousands)			
Research and development	$ 134,852	$ 222,519	$ (87,667)	(39)%
General and administrative	59,392	67,199	(7,807)	(12)%
Restructuring costs	30,080	—	30,080	nm
Total operating expenses	$ 224,324	$ 289,718	$ (65,394)	(23)%

nm = not meaningful

Total operating expenses consist of research and development ("R&D") expenses, general and administrative ("G&A") expenses, and restructuring costs. Our operating expenses were $224.3 million and $289.7 million for the years ended December 31, 2025, and 2024, 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, and preclinical activities related to our discovery programs. We also incurred wind down costs for programs that we are no longer advancing in clinical development, including birtamimab and PRX012.

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 decreased by $87.7 million for the year ended December 31, 2025, compared to the prior year. The decrease for the year ended December 31, 2025, was primarily due to lower clinical trial expenses primarily related to PRX012 wind down, lower personnel expenses and lower manufacturing and consulting expenses.

The following table sets forth the R&D expenses for our major programs (specifically, programs with successful first dosing in a Phase 1 clinical trial and have material expenditures in the periods presented), which were birtamimab, PRX012, PRX019, and other R&D expenses for the years ended December 31, 2025, and 2024, (in thousands):

	Year Ended December 31,	
	2025	2024
Birtamimab (NEOD001)	$ 53,455	$ 85,649
PRX012	54,020	116,359
PRX019[1]	8,081	5,035
Other R&D[2]	19,296	15,476
Total research and development	$ 134,852	$ 222,519

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

(2) *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, close out costs for programs that we are no longer advancing, and immaterial costs incurred on ongoing partnered programs.*

General and Administrative Expenses

Our G&A expenses decreased by $7.8 million, for the year ended December 31, 2025, compared to the prior year primarily due to lower personnel and consulting expenses.

Restructuring Costs

In June 2025, we commenced a restructuring plan following our decision in May 2025 to discontinue further development of birtamimab. We have incurred aggregate restructuring charges of approximately $30.1 million for the year ended December 31, 2025.

Restructuring charges incurred under this plan primarily consist of employee termination benefits in connection with the reduction in force announced in June 2025 and contract termination costs. Employee termination benefits include severance costs, employee-related benefits, and noncash share-based compensation expense related to the acceleration of the vesting of certain stock options. The vast majority of the employee termination benefits were paid out during the year ended December 31, 2025. We may also incur additional costs not currently contemplated due to events that may occur as a result of, or that are associated with, the restructuring plan. See Note 11, "Restructuring" to the Consolidated Financial Statements for more information.

Other Income (Expense)

	Year Ended December 31,		Change	
	2025	2024	$	%
	(Dollars in thousands)			
Interest income	$ 14,139	$ 25,816	$ (11,677)	(45)%
Other expense, net	(328)	(185)	(143)	77 %
Total other income (expense), net	$ 13,811	$ 25,631	$ (11,820)	(46)%

Interest income decreased by $11.7 million for the year ended December 31, 2025, 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 expense, net for the year ended December 31, 2025, was primarily foreign exchange losses from transactions with vendors denominated in euros.

Provision for (benefit from) Income Taxes

	Year Ended December 31,		Change	
	2025	2024	$	%
	(Dollars in thousands)			
Provision for (benefit from) income taxes	$ 43,263	$ (6,620)	$ 49,883	(754)%

On July 4, 2025, the One Big Beautiful Bill Act ("OBBBA") was signed into law. The OBBBA includes a broad range of U.S. tax reform measures, including, among other provisions, the immediate expensing of U.S. research and development expenditures. In accordance with ASC 740, the Company has recognized the effects of the new tax law in the period of enactment, and unamortized Section 174 balances will be recognized over the remaining amortization period. As the Company maintains a full valuation allowance on its deferred tax assets, the legislation did not have a material impact on our consolidated financial statements for the year ended December 31, 2025.

Provision for income taxes increased by $49.9 million for the year ended December 31, 2025, compared to prior year primarily due to recording a valuation allowance for the federal deferred tax assets, mainly relating to share-based compensation and R&D expenditure capitalized in previous years.

No tax benefit has been recorded related to tax losses recognized in Ireland or the U.S. and any deferred tax assets for those losses are offset by a valuation allowance.

Comparison of the years ended December 31, 2024 and 2023

Refer to "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations—Results of Operations" in our 2024 Annual Report on Form 10-K for a discussion of the results of operations for the year ended December 31, 2024 compared to the year ended December 31, 2023.

Liquidity and Capital Resources

Overview

	December 31,	
	2025	2024
	(Dollars in thousands)	
Working capital	$ 274,350	$ 436,911
Cash and cash equivalents	$ 307,531	$ 471,388
Total assets	$ 326,804	$ 547,108
Total liabilities	$ 46,330	$ 60,182
Total shareholders' equity	$ 280,474	$ 486,926

Working capital was $274.4 million as of December 31, 2025, a decrease of $162.6 million from working capital of $436.9 million as of December 31, 2024. This decrease in working capital during the year ended December 31, 2025, was primarily attributable to cash used in operating activities of $163.6 million.

As of December 31, 2025, we had $307.5 million in cash and cash equivalents. Based on our current business plans, we believe that our existing cash and cash equivalents at December 31, 2025 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 our 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, 2025, $232.5 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 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; 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,		
	2025	**2024**	**2023**
Net cash used in operating activities	$ (163,580)	$ (150,050)	$ (133,906)
Net cash used in investing activities	(138)	(298)	(2,773)
Net cash provided by (used in) financing activities	(139)	1,554	45,103
Net decrease in cash, cash equivalents and restricted cash	$ (163,857)	$ (148,794)	$ (91,576)

Cash Used in Operating Activities

Net cash used in operating activities was $163.6 million for the year ended December 31, 2025, which was primarily due to ongoing research and development activities, general and administrative expenses to support those activities (adjusted to exclude non-cash charges for share-based compensation expense) and payments related to our restructuring activities, partially offset by interest income on investments.

Cash Used in Investing Activities

Net cash used in investing activities was $138 thousand for the year ended December 31, 2025, which consisted of expenditures to purchase property and equipment.

Cash Provided by (Used in) Financing Activities

Net cash used in financing activities was $139 thousand for the year ended December 31, 2025, which consisted of expenditures related to our at-the-market offering.

Years ended December 31, 2024 and 2023

Refer to "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations — Liquidity and Capital Resources" in our 2024 and 2023 Annual Report on Form 10-K for a discussion of the cash flows for the years ended December 31, 2024 and 2023, respectively.

Off-Balance Sheet Arrangements

At December 31, 2025, 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, 2025, consisted of minimum cash payments under operating leases of $9.1 million, purchase obligations of $3.1 million (of which $2.7 million is included in current liabilities), obligations under our restructuring plan of $13.3 million (of which all of it is included in current liabilities), and contractual obligations under license agreements of $50 thousand. 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 our 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 2025, we renewed both leases, each for another

one year term with termination dates in July 2026. 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 $9.0 million remains outstanding as of December 31, 2025

The following is a summary of our contractual obligations as of December 31, 2025 (in thousands):

	Total	2026	2027	2028	2029	Thereafter
Operating leases [1]	$ 9,093	$ 3,301	$ 3,269	$ 2,523	$ —	$ —
Purchase obligations [2]	3,077	3,077	—	—	—	—
Obligations under the restructuring plan [3]	13,303	13,303	—	—	—	—
Contractual obligations under license agreements	50	35	15	—	—	—
Total	$ 25,523	$ 19,716	$ 3,284	$ 2,523	$ —	$ —

[1] *See Note 6, "Commitments and Contingencies" to our Consolidated Financial Statements.*

[2] *As of the filing date, there were no material changes to our Purchase obligations subsequent to December 31, 2025*

[3] *Includes cash obligations under our restructuring plan. For additional information, see Note 11, "Restructuring" to our Consolidated Financial Statements.*

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 2026 net cash used in operating and investing activities to be approximately $50 million to $55 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 $328,000, $185,000 and $458,000 during the years ended December 31, 2025, 2024 and 2023, 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. 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

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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, 2025 and 2024, the related consolidated statements of operations, cash flows, and shareholders' equity for each of the years in the three-year period ended December 31, 2025, 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, 2025, 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, 2025 and 2024, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2025, 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, 2025 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 Matters

Critical audit matters are matters arising from the current period audit of the consolidated financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. We determined that there are no critical audit matters.

/s/ KPMG LLP

We have served as the Company's auditor since 2012.

San Francisco, California
February 27, 2026

Prothena Corporation plc and Subsidiaries
Consolidated Balance Sheets
(in thousands, except share and per share data)

	December 31,	
	2025	**2024**
Assets		
Current assets:		
Cash and cash equivalents	$ 307,531	$ 471,388
Prepaid expenses and other current assets	7,662	14,024
Total current assets	315,193	485,412
Non-current assets:		
Property and equipment, net	2,144	3,081
Operating lease right-of-use assets	8,125	10,708
Deferred tax assets	—	43,239
Restricted cash, non-current	860	860
Other non-current assets	482	3,808
Total non-current assets	11,611	61,696
Total assets	$ 326,804	$ 547,108
Liabilities and Shareholders' Equity		
Current liabilities:		
Accounts payable	$ 5,875	$ 7,770
Accrued research and development	4,329	13,428
Deferred revenue, current	2,664	8,850
Restructuring liability	13,303	—
Lease liability, current	2,886	2,610
Other current liabilities	11,786	15,843
Total current liabilities	40,843	48,501
Non-current liabilities:		
Deferred revenue, non-current	—	3,448
Lease liability, non-current	5,487	8,233
Total non-current liabilities	5,487	11,681
Total liabilities	46,330	60,182
Commitments and contingencies (Note 6)		
Shareholders' equity:		
Euro deferred shares, €22 nominal value:	—	—
Authorized shares — 10,000 at December 31, 2025 and 2024		
Issued and outstanding shares — none at December 31, 2025 and 2024		
Ordinary shares, $0.01 par value:	538	538
Authorized shares — 100,000,000 at December 31, 2025 and 2024		
Issued and outstanding shares — 53,832,982 and 53,826,982 at December 31, 2025 and 2024, respectively		
Additional paid-in capital	1,626,369	1,588,729
Accumulated deficit	(1,346,433)	(1,102,341)
Total shareholders' equity	280,474	486,926
Total liabilities and shareholders' equity	$ 326,804	$ 547,108

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,		
	2025	**2024**	**2023**
Collaboration revenue	$ 9,634	$ 135,107	$ 91,320
Revenue from license and intellectual property	50	50	50
Total revenue	9,684	135,157	91,370
Operating expenses:			
Research and development	134,852	222,519	220,571
General and administrative	59,392	67,199	61,835
Restructuring costs	30,080	—	—
Total operating expenses	224,324	289,718	282,406
Loss from operations	(214,640)	(154,561)	(191,036)
Other income (expense):			
Interest income	14,139	25,816	31,014
Other expense, net	(328)	(185)	(458)
Total other income, net	13,811	25,631	30,556
Loss before income taxes	(200,829)	(128,930)	(160,480)
Provision for (benefit from) income taxes	43,263	(6,620)	(13,452)
Net loss	$ (244,092)	$ (122,310)	$ (147,028)
Basic and diluted net loss per ordinary share	$ (4.53)	$ (2.27)	$ (2.76)
Shares used to compute basic and diluted net loss per share	53,829	53,772	53,216

See accompanying Notes to Consolidated Financial Statements.

Prothena Corporation plc and Subsidiaries
Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,		
	2025	**2024**	**2023**
Operating activities			
Net loss	$ (244,092)	$ (122,310)	$ (147,028)
Adjustments to reconcile net loss to cash used in operating activities:			
Depreciation	895	893	928
Share-based compensation	37,640	45,964	40,914
Deferred income taxes	43,239	(9,346)	(15,689)
Reduction in the carrying amount of right-of-use assets	2,807	2,692	7,484
Loss on disposal of fixed assets	104	—	15
Changes in operating assets and liabilities:			
Accounts receivable	—	5,159	(5,159)
Prepaid expenses and other assets	10,628	2,539	(2,537)
Deferred revenue	(9,634)	(55,107)	(29,330)
Restructuring liability	13,303	—	—
Accounts payable, accruals and other liabilities	(15,776)	(18,298)	22,855
Operating lease liabilities	(2,694)	(2,236)	(6,359)
Net cash used in operating activities	(163,580)	(150,050)	(133,906)
Investing activities			
Purchases of property and equipment	(138)	(298)	(2,810)
Proceeds from disposal of fixed assets	—	—	37
Net cash used in investing activities	(138)	(298)	(2,773)
Financing activities			
Proceeds from issuance of ordinary shares in public offering, net	—	—	20,689
Proceeds from issuance of ordinary shares in at-the market offering, net	(139)	(353)	2,894
Proceeds from issuance of ordinary shares upon exercise of stock options	—	1,907	21,520
Net cash provided by (used in) financing activities	(139)	1,554	45,103
Net decrease in cash, cash equivalents and restricted cash	(163,857)	(148,794)	(91,576)
Cash, cash equivalents and restricted cash, beginning of the year	472,248	621,042	712,618
Cash, cash equivalents and restricted cash, end of the year	$ 308,391	$ 472,248	$ 621,042
Supplemental disclosures of cash flow information			
U.S. Federal	$ 900	$ 3,110	$ 1,467
U.S. State and Local	31	62	87
Cash paid for income taxes, net	$ 931	$ 3,172	$ 1,554
Supplemental disclosures of non-cash investing and financing activities			
Acquisition of property and equipment included in accounts payable and accrued liabilities	$ —	$ 75	$ 237
Right-of-use assets obtained in exchange for lease obligations	$ 224	$ 217	$ 3,810
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

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,		
	2025	2024	2023
Cash and cash equivalents	$ 307,531	$ 471,388	$ 618,830
Restricted cash, current	—	—	1,352
Restricted cash, non-current	860	860	860
Total cash, cash equivalents and restricted cash, end of the year	$ 308,391	$ 472,248	$ 621,042

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, 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 $153 thousand	42,361	—	3,071	—	3,071
Net loss	—	—	—	(147,028)	(147,028)
Balances at December 31, 2023	**53,682,117**	**537**	**1,540,859**	**(980,031)**	**561,365**
Share-based compensation			45,964		45,964
Issuance of ordinary shares upon exercise of stock options	125,615	1	1,906		1,907
Issuance of ordinary shares upon vesting of restricted stock units	19,250	—	—		—
Net loss				(122,310)	(122,310)
Balances at December 31, 2024	**53,826,982**	**538**	**1,588,729**	**(1,102,341)**	**486,926**
Share-based compensation			37,640		37,640
Issuance of ordinary shares upon vesting of restricted stock units	6,000	—	—		—
Net loss				(244,092)	(244,092)
Balances at December 31, 2025	**53,832,982**	**$ 538**	**$ 1,626,369**	**$ (1,346,433)**	**$ 280,474**

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 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 pipeline includes both wholly-owned and partnered programs being developed for the potential treatment of diseases including Parkinson's disease, ATTR amyloidosis with cardiomyopathy, Alzheimer's disease, Amyotrophic lateral sclerosis (ALS) and a number of other neurodegenerative diseases. Prothena is developing and applying its proprietary CYTOPE® technology to target a broad spectrum of intracellular targets in the brain and periphery.

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, 2025, the Company had an accumulated deficit of $1.3 billion and cash and cash equivalents of $307.5 million.

Based on the Company's business plans, management believes that the Company's cash and cash equivalents at December 31, 2025, 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, 2025, the Company had $0.9 million of restricted cash held by a bank in certificate of deposit as collateral to a standby letter of credit under certain operating lease. 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, 2025, 2024 and 2023.

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, 2025 and 2024, 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, 2025, 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 estimates 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.

Restructuring Charges

The Company commenced a restructuring plan in June 2025. Associated restructuring charges consist of postemployment benefits related to the reduction of its workforce, contract termination costs, and other costs. Liabilities for costs associated with a restructuring activity are measured at fair value and are recognized when the liability is incurred. Postemployment benefits are recorded at the date the entity notifies the employee, unless the employee must provide future service, in which case the benefits are expensed ratably over the future service period. Liabilities for ongoing benefits are recorded when restructuring activities are probable and the benefit amounts are estimable. Costs related to contracts without future benefit or contract termination are recognized at fair value at the earlier of the contract termination or the cease-use dates. Other exit-related costs are expensed as incurred. Other costs primarily consist of legal, consulting, and other costs related to employee terminations, and are expensed when incurred. Termination benefits are calculated based on regional benefit practices and local statutory requirements.

The recognition of restructuring charges requires the Company to make certain judgments and estimates regarding the nature, timing and amount of costs associated with the restructuring plan. To the extent the Company's actual results differ from its estimates and assumptions, the Company may be required to revise the estimates of future liabilities, requiring the recognition of additional restructuring charges or the reduction of liabilities already recognized. Such changes to previously estimated amounts may be material to the consolidated financial statements. Changes in the estimates of the restructuring charges are recorded in the period the change is determined. At the end of each reporting period, the Company evaluates the remaining accrued balances to ensure that no excess accruals are retained and the utilization of the provisions are for their intended purpose in accordance with developed restructuring plans. See Note 11, "Restructuring" for additional information regarding restructuring charges.

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. In general, 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. In RSUs with front-loaded vesting, share-based compensation expense is recognized ratably based on the number of RSU shares that vest in each period. The fair value of RSUs is based on the closing market price of the Company's ordinary shares on the date of grant. 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).

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.

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. Based upon the weight of available evidence, including the outcome of the Phase 3 AFFIRM-AL clinical trial for birtamimab and the announced corporate restructuring, including a substantial workforce reduction, management believes that it is not more likely than not the Company will realize the benefits of its federal and state DTAs. Accordingly, in the year ended December 31, 2025, the Company recorded a full valuation allowance against its federal and state DTAs and continues to record a full valuation allowance against its Irish DTAs. 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 and Other Risks and Uncertainties

Financial instruments that potentially subject the Company to concentration of credit risk consist of cash and cash equivalents. 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 $328,000, $185,000 and $458,000 during the years ended December 31, 2025, 2024 and 2023,

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.

The Company's revenue during the years ended December 31, 2025, 2024 and 2023 was primarily from collaboration revenue recognized under the Company's Collaboration Agreement with BMS. The Company derived its revenue during the years ended December 31, 2025, 2024 and 2023 from foreign countries and none from Ireland.

As of December 31, 2025, and 2024, $2.1 million and $3.1 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.

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 ("CODM") 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 the 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 Sheets.

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,		
	2025	2024	2023
Birtamimab (NEOD001)	$ 53,455	$ 85,649	$ 68,831
PRX012	54,020	116,359	102,767
PRX019	8,081	5,035	7,703
Other R&D	19,296	15,476	41,270
Total R&D	$ 134,852	$ 222,519	$ 220,571

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.

There have been no other recent accounting pronouncements or changes in accounting pronouncements during fiscal 2025 that are of significance or potential significance to the Company.

Recently Adopted Accounting Pronouncement

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 Company adopted this standard on a retrospective basis for the year ended December 31, 2025 and has included these enhanced income tax disclosures in Note 10, "Income Taxes". The further disaggregation of income taxes paid are shown within the Supplemental disclosures of cash flow information under the Consolidated Statements of Cash Flows.

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 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 $275.4 million and $440.3 million in money market funds included in cash and cash equivalents at December 31, 2025, and 2024, 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,	
	2025	**2024**
Prepaid R&D expenses	$ 5,270	$ 12,029
Prepaid G&A expenses	639	830
Other	1,753	1,165
Prepaid and other current assets	$ 7,662	$ 14,024

Property and Equipment, net

Property and equipment, net consisted of the following (in thousands):

	December 31,	
	2025	2024
Machinery and equipment	$ 7,068	$ 9,137
Purchased computer software	2,128	2,252
	9,196	11,389
Less: accumulated depreciation and amortization	(7,052)	(8,308)
Property and equipment, net	$ 2,144	$ 3,081

Depreciation expense was $0.9 million, $0.9 million, and $0.9 million for the years ended December 31, 2025, 2024 and 2023, respectively.

Other Current Liabilities

Other current liabilities consisted of the following (in thousands):

	December 31,	
	2025	2024
Payroll and related expenses	$ 11,350	$ 14,468
Professional services	222	445
Other	214	930
Other current liabilities	$ 11,786	$ 15,843

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,		
	2025	2024	2023
Numerator:			
Net loss	$ (244,092)	$ (122,310)	$ (147,028)
Denominator:			
Weighted-average ordinary shares outstanding used in per share calculations	53,829	53,772	53,216
Net loss per share:			
Basic and diluted net loss per ordinary share	$ (4.53)	$ (2.27)	$ (2.76)

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, 2025, 2024 and 2023, 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,		
	2025	2024	2023
Stock options to purchase ordinary shares	10,289	11,107	9,866
Restricted Stock Units (RSU)	1,091	6	25
Total	11,380	11,113	9,891

6. Commitments and Contingencies

Lease Commitments

As of December 31, 2025, the Company currently has three leases relating to its facilities in the United States and Dublin, Ireland.

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 2025, the Company renewed both leases, each for another one year term with termination dates in July 2026.

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, 2025, the Brisbane Sublease has a remaining lease term of 2.8 years.

Total operating lease cost for the Brisbane Sublease was $3.2 million, $3.2 million and $1.3 million for the years ended December 31, 2025, 2024 and 2023, respectively. Total cash paid against the operating lease liability was $3.1 million, $2.7 million and $0.4 million for the years ended December 31, 2025, 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, 2025, 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, 2025 (in thousands):

Year Ended December 31,	Operating Leases
2026	$ 3,301
2027	3,269
2028	2,523
Thereafter	—
Total	$ 9,093
Less: Present value adjustment (imputed interest)	(720)
Total lease liability	$ 8,373
Less: Lease liability, current	(2,886)
Lease liability, non-current	$ 5,487

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, 2025, and 2024.

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, 2025, the Company had non-cancelable purchase commitments to suppliers for $3.1 million of which $2.7 million is included in current liabilities, obligations under the Company's restructuring plan of $13.3 million (of which all of it is included in current liabilities) and contractual obligations under license agreements of $50 thousand. The following is a summary of the Company's non-cancelable purchase commitments and contractual obligations as of December 31, 2025 (in thousands):

	Total	2026	2027	2028	2029	Thereafter
Purchase Obligations [1]	$ 3,077	$ 3,077	$ —	$ —	$ —	$ —
Contractual obligations under license agreements	50	35	15	—	—	—
Obligations under restructuring plan[2]	13,303	13,303	—	—	—	—
Total	$ 16,430	$ 16,415	$ 15	$ —	$ —	$ —

[1] *Purchase obligations consist of non-cancelable purchase commitments to suppliers and contract research organizations.*

[2] *Includes cash obligations under our restructuring plan. For additional information, see Note 11, "Restructuring" to the Consolidated Financial Statements.*

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 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 term of the License Agreement will continue on a Licensed Product-by-Licensed Product and country-by-country basis until the expiration of all Roche Royalty Terms with respect to all Licensed Products. 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, 2025, and December 31, 2024, 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.

Roche did not achieve any milestones under the License Agreement during the years ended December 31, 2025 and 2024, respectively.

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.

Term and Termination

The term of the Collaboration Agreement expired on May 24, 2024.

Performance Obligations

At inception of the Collaboration Agreement, there were a total of six options, including US Rights and Global Rights to acquire an exclusive license to develop, manufacture and commercialize antibodies targeting the applicable Collaboration Target in the U.S. (each, a "US License") or globally (each, 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, 2025 of $2.7 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.

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. 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 in such country of sale, (ii) expiration of any regulatory exclusivity for the Collaboration Product in such country of sale, and (iii) an agreed period of time after the first commercial sale of the Collaboration Product in such country of sale (the "Royalty Term"). The term of the Tau Global License Agreement will continue on a Licensed Product-by-Licensed Product and country-by-country basis until the expiration of all Royalty Terms with respect to all Licensed Products.

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. BMS will continue to pay royalties on a Collaboration Product-by-Collaboration Product and country-by-country basis until the end of the Royalty Term. The term of the PRX019 Global License Agreement will continue on a Licensed Product-by-Licensed Product and country-by-country basis until the expiration of all Royalty Terms with respect to all Licensed Products.

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

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.

Revenue and Expense Recognition

Collaboration revenue from BMS was $9.6 million, $135.1 million and $91.3 million for the year ended December 31, 2025, 2024 and 2023, respectively. For the year ended December 31, 2025, collaboration revenue was related to the Company's partial performance of its PRX019 Phase 1 Clinical Trial Obligation.

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.

As of December 31, 2025, the aggregate amount of the transaction price allocated to the performance obligations that are unsatisfied was $2.7 million. The Company had nil and nil accounts receivable from BMS at December 31, 2025, and December 31, 2024, respectively.

Deferred Revenue

The deferred revenue balance at the beginning of the fiscal year was $12.3 million. During the year ended December 31, 2025, $9.6 million of deferred revenue was recognized as collaboration revenue related to the PRX019 Phase 1 Clinical Trial Obligation performed. As of December 31, 2025, the total deferred revenue balance of $2.7 million classified as current deferred revenue, relates to outstanding performance obligations related to the PRX019 Phase 1 Clinical Trial Obligation. The deferred revenue balance will be recognized as the remaining services are performed.

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.

BMS did not achieve any milestones under either the Tau Global License Agreement or the PRX019 Global License Agreement during the years ended December 31, 2025, 2024 and 2023, 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.

Contingent Consideration/Milestone Accounting

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. Novo Nordisk did not achieve any milestones under the share purchase agreement during the years ended December 31, 2025, 2024 and 2023, respectively.

Revenue Recognition

No revenue was recognized related to the transaction during the years ended December 31, 2025, 2024 and 2023, respectively. There are no remaining performance obligations under this agreement. The Company had no accounts receivable from Novo Nordisk as of December 31, 2025, and 2024, respectively.

8. Shareholders' Equity

Ordinary Shares

As of December 31, 2025, the Company had 100,000,000 ordinary shares authorized for issuance with a par value of $0.01 per ordinary share and 53,832,982 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, 2025, 16,780,773 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, 2025, 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, 2025. 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 year ended December 31, 2023, the Company sold and issued 42,361 ordinary shares pursuant to the December 2021 Distribution Agreement under the December 2021 Prospectus, with total gross proceeds of approximately $3.2 million, before deducting underwriting discounts, commissions, and other offering expenses paid by the Company of $0.1 million.

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, 2025 and 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 2025, 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, 2025, the number of ordinary shares authorized under the 2018 LTIP was 18,620,433. Upon adoption of the 2018 LTIP, no new awards are permitted under the 2012 LTIP.

As of December 31, 2025, the number of ordinary shares authorized under the 2020 EIIP was 1,485,000 and 666,163 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 RSU awards generally vest over either two or three years. As of December 31, 2025, 5,400,701 ordinary shares remained available for grant under the Company's equity incentive plans.

Share-based Compensation Expense

Share-based compensation expense recorded in these Consolidated Financial Statements was based on awards granted under the 2012 LTIP, the 2018 LTIP, and the 2020 EIIP. The estimated forfeiture rate as of December 31, 2025 was 11%. 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, 2025, is $33.0 million. The weighted-average period over which this unearned share-based compensation is expected to be recognized is 2.51 years.

The following table summarizes share-based compensation expense for the periods presented (in thousands):

	Year Ended December 31,		
	2025	2024	2023
Research and development	$ 14,065	$ 20,931	$ 19,211
General and administrative	21,494	25,033	21,703
Restructuring costs [1]	2,081	—	—
Total share-based compensation expense	$ 37,640	$ 45,964	$ 40,914

[1] *Restructuring costs for the year ended December 31, 2025 includes $2.1 million of share-based compensation expense related to the contractual acceleration of vesting of certain option awards granted to executive officers.*

The Company recognized no tax benefits for the year ended December 31, 2025 due to the Company's full valuation allowance on its deferred tax assets. The Company recognized tax benefits from share-based awards of $8.3 million and $7.2 million for the years ended December 31, 2024 and 2023, respectively.

The fair value of the options granted to employees and non-employee directors during the years ended December 31, 2025, 2024 and 2023 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,								
	2025			2024			2023		
Expected volatility	76.5%	-	79.0%	74.5%	-	78.6%	76.4%	-	90.1%
Risk-free interest rate	3.8%	-	4.4%	3.5%	-	4.7%	3.5%	-	4.8%
Expected dividend yield		—%			—%			—%	
Expected term (in years)	4.8	-	5.8	4.6	-	5.7	4.4	-	5.4
Weighted average grant date fair value		$9.49			$18.69			$37.32	

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, 2025:

	Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2024	11,107,373	$ 28.70	6.16	$ 3,401
Granted	2,086,686	14.26		
Exercised	—	—		
Forfeited	(1,409,899)	28.69		
Expired	(1,494,866)	39.64		
Outstanding at December 31, 2025	10,289,294	$ 24.18	5.03	$ 402
Vested and expected to vest at December 31, 2025	9,995,785	$ 24.26	4.92	$ 385
Exercisable at December 31, 2025	7,838,889	$ 24.56	3.95	$ 22

The total intrinsic value of options exercised was nil, $1.3 million, and $52.1 million during the years ended December 31, 2025, 2024 and 2023, 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, 2025:

	Number of Units	Weighted Average Grant-Date Fair Value	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Unvested at December 31, 2024	6,000	$ 51.80	0.71	$ 83
Units Granted	1,298,136	8.65		
Units Vested	(6,000)	51.80		
Units Forfeited	(207,358)	14.04		
Unvested at December 31, 2025	1,090,778	$ 7.63	1.08	$ 10,417
Unvested and expected to vest at December 31, 2025	964,269	$ 7.61	1.03	$ 9,209

As of December 31, 2025, total compensation cost not yet recognized related to unvested RSUs was $6.2 million, which is expected to be recognized over a weighted-average period of 2.53 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,		
	2025	2024	2023
Ireland	$ (191,818)	$ (129,602)	$ (153,920)
U.S.	(9,011)	672	(6,560)
Loss before provision for income taxes	$ (200,829)	$ (128,930)	$ (160,480)

Components of the provision for income taxes for each of the fiscal periods presented consisted of the following (in thousands):

	Year Ended December 31,		
	2025	2024	2023
Current:			
U.S. Federal	$ 9	$ 2,676	$ 2,200
U.S. State	15	50	37
Ireland	—	—	—
Total current provision for income taxes	$ 24	$ 2,726	$ 2,237
Deferred:			
U.S. Federal	$ 43,047	$ (9,298)	$ (15,647)
U.S. State	192	(48)	(42)
Ireland	—	—	—
Total deferred provision for (benefit from) income taxes	$ 43,239	$ (9,346)	$ (15,689)
Provision for (benefit from) income taxes	$ 43,263	$ (6,620)	$ (13,452)

The Company recorded a net tax shortfall (windfall) from stock option exercises of nil, $1.0 million, and $(3.5) million for the years ended December 31, 2025, 2024 and 2023 respectively, all of which were recorded as part of its income tax provision in the Consolidated Statements of Operations.

The Company is domiciled in Ireland. The provision for income taxes differs from the statutory tax rate of 12.5% applicable to Ireland primarily due to Irish and U.S. net operating losses for which a tax provision benefit is not recognized, U.S. income taxed at different rates, and the recognition of a full valuation allowance against deferred tax assets. Following is a reconciliation between income taxes computed at the Irish statutory tax rate and the provision for (benefit from) income taxes for each of the fiscal periods presented (in thousands):

	Year Ended December 31,					
	2025		2024		2023	
	Amount	Percent	Amount	Percent	Amount	Percent
Taxes at the Irish Statutory Rate	$ (25,104)	12.50 %	$ (16,116)	12.50 %	$ (20,060)	12.50 %
Nontaxable or Nondeductible Items:						
Share-Based Payments	791	(0.39)%	1,404	(1.09)%	1,441	(0.90)%
Income not subject to tax	—	— %	(2,560)	1.99 %	—	— %
Other	277	(0.14)%	432	(0.34)%	—	— %
Other						
Income tax at rates other than applicable statutory rate	(952)	0.47 %	1,105	(0.86)%	474	(0.30)%
Changes in Valuation Allowance	23,861	(11.88)%	15,819	(12.27)%	17,325	(10.80)%
Foreign Tax Effects:						
United States						
Share-Based Payments	11,311	(5.63)%	5,687	(4.41)%	(743)	0.46 %
Cross-Border Tax Laws	—	— %	(4,790)	3.72 %	(4,738)	2.95 %
Research and Development Credit	(1,638)	0.82 %	(5,780)	4.48 %	(4,802)	2.99 %
Changes in Valuation Allowance	35,641	(17.75)%	(1,928)	1.50 %	(1,410)	0.88 %
Other	(924)	0.46 %	107	(0.08)%	(939)	0.59 %
Provision for (benefit from) income taxes	$ 43,263	(21.54)%	$ (6,620)	5.14 %	$ (13,452)	8.37 %

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, 2025, and 2024 are as follows (in thousands):

	December 31,	
	2025	2024
Deferred tax assets:		
Net operating loss carryforwards	$ 203,434	$ 171,191
Tax credits	25,870	23,968
Lease liabilities	2,051	2,424
Accruals and other	1,974	1,521
Capitalized R&D	27,472	33,951
Share-based compensation	7,956	11,810
Gross deferred tax assets	268,757	244,865
Valuation allowance	(266,576)	(198,869)
Net deferred tax assets	2,181	45,996
Deferred tax liability:		
Operating lease right-of-use assets	(1,989)	(2,393)
Fixed Assets	(192)	(364)
Net deferred tax assets	$ —	$ 43,239

The Company's deferred tax assets ("DTAs") are composed primarily of its Irish subsidiaries' net operating loss carryforwards, federal net operating loss carryforwards and California net operating loss carryforwards available to reduce future taxable income of the Company's U.S. subsidiaries, federal and California tax credit carryforwards, capitalized R&D, share-based compensation, and other temporary differences.

As of each reporting date, the Company considers new evidence that could affect the future realization of DTAs by jurisdiction. Valuation allowances are established if there is uncertainty that a portion or all of the DTAs will not be realized. The ultimate realization of a DTA is dependent upon the generation of future taxable income of the proper character in appropriate jurisdictions to obtain benefit from the reversal of temporary differences and net operating loss carryforwards.

Management performs an assessment of its DTA each period. Based upon the weight of available evidence, including the outcome of the Phase 3 AFFIRM-AL clinical trial for birtamimab and the announced corporate restructuring, including a substantial workforce reduction, management believes that it is not more likely than not the Company will realize the benefits of its federal DTAs. Accordingly, the Company recorded an expense to establish a valuation allowance of $43.2 million in the year ended December 31, 2025. The Company had a full valuation allowance against its federal, state and Irish DTAs as of December 31, 2025.

For the year ended December 31, 2025, the Company recorded a decrease in DTA of $43.2 million, primarily due to the recognition of full valuation allowance. 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.

As of December 31, 2025, certain of the Company's Irish entities had trading loss carryovers of $1.4 billion and non-trading loss carryovers of $25.7 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 profits in the company in which they arise. In addition, as of December 31, 2025, the Company had federal and state net operating loss carryforwards of approximately $14.1 million and $211.0 million, respectively, which are available to reduce future taxable income, if any, for the Company's U.S. subsidiary. The federal net operating loss has an indefinite carryforward period but is limited to offset 80% of taxable income in the year utilized. 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 $19.8 million and $22.0 million, respectively, at December 31, 2025. 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.

The Company's U.S. subsidiaries' cash balances at December 31, 2025, 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, 2025 is not practicable because of the complexity and variety of assumptions necessary to compute the tax.

On July 4, 2025, the U.S. enacted tax reform legislation through the One Big Beautiful Bill Act. As a result of the enactment of the legislation, the Company recorded $0.4 million of tax benefit for year ended December 31, 2025, primarily related to changes in the capitalization requirements of U.S. research and development activities.

A reconciliation of the beginning and ending amounts of unrecognized tax benefits is as follows (in thousands):

	2025	2024
Gross Unrecognized Tax Benefits at January 1	$ 15,427	$ 13,354
Additions for tax positions taken in the current year	1,101	2,201
Reductions for tax positions taken in the prior year	(619)	(128)
Gross Unrecognized Tax Benefits at December 31	$ 15,909	$ 15,427

If recognized, none of the Company's unrecognized tax benefits as of December 31, 2025, would reduce its annual effective tax rate, primarily due to corresponding adjustments to its deferred tax valuation allowance. As of December 31, 2025, the Company has not recorded a liability for potential interest or penalties.

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 IRS concluded its examination of the Company's U.S. subsidiaries for tax year 2021, with no adjustments arising. There were no other ongoing income tax audits as of December 31, 2025. 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, 2025, the Company's assessment did not result in a material change in unrecognized tax benefits. The tax years 2013 to 2025 remain subject to examination by the U.S taxing authorities and the tax years 2020 to 2025 remain subject to examination by the Irish taxing authorities as of December 31, 2025.

11. Restructuring

In June 2025, the Company commenced a restructuring plan following the Company's May 23, 2025 announcement of its decision to discontinue further development of birtamimab.

The Company incurred aggregate restructuring charges of approximately $30.1 million for the year ended December 31, 2025. Restructuring charges primarily consisted of employee termination benefits in connection with the reduction in force announced in June 2025 and contract termination costs primarily associated with exit fees relating to third-party manufacturers that were contracted for commercial supplies of birtamimab. Employee termination benefits include severance costs, employee-related benefits, and non-cash share-based compensation expense related to the acceleration of the vesting of certain stock options. Charges and other costs related to the restructuring plan are presented as restructuring costs in the Consolidated Statements of Operations. The vast majority of the termination benefits were paid out during the year ended December 31, 2025. The Company may also incur additional costs not currently contemplated due to events that may occur as a result of, or that are associated with, the restructuring plan.

The following table summarizes the restructuring liability and utilization by cost type associated with the restructuring activities during the year ended December 31, 2025 (in thousands):

	Restructuring Liability			
	Termination Benefits	Contract Termination Costs	Other	Total
Balance at December 31, 2024	$ —	$ —	$ —	$ —
Restructuring Charges	17,281	12,291	508	30,080
Adjustment for non-cash charges	(2,081)	(37)	(499)	(2,617)
Reduction for cash payments	(14,108)	(38)	(9)	(14,155)
Foreign Exchange	(1)	(4)	—	(5)
Balance at December 31, 2025	$ 1,091	$ 12,212	$ —	$ 13,303

The total amount expected to be incurred at inception in connection with the restructuring plan was $32.6 million. The cumulative amount incurred to date was $30.1 million as of December 31, 2025. The restructuring liability is included in current liabilities on the Consolidated Balance Sheets as of December 31, 2025.

12. 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 $1.4 million, $1.9 million and $1.7 million for the years ended December 31, 2025, 2024 and 2023, 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 $167,000, $181,000, and $152,000 in the years ended December 31, 2025, 2024 and 2023, 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, 2025, 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, 2025, 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, 2025, our internal control over financial reporting was effective. The effectiveness of our internal control over financial reporting as of December 31, 2025, 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, 2025, 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

During the quarter ended December 31, 2025, no director or officer (as defined in Rule 16a-1(f) under the Exchange Act) of the Company adopted or terminated any Rule 10b5-1 trading arrangements or non-Rule 10b5-1 trading arrangements (in each case, as defined in Item 408(a) of Regulation S-K).

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 14, 2026 (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	57	President and Chief Executive Officer, Director	2016
Michael J. Malecek	60	Chief Legal Officer and Company Secretary	2019
Tran B. Nguyen	52	Chief Financial Officer	2013
		Chief Strategy Officer	2021
Brandon S. Smith	51	Chief Operating Officer	2021
Chad J. Swanson	54	Chief Development Officer	2024
Karin L. Walker	62	Chief Accounting Officer	2013
Wagner M. Zago	53	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.

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 was filed as Exhibit 19.1 to our Annual Report on Form 10-K for the year ended 2024. From time to time, Prothena may engage in transactions in Prothena's securities. It is our policy to comply with all applicable federal and state securities laws or stock exchange listing standards when engaging in transactions in Prothena's securities.

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(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	
10.2(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	
10.2(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	
10.3(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)	

Exhibit No.	Description	Previously Filed				Filed Herewith
		Form	File No.	Filing Date	Exhibit	
10.3(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)	
10.4(a)+	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	
10.4(b)+	Amendment Number One to Global License Agreement, dated as of October 15, 2025, by and between Prothena Biosciences Limited and Celgene Switzerland LLC					X
10.5+	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	
10.6+	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	
10.7(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)	
10.7(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)	
10.8#	Prothena Corporation plc Amended and Restated 2012 Long Term Incentive Plan	8-K	001-35676	5/23/2017	10.1	
10.9(a)#	Prothena Corporation plc 2018 Long Term Incentive Plan	8-K	001-35676	5/18/2018	10.1	
10.9(b)#	First through Sixth Amendments to the Prothena Corporation plc 2018 Long Term Incentive Plan					X
10.10(a)#	Prothena Corporation plc 2020 Employment Inducement Incentive Plan	10-Q	001-35676	5/6/2020	10.2	
10.10(b)#	First through Fourteenth Amendments to the Prothena Corporation plc 2020 Employment Inducement Incentive Plan	10-K	001-35676	2/22/2024	10.23	
10.11#	Form of Deed of Indemnification between Prothena Corporation plc and its Directors and Officers	8-K	001-35676	12/11/2014	10.1	
10.12#	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	
10.13#	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	
10.14#	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	

Exhibit No.	Description	Previously Filed				Filed Herewith
		Form	File No.	Filing Date	Exhibit	
10.15#	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	
10.16#	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	
10.17#	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	
10.18#	Form of Restricted Share Unit Award Agreement between Prothena Corporation plc and its Named Executive Officers under the Prothena Corporation plc 2018 Long Term Incentive Plan	10-Q	001-35676	8/4/2025	10.2	
10.19#	Employment Agreement, dated September 30, 2016, between Prothena Biosciences Inc and Gene G. Kinney	8-K	001-35676	11/4/2016	10.1	
10.20#	Form of Employment Agreement between Prothena Biosciences Inc and its Named Executive Officers (other than CEO)	8-K	001-35676	7/30/2025	10.1	
19.1	Prothena Corporation plc Insider Trading Compliance Policy	10-K	001-35676	2/27/2025	19.1	
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

Exhibit No.	Description	Previously Filed				Filed Herewith
		Form	File No.	Filing Date	Exhibit	
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, 2026

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, 2026
/s/ Tran B. Nguyen Tran B. Nguyen	Chief Strategy Officer and Chief Financial Officer (Principal Financial Officer)	February 27, 2026
/s/ Karin L. Walker Karin L. Walker	Chief Accounting Officer (Principal Accounting Officer)	February 27, 2026
/s/ Daniel G. Welch Daniel G. Welch	Chair of the Board	February 27, 2026
/s/ Richard T. Collier Richard T. Collier	Director	February 27, 2026
/s/ Shane M. Cooke Shane M. Cooke	Director	February 27, 2026
/s/ William H. Dunn, Jr. William H. Dunn, Jr., M.D.	Director	February 27, 2026
/s/ Lars G. Ekman Lars G. Ekman, M.D., Ph.D.	Director	February 27, 2026
/s/ Helen S. Kim Helen S. Kim	Director	February 27, 2026
/s/ Dennis J. Selkoe Dennis J. Selkoe, M.D.	Director	February 27, 2026