

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, 2022

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
(State or other jurisdiction of
incorporation or organization)

98-1111119
(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:

<u>Title of Each Class</u>	<u>Trading Symbol</u>	<u>Name of Each Exchange on Which Registered</u>
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

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, 2022, 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 \$955.8 million, based on the last reported sale of the registrant's ordinary shares on the Nasdaq Global Market on such date.

52,564,434 of the Registrant's ordinary shares, par value \$0.01 per share, were outstanding as of February 17, 2023.

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 16, 2023, 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, 2022.

PROTHENA CORPORATION PLC
Annual Report on Form 10-K
For the Year Ended December 31, 2022

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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 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; plans for future clinical studies of our drug candidates; our potential to advance, initiate, and complete investigational new drug (“IND”) enabling studies for our discovery and preclinical programs; 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 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 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 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 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;
 - government regulation of our industry;
 - the volatility of the market price of our ordinary shares;
 - the outbreak of the novel strain of coronavirus SARS-CoV-2 and the emergence of variant strains;
 - the Russian invasion of Ukraine; and
 - business disruptions.
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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 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.
 - The COVID-19 pandemic has adversely affected our business and could have a material adverse effect on our liquidity, results of operations, financial condition, or business, including our nonclinical and clinical development programs.
 - 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.
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PART I

ITEM 1. BUSINESS

Overview

Prothena is a late-stage clinical biotechnology company with expertise in protein dysregulation and a pipeline of investigational therapeutics with the potential to change the course of devastating neurodegenerative and rare peripheral amyloid diseases.

Fueled by our deep scientific expertise built over decades of research, we are advancing a pipeline of therapeutic candidates for a number of indications and novel targets for which our ability to integrate scientific insights around neurological dysfunction and the biology of misfolded proteins can be leveraged. Our wholly-owned programs include birtamimab for the potential treatment of AL amyloidosis and a portfolio of programs for the potential treatment of Alzheimer's disease including PRX012, which targets Amyloid beta ($A\beta$), and PRX123, a novel dual $A\beta$ -tau vaccine. Our partnered programs include prasinezumab, in collaboration with Roche for the potential treatment of Parkinson's disease and other related synucleinopathies, and programs that target tau (PRX005), TDP-43, and an undisclosed target (PRX019) in collaboration with Bristol Myers Squibb (BMS) for the potential treatment of Alzheimer's disease, amyotrophic lateral sclerosis (ALS), and other neurodegenerative diseases. We are also entitled to certain potential milestone payments pursuant to our share purchase agreement with Novo Nordisk pertaining to our ATTR amyloidosis business (NNC6019, formerly PRX004).

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

Our Strategy

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

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

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

Our plan is to become a fully integrated research, development, and commercial biotechnology company. Three late-stage programs in our pipeline are ongoing, including AFFIRM-AL, a registration-enabling Phase 3 study of birtamimab in Mayo Stage IV patients with AL amyloidosis being conducted under a Special Protocol Assessment (SPA) agreement with FDA with significance level of $p \leq 0.10$, a Phase 2b PADOVA study of prasinezumab in patients with early Parkinson's disease being conducted by Roche, and a Phase 2 study of NNC6019 (formerly PRX004) in patients with ATTR cardiomyopathy being conducted by Novo Nordisk. In addition, we are advancing a robust portfolio of Alzheimer's disease programs designed to target the underlying disease pathology. These programs include PRX012, an anti- $A\beta$ antibody designed to be best-in-class and dosed subcutaneously; PRX005, an investigational antibody that specifically targets a key epitope within the microtubule binding region (MTBR) of tau, and a potential best-in-class treatment, which is partnered with BMS; and PRX123, a dual $A\beta$ -tau vaccine for the treatment and prevention of Alzheimer's disease.

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 A β plays in Alzheimer's disease pathology and discovering the biological cause of amyloid related imaging abnormalities ("ARIA"). These findings led to the development of a drug discovery and development organization that generated first-in-class clinical candidates in Alzheimer's disease, Parkinson's disease, and AL and ATTR amyloidosis.

Key elements of our biology-directed discovery engine include:

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

Once we formulate a novel hypothesis or approach, we determine how to optimally intervene against a known target. We employ a combination of our understanding of normal protein structure, computational antibody design technologies, and an empirical and unbiased screening process to determine the optimal epitope to target on a pathogenic protein. Through our detailed screening process, we attempted 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 A β , tau, alpha-synuclein, light chain, and transthyretin to relevantly influence biology and achieve clinical benefit across a number of indications.

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

Today, one of the elements that distinguishes Prothena is that our pipeline has matured beyond demonstrating target engagement via downstream biomarkers. Instead, our internally discovered pipeline has generated multiple proof points that our molecules have successfully influenced biology in a manner that translates into clinical benefit. We've most recently demonstrated this in AL amyloidosis, ATTR amyloidosis, and Parkinson's disease where preclinical findings in our programs have translated to positive clinical data.

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

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

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

AL amyloidosis and ATTR amyloidosis are diseases caused by misfolded, pathogenic forms of light chain (AL) or transthyretin (ATTR) protein that deposit as amyloid in vital organs such as the heart. Current therapeutic approaches seek to reduce the production of new pathogenic AL or ATTR protein in order to slow the formation of new amyloid deposits. However, simply reducing new pathogenic protein production may not be adequate for patients who are at high risk of early mortality due to the substantial existing amyloid deposition in their vital organs. The therapeutic approaches we are developing with birtamimab for AL amyloidosis and NNC6019 (formerly PRX004) for ATTR amyloidosis, are investigational monoclonal antibodies designed to clear the pathogenic amyloid deposits. Birtamimab and NNC6019 are designed to target and clear amyloid deposited in organs in order to improve organ function. Current therapies do not adequately address the needs of patients with AL and ATTR amyloidosis who have advanced stages of cardiac disease due to amyloid deposition. Improving survival for these patients is an area of urgent need which directly aligns with birtamimab and NNC6019's differentiated deleter mechanism that targets the amyloid that causes organ dysfunction and failure and puts patients at risk for early mortality.

Moving forward, we intend to advance new discovery-stage therapeutics for other diseases of protein dysregulation with unmet medical needs. Our discovery effort targeting TDP-43 for the potential treatment of amyotrophic lateral sclerosis (ALS) is an example of this.

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

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

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

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

We rely on, and will expand as appropriate, strong internal talent with expertise in our core areas of focus. We also rely on external resources, as needed, to execute efficiently on our clinical development and other business objectives. We engage and collaborate with consultants and advisors with certain scientific, clinical or other functional and/or disease area expertise to help us execute specific activities related to our programs. This may include activities such as testing and characterizing our potential therapeutic candidates and gaining feedback and guidance on our programs through advisory boards.

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

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

Our Research and Development Pipeline

Our clinical research and development pipeline includes five therapeutic antibody programs in clinical development: birtamimab for the potential treatment of AL amyloidosis; prasinezumab, in collaboration with Roche, for the potential treatment of Parkinson’s disease and other related synucleinopathies; NNC6019, which is being developed by Novo Nordisk, for the potential treatment of ATTR amyloidosis; PRX012 for the potential treatment of Alzheimer’s disease; and PRX005, in collaboration with BMS, for the potential treatment of Alzheimer’s disease.

In addition to our clinical development pipeline, we have a number of discovery- and late-preclinical-stage programs targeting proteins implicated in neurological diseases including A β and tau for the potential treatment and prevention of Alzheimer’s disease and other neurodegenerative disorders, and TDP-43 for the potential treatment of amyotrophic lateral sclerosis. TDP-43 and a third undisclosed neurodegenerative target are the focus of our collaboration with BMS. We have also prioritized and selected the lead candidate for our Alzheimer’s disease vaccine program, PRX123.

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:

PROGRAM/ INDICATION	PROTEIN TARGET	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	COMMERCIAL RIGHTS
Birtamimab AL amyloidosis	Kappa & Lambda Light Chain	AFFIRM-AL (Phase 3 study, under SPA ¹ agreement with FDA)					prothena
Prasinezumab Parkinson’s disease	α -Synuclein (C-terminus)	PASADENA (Phase 2 study) PADOVA (Phase 2b study)					prothena Roche
NNC6019 (PRX004) ATTR amyloidosis	Transthyretin (misTTR)	Phase 2 study ongoing					Novo Nordisk
PRX005 Alzheimer’s disease	Tau (MTBR)	Phase 1 study ongoing					Bristol Myers Squibb
PRX012 Alzheimer’s disease	A β (N-terminus)	Phase 1 study ongoing					prothena
PRX123 Alzheimer’s disease	A β + Tau	Lead prioritized					prothena
PRX019 Neurodegeneration	Undisclosed Target	Lead prioritized					Bristol Myers Squibb
TDP-43 ALS	TDP-43						Bristol Myers Squibb
Undisclosed AD In Down syndrome	Undisclosed Target						prothena

References: mAb Small Molecule Vaccine Undisclosed

¹ Primary endpoint of all-cause mortality at p \leq 0.10 under the Special Protocol Assessment (SPA) agreement with FDA; A β , A β ; AD, Alzheimer’s disease; ALS, amyotrophic lateral sclerosis; mAb, monoclonal antibody

Birtamimab for the Potential Treatment of AL Amyloidosis

About Birtamimab and AL Amyloidosis

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

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

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

Clinical Development Program for Birtamimab

Early Development

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

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

On December 12, 2022, we presented in an oral presentation at the 64th American Society of Hematology Annual Meeting and Exposition in New Orleans, Louisiana, data from the completed VITAL study demonstrating that in a post hoc analysis of patients with Mayo Stage IV AL amyloidosis, a statistically significant survival benefit was observed through 9-months for those treated with birtamimab. The survival benefit of birtamimab in VITAL remained consistent when adjusted for key baseline variables in patients with Mayo Stage IV AL amyloidosis.

Confirmatory Phase 3 AFFIRM-AL Study Design under SPA Agreement with the FDA

Based on further analyses of data from the VITAL study and multiple in-depth discussions with the FDA, Prothena announced plans on February 1, 2021, to advance birtamimab into the confirmatory Phase 3 AFFIRM-AL study in patients with Mayo Stage IV AL amyloidosis. AFFIRM-AL is a registration-enabling Phase 3 study that is being conducted with a primary endpoint of all-cause mortality at $p < 0.10$ under a Special Protocol Assessment (SPA) agreement with the FDA. Topline data from AFFIRM-AL is expected in 2024.

AFFIRM-AL is an ongoing global, multi-center, double-blind, placebo-controlled, 2:1 randomized, time-to-event study expected to enroll approximately 150 newly diagnosed, treatment naïve patients with AL amyloidosis categorized as Mayo Stage IV. It has been designed to evaluate the primary endpoint of all-cause mortality with a significance level of $p \leq 0.10$.

Secondary endpoints will assess change from baseline to month 9 in quality of life as measured by SF-36v2 PCS and functional capacity as measured by 6MWT distance.

An interim analysis will be conducted when approximately 50% of the events have occurred, allowing the independent data monitoring committee to recommend either continuing the study or stopping early for overwhelming efficacy. Patients will receive 24 mg/kg of birtamimab or placebo by intravenous infusion every 28 days, with all patients receiving concurrent standard of care therapy consisting of a first line bortezomib-containing regimen.

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

Prior to initiating clinical trials, we tested the efficacy of prasinezumab in various cellular and animal models of α -synuclein-related disease. In transgenic mouse models of Parkinson's disease, passive immunization with 9E4, the murine version of prasinezumab, reduced the appearance of α -synuclein pathology, protected synapses and improved performance by the mice in behavioral testing.

Phase 2b PADOVA Study

A Phase 2b study (PADOVA) to further assess the efficacy of prasinezumab in an expanded patient population is being conducted by Roche. PADOVA is a Phase 2b, randomized, double-blind, placebo-controlled, multicenter study to evaluate the efficacy and safety of prasinezumab in patients with early Parkinson's disease who are on stable symptomatic (levodopa) medication. The study intends to enroll 575 patients randomized to receive either prasinezumab or placebo via intravenous infusion every 4 weeks. The primary endpoint is time to meaningful progression on motor signs of the disease, as assessed by ≥ 5 point increase in Movement Disorder Society – Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III score from baseline. Topline data from PADOVA is expected in 2024.

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 study 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.

Phase 2 PASADENA Study

The results from the Phase 1 study further supported advancing prasinezumab into the Phase 2 PASADENA Study. PASADENA is a two-part Phase 2 clinical study in early Parkinson's disease patients that is being conducted by Roche. Part 1 was a randomized, double-blind, placebo-controlled, three-arm study 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 study must not have been on dopaminergic therapy and were not expected to require dopaminergic therapy for at least 52 weeks. Part 2 of the study was a 52-week blinded extension phase in which patients from the placebo arm of the study 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 study were presented in a Top Abstract oral presentation at the International Parkinson and Movement Disorder Society's MDS Virtual Conference 2020. While the study 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 the PASADENA study, 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 study 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 study 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.

In October 2020, we announced that Roche and Prothena will advance prasinezumab into a late-stage Phase 2b study in patients with early Parkinson's disease. The study is designed to further assess the efficacy of prasinezumab by expanding upon the patient population enrolled in PASADENA to include patients with early Parkinson's disease on stable levodopa therapy.

Prasinezumab is the first potentially disease-modifying, anti-alpha-synuclein antibody to demonstrate signals of efficacy on multiple pre-specified secondary and exploratory clinical endpoints in patients with early Parkinson's disease and advance into late-stage development.

Phase 1 Studies

During 2014, together with Roche, we advanced prasinezumab into clinical development with the initiation of two Phase 1 studies. Results of the first study, 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 study. Results of the second study, a Phase 1b double-blind, placebo-controlled, multiple ascending dose study demonstrated an acceptable safety and tolerability profile at all dose levels tested in patients with Parkinson's disease, meeting the primary objective of the study. 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 study 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 study 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 study of prasinezumab in patients with early Parkinson's disease. The start of the Phase 2 PASADENA study 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 study of prasinezumab in patients with early Parkinson's disease. The start of the Phase 2b PADOVA study 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 million of a total \$755 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 million in 2021, Roche is also obligated to pay:

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

Roche bore 100% of the cost of conducting the research collaboration under the License Agreement during the research term, which expired December 31, 2017. In May 2021, the Company exercised its rights under the terms of License Agreement to receive potential U.S. commercial sales milestone and royalties, in lieu of a U.S. profit and loss share for prasinezumab in

Parkinson's disease. Thus in the U.S. through May 28, 2021, the parties shared all development costs, all of which were allocated 70% to Roche and 30% to the Company, for prasinezumab in the Parkinson's disease indication. If the Company opts in to participate in co-development and co-funding for any other Licensed Products and/or indications, the parties will share all development and commercialization costs, as well as profits, all of which will be allocated 70% to Roche and 30% to the Company. In addition, we have an option under the License Agreement to co-promote prasinezumab in the U.S. in the Parkinson's disease indication. If we exercise such option, we may also elect to co-promote additional licensed products in the U.S. approved for Parkinson's disease or other indications calling on the same prescriber. Outside the U.S., Roche has responsibility for developing and commercializing the licensed products.

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

NNC6019 (formerly PRX004) for the Potential Treatment of ATTR Amyloidosis

NNC6019 (formerly PRX004) 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.

NNC6019's proposed mechanism of action is to deplete both circulating non-native TTR to prevent further deposition and deposited amyloid to improve organ function. NNC6019 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 study with NNC6019 in patients with hereditary forms of ATTR amyloidosis, in which NNC6019 was demonstrated to be safe and well tolerated.

ATTR Amyloidosis Business Acquired by Novo Nordisk

On July 12, 2021, we announced that we and Novo Nordisk entered into a definitive purchase agreement under which Novo Nordisk acquired our clinical stage antibody NNC6019 (formerly PRX004) 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, including a \$40 million clinical milestone payment that we announced on November 21, 2022.

A Phase 2 study of NNC6019 in patients with ATTR cardiomyopathy is being conducted by Novo Nordisk (NCT05442047). Topline data is expected in 2024.

PRX005 for the Potential Treatment of Alzheimer's Disease

PRX005 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, PRX005 demonstrated significant reduction of intraneuronal tau pathology and progression protection against behavioral deficit in a tau transgenic mouse model and complete blockade of neuronal tau internalization in vitro.

In June 2021, we announced that BMS exercised its option under the global neuroscience research and development collaboration to enter into an exclusive U.S. license for PRX005. BMS paid Prothena \$80 million for this option following the execution of a US License Agreement for PRX005 and transfer of the underlying license.

Phase 1 Studies

In this first-in-human, randomized, placebo controlled, single ascending dose (SAD) study, healthy volunteers (n=19) were enrolled into three PRX005 dose level cohorts (low, medium or high dose) and randomized in a 3:1 drug to placebo ratio. Study participants received a single dose of PRX005 or placebo intravenously (IV) and were followed for up to two months. The results of the study found all three dose level cohorts of PRX005 to be generally safe and well tolerated, meeting the Phase 1 SAD study primary objective. None of the treatment emergent adverse events (TEAE) were serious. No clinically relevant changes were observed in other safety parameters. PRX005 also met key pharmacokinetic (PK) and immunogenicity secondary endpoints. Plasma drug concentrations of PRX005 increased in a dose-proportional manner. Furthermore, PRX005 exposure in cerebrospinal fluid (CSF) was measured in the high dose cohort and based on the robust exposure of PRX005 in the CSF (day 29 CSF:Plasma ratio=0.2%), substantial target engagement is expected in the CNS. PRX005 had a desirable immunogenicity profile with no persistent PRX005-induced antidrug antibodies (ADAs) observed. A multiple ascending dose portion of the Phase 1 study is ongoing. Topline data from the Phase 1 study is expected in 2023.

Global Neuroscience Research and Development Collaboration with Bristol Myers Squibb

This global neuroscience research and development collaboration is focused on three proteins implicated in the pathogenesis of several neurodegenerative diseases, including tau, TDP-43, and an undisclosed target. PRX005 is designed to

be a best-in-class anti-tau, MTBR-specific antibody for the potential treatment of AD and, with the initiation of the Phase 1 study, is the first program to advance to the clinic from this collaboration. After receiving the \$80 million payment described above, we have received a total of \$230 million pursuant to the collaboration and we are eligible to receive up to an additional \$160 million for U.S. rights, up to \$165 million for global rights, and up to \$1.7 billion for regulatory and commercial milestone payments for a total of up to \$2.2 billion plus potential tiered commercial sales royalties across multiple programs.

In March 2018, we entered into the Master Collaboration Agreement (the “Collaboration Agreement”) with Celgene (which was acquired by BMS in November 2019), under which Celgene (now BMS) may elect in its sole discretion to exclusively license rights to develop and commercialize antibodies targeting tau, TDP-43 and an undisclosed target. The Collaboration Agreement became effective on March 20, 2018, which triggered an upfront payment to us of \$100 million, as well as a further payment of approximately \$50 million to subscribe for 1,174,536 of the Company’s ordinary shares at a price of \$42.57 per share, pursuant to a Share Subscription Agreement (the “SSA”) as described further below.

In June 2021, we announced that BMS exercised its option under the global neuroscience research and development collaboration to enter into an exclusive U.S. license for PRX005. BMS paid Prothena \$80.0 million following the execution of a US License Agreement for PRX005 and transfer of the underlying license.

On a program-by-program basis, following Prothena’s filing of an investigational new drug application (IND) for the additional two collaboration programs, BMS may elect in its sole discretion to exercise its right to receive an exclusive license to develop and commercialize antibodies targeting the applicable Collaboration Target in the U.S. (the “US Rights”). If BMS exercises the US Rights for a collaboration program, it is obligated to pay Prothena an exercise fee of approximately \$80 million per program. Thereafter, BMS would have decision making authority over development activities, and all regulatory, manufacturing and commercialization activities, for antibody products targeting the relevant Collaboration Target (the “Collaboration Products”) in the U.S.

On a program-by-program basis, following completion of a Phase 1 clinical trial for a collaboration program for which BMS has previously exercised its US Rights, BMS may elect in its sole discretion to exercise its right with respect to such collaboration program to receive a worldwide, exclusive license to develop and commercialize antibodies targeting the applicable Collaboration Target (the “Global Rights”). If BMS exercises its Global Rights, BMS would be obligated to pay Prothena an additional exercise fee of \$55 million for such collaboration program. The Global Rights would then replace the US Rights for that collaboration program, and BMS would have decision making authority over developing, obtaining and maintaining regulatory approval for, manufacturing and commercializing the Collaboration Products worldwide.

After exercise of Global Rights for a collaboration program, Prothena is eligible to receive up to \$562.5 million in regulatory and commercial milestones per program. For obtaining either US Rights or Global Rights for such collaboration program, Prothena will also be eligible to receive tiered royalties on net sales of Collaboration Products ranging from high single digit to high teen percentages, on a weighted average basis depending on the achieving of certain net sales thresholds. Such exercise fees, milestones and royalty payments are subject to certain reductions as specified in the Collaboration Agreement, the agreement for US Rights and the agreement for Global Rights.

BMS will continue to pay royalties on a Collaboration Product-by-Collaboration Product and country-by-country basis, until the latest of (i) expiration of certain patents covering the Collaboration Product, (ii) expiration of all regulatory exclusivity for the Collaboration Product, and (iii) an agreed period of time after the first commercial sale of the Collaboration Product in the applicable country (the “Royalty Term”).

The research term under the Collaboration Agreement continues for a period of six (6) years, which BMS may extend for up to two additional 12-month periods by paying an extension fee of \$10 million per extension period. The term of Collaboration Agreement continues until the last to occur of the following: (i) expiration of the research term, (ii) expiration of all US Rights terms, and (iii) expiration of all Global Rights terms.

The term of any agreement for US Rights or Global Rights would continue on a Collaboration Product-by-Collaboration Product and country-by-country basis until the expiration of all Royalty Terms under such agreement.

The Collaboration Agreement may be terminated (i) by either party on a program-by-program basis if the other party remains in material breach of the Collaboration Agreement following a cure period to remedy the material breach, (ii) by BMS at will on a program-by-program basis or in its entirety, (iii) by either party, in its entirety, upon insolvency of the other party, or (iv) by Prothena, in its entirety, if BMS challenges a patent licensed by Prothena to BMS under the Collaboration Agreement.

Under the SSA, BMS is subject to certain transfer and standstill restrictions, including a restriction on acquiring more than 9.9% of the Company's share capital for a specified period of time following the closing of the subscription of 1,174,536 of the Company's ordinary shares (Shares), or earlier upon announcement of the intent to consummate a change of control of the Company by the Company or a third party, or expiration or termination of the Collaboration Agreement. In addition, BMS will be entitled to request the registration of the Shares on Form S-3ASR or Form S-3 following termination of the transfer restrictions if the Shares cannot be resold without restriction pursuant to Rule 144 promulgated under the Securities Act of 1933, as amended.

PRX012 for the Potential Treatment of Alzheimer's Disease

PRX012 is an investigational antibody that targets A β , 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 A β 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-A β 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 A β than aducanumab that also neutralized soluble, toxic (i.e., oligomeric) A β species. Preclinical studies also showed that our antibodies recognize A β pathology to a greater extent than aducanumab, demonstrating more extensive plaque area binding at lower antibody concentrations, which are estimated to be clinically relevant exposures in the central nervous system following systemic dosing.

We are advancing our lead candidate, PRX012, as a next-generation approach for subcutaneous administration to improve access for patients with 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 study 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. A multiple ascending dose portion of the Phase 1 study is ongoing. Topline data from the Phase 1 study is expected in 2023.

Our Discovery and Preclinical Programs

We are also advancing several discovery and preclinical-stage programs for neurological diseases with significant unmet medical needs such as Alzheimer's disease and amyotrophic lateral sclerosis (ALS). Our discovery and pre-clinical pipeline includes our proprietary dual A β -tau vaccine program, as well as two programs (TDP-43 and an undisclosed target (PRX019)) that are the focus of our collaboration with BMS.

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

PRX123, a Dual A β -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 A β and tau proteins. Preclinical models suggest that A β 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 A β 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 A β 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-A β and anti-tau antibodies to enable phagocytosis of A β and to neutralize tau. These findings provided proof of concept in multiple preclinical species. We expect to file an IND for PRX123 with the FDA in 2023.

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, record-keeping, 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. Non-compliance 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 approval until manufacturing or other alleged deficiencies are brought into compliance. The FDA and other comparable regulatory authorities also have the authority to cause the withdrawal of approval of a marketed product or to impose additional labeling or distribution restrictions.

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

Product Approval

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

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

Nonclinical tests assess the potential safety and pharmacologic effects of a product candidate in in vitro and/or in vivo studies. The results of these studies must be submitted to the FDA as part of an IND before human testing may proceed. An IND is a request for authorization from the FDA to manufacture and administer an investigational drug or biologic product to

humans. The IND includes the proposed protocol(s) and general investigational plan for human studies. The IND also includes results of nonclinical studies and other human studies, as appropriate, as well as manufacturing information, analytical data and any other available data or literature to support the use of the investigational new drug. An IND must become effective before human clinical trials may be initiated. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises full or partial concerns or questions related to initiation of the proposed clinical trial(s). In such a case, the IND may be placed on a full or partial clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial(s) may begin. Accordingly, submission of an IND may or may not result in the FDA allowing a clinical trial(s) to commence as planned.

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

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

- *Phase 1.* Phase 1 includes the initial introduction of an investigational product into humans. Phase 1 clinical trials are typically more closely monitored and may be conducted in patients with the target disease or condition or in healthy volunteers. These studies are designed to evaluate the safety, appropriate dosage, metabolism and pharmacologic actions of the investigational product in humans, the side effects associated with increasing doses, and if possible, to gain early evidence on effectiveness. During Phase 1 clinical trials, sufficient information about the investigational product's pharmacokinetics and pharmacological effects may be obtained to permit the design of well-controlled Phase 2 and Phase 3 clinical trials. The total number of participants included in Phase 1 clinical trials varies, but is generally in the range of 20 to 80;
- *Phase 2.* Phase 2 includes controlled clinical trials conducted to preliminarily or further evaluate the efficacy and safety of the investigational product for a specific indication(s) in patients with the disease or condition under study, to determine dosage(s) for further studies, and to identify possible adverse side effects and safety risks associated with the product. Phase 2 clinical trials are typically well-controlled, closely monitored, and conducted in a patient population, usually involving no more than several hundred participants; and
- *Phase 3.* Phase 3 clinical trials are generally well controlled clinical trials conducted in an expanded patient population generally at geographically dispersed clinical trial sites. They are performed after preliminary evidence suggesting effectiveness and safety of the product has been obtained, and are intended to further evaluate efficacy and safety, to establish the overall benefit-risk relationship of the investigational product, and to provide an adequate basis for product approval. Phase 3 clinical trials usually involve several hundred to several thousand participants.

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

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

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

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

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

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

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

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

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

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

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

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

European Union. In the EU, there are several pathways for marketing approval, depending on the type of product for which approval is sought. Under the centralized procedure, a sponsor submits a single application to the EMA. The marketing application is similar to the BLA submitted to 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 EU member states.

In addition to the centralized procedure, the EU also has: (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 record-keeping, reporting of adverse events, and submitting product deviation reports to notify the FDA of unanticipated changes in distributed products. Additionally, any significant change in the approved product or in how it is manufactured, including changes in formulation or the site of manufacture, generally require prior FDA approval of a supplemental BLA. The packaging and labeling of all products developed by us are also subject to FDA approval and ongoing regulation and oversight.

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

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

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

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

The U.S. Foreign Corrupt Practices Act (the “FCPA”), the Irish Criminal Justice (Corruption Offences) Act 2018 (the “Irish Corruption Act”) and the U.K. Bribery Act prohibit companies and their representatives from offering, promising, authorizing or making payments to governmental officials (and certain private individuals under the Irish Corruption Act and the U.K. Bribery Act) for the purpose of obtaining or retaining business abroad. In many countries, the healthcare professionals we interact with may meet the definition of a government official for purposes of the FCPA. Failure to comply with domestic or non-domestic laws could result in various adverse consequences, including possible delay in approval or refusal to approve a product, recalls, seizures, withdrawal of an approved product from the market, the imposition of civil or criminal sanctions and the prosecution of executives overseeing our international operations.

Orphan Drugs

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

Pharmaceutical Coverage, Pricing and Reimbursement

Sales of our products will depend, in part, on the extent to which our products will be covered by third-party payors, such as federal, state and other government health care programs, commercial insurance and managed healthcare organizations. These third-party payors are increasingly reducing reimbursements for medical products, drugs and services. In addition, the U.S. government, state legislatures and other governments have continued implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost- containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our drug candidates or a decision by a third-party payor to not cover our drug candidates could reduce physician usage of our products once approved and have a material adverse effect on our sales, results of operations and financial condition.

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. Such laws include, without limitation, anti-kickback, fraud and abuse, false claims, privacy and security and physician sunshine laws and regulations. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to operate our business and our financial results.

Intellectual Property

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

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

We own or hold exclusive licenses to a number of issued patents and pending patent applications in the U.S. and other jurisdictions, including Patent Cooperation Treaty applications. As of December 31, 2022, our patent portfolio included the following families of patents or patent applications that we own or have exclusively licensed from other parties:

- Approximately 8 patent families related to AL or AA amyloidosis, including our birtamimab program, including a composition of matter patent anticipated to expire 2029 (subject to potential adjustments in patent term as described below);
- Approximately 16 patent families related to Parkinson's disease and other synucleinopathies, including our prasinezumab program, including a composition of matter patent anticipated to expire in 2032 (subject to potential adjustments in patent term as described below);
- Approximately 10 patent families related to passive immunotherapy for Alzheimer's disease, including our PRX005 and PRX012 programs; and
- Approximately 17 patent families related to other potential targets of intervention and diseases, including PRX019, and other product candidates including vaccines.

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

The term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration of a U.S. patent as compensation for the patent term lost during diligent clinical development and the FDA regulatory review process, which together are the regulatory review period. The U.S. Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under a regulatory review period. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent can be extended for each first regulatory review period for a product. Moreover, a patent can only be extended once, and thus, if a single patent is applicable to multiple products, it can only be extended based on one product. Similar provisions are available in Europe and other jurisdictions to extend the term of a patent that covers an approved drug. When possible, depending upon the length of clinical trials and other factors involved in the filing of a BLA or NDA, we expect to apply for patent term extensions for patents covering our product candidates and their methods of use.

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

University of California License Agreement: Under a License Agreement with The Regents of the University of California, we have exclusively licensed from the University of California its joint ownership interest in certain patents jointly

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

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

Competition

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

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

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

Manufacturing

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 the ongoing Phase 2 and any subsequent clinical trials for prasinezumab. We are dependent on Roche to manufacture these clinical supplies.

NNC6019 (formerly PRX004) - Rentschler Biopharma SE ("Rentschler") manufactured clinical supplies of our drug candidate NNC6019 for our completed Phase 1 clinical trial. On July 8, 2021, we sold shares of one of our wholly-owned subsidiaries to Novo Nordisk. In connection with the transaction, Novo Nordisk acquired our ATTR amyloidosis business, including our drug candidate NNC6019. We are dependent on Novo Nordisk, and its third party manufacturers if applicable, to manufacture clinical supplies of NNC6019.

Birtamimab - BI manufactured clinical supplies of our drug candidate birtamimab for our prior Phase 1, Phase 2 (PRONTO) and Phase 3 (VITAL) clinical trials. Rentschler is our third-party manufacturer of drug substance for our Phase 3 (AFFIRM-AL) clinical trial. Such drug substance manufactured by Rentschler has been demonstrated to be comparable to the drug substance manufactured by BI. Catalent Pharma Solutions, LLC ("Catalent") is our third-party manufacturer of drug product for our Phase 3 (AFFIRM-AL) clinical trial, and this drug product has been demonstrated to be comparable to the drug

product produced by BI. We are dependent on Rentschler and Catalent to manufacture clinical supplies for our Phase 3 (AFFIRM-AL) clinical trial.

PRX005 - Catalent is our third-party manufacturer of drug substance and Berkshire Sterile Manufacturing, LLC (“Berkshire”) is our third-party manufacturer for drug product. We are dependent on Catalent and Berkshire to manufacture clinical supplies for our Phase 1 clinical trial and any subsequent clinical trials for PRX005.

PRX012 - Catalent is our third-party manufacturer of drug substance and Berkshire is our third-party manufacturer for drug product. We are dependent on Catalent and Berkshire to manufacture clinical supplies for our planned Phase 1 clinical trial and any subsequent clinical trials for PRX012.

Research and Development

Our research and development expenses totaled \$135.6 million, \$82.3 million, and \$74.9 million in 2022, 2021, and 2020, 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, 2022, we had 127 employees, including 19 holding M.D. and/or Ph.D. degrees. Of our employees, 92 were engaged in research and development activities and the remainder were working in general and administrative areas.

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

Our human capital management strategy also embraces diversity, equity, and inclusion. As of December 31, 2022, we employed approximately 63% women and 37% men, and approximately 45% of our employees are racially or ethnically diverse. Our executive team, including employees at or above the vice president level, includes approximately 45% women, and approximately 28% 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. In addition, specifically in response to the COVID-19 pandemic, we implemented masking and social distancing policies, and other safety measures at our facilities. Additionally, because we enabled 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, including with respect to policies on diversity, equity, and inclusion; workplace environment and safety; and corporate culture.

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 income (losses) of \$(116.9) million, \$67.0 million and \$(111.1) million for the years ended December 31, 2022, 2021 and 2020, respectively. As of December 31, 2022, we had an accumulated deficit of \$833.0 million. We expect to continue to incur substantial losses for the foreseeable future as we:

- support the Phase 3 AFFIRM-AL clinical trial for birtamimab, the Phase 1 clinical trial for PRX005, the Phase 1 clinical trial for PRX012, and potential additional clinical trials for these and other programs;
- develop and possibly commercialize our drug candidates, including birtamimab, prasinezumab, PRX005, PRX012, and PRX123;
- undertake nonclinical development of other drug candidates and initiate clinical trials, if supported by nonclinical data;
- pursue our early stage research and seek to identify additional drug candidates; and
- potentially acquire rights from third parties to drug candidates or technologies through licenses, acquisitions, or other means.

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

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

As of December 31, 2022, we had cash and cash equivalents of \$710.4 million. Although we believe, based on our current business plans, that our existing cash and cash equivalents will be sufficient to meet our obligations for at least the next twelve months, we anticipate that we will require additional capital in order to continue the research and development, and

eventual commercialization, of our drug candidates. Our future capital requirements will depend on many factors that are currently unknown to us, including, without limitation:

- the timing of progress, results, and costs of our clinical trials, including the Phase 3 clinical trial for birtamimab, the Phase 2 clinical trial for prasinezumab being conducted by Roche, the Phase 2b clinical trial for prasinezumab being conducted by Roche, the Phase 2 clinical trial for NNC6019 (formerly PRX004) being conducted by Novo Nordisk, the Phase 1 clinical trial for PRX005, and the Phase 1 clinical trial for PRX012;
- the timing, initiation, progress, results, and costs of these and our other research, development, and possible commercialization activities;
- the results of our research and nonclinical and clinical studies;
- 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 and the recent disruptions to, and volatility in, the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic and geopolitical turmoil, including the Russian invasion of Ukraine. 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 December 2021 Distribution Agreement (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.

The United Kingdom's withdrawal from the European Union could have a negative effect on global economic conditions and financial markets, European Union regulatory procedures and our business.

Following a national referendum and enactment of legislation by the government of the United Kingdom, the United Kingdom formally withdrew from the European Union ("EU") on January 31, 2020, commonly referred to as Brexit. The United Kingdom remained in the EU customs union and the single market for a transition period which expired on December 31, 2020. On December 24, 2020, the United Kingdom and the EU reached agreement in principle on their future trading relationship and entered into the EU-UK Trade and Cooperation Agreement which was formally ratified by the parties and as of May 1, 2021, is fully in force. However, because the agreement merely sets forth a framework in many respects and will require complex additional bilateral negotiations between the United Kingdom and the EU as both parties continue to work on the rules for implementation, significant political and economic uncertainty remains as to aspects of the future relationship between the United Kingdom and the EU. The uncertainty surrounding Brexit has had and may continue to have a material adverse effect on global economic conditions and the stability of global financial markets, and may significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. Any of these factors could depress economic activity and restrict access to capital, which could have a material adverse effect on our business, financial condition, results of operations, and/or growth prospects.

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

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

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

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

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

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

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

We may be adversely affected by earthquakes, natural disasters, and adverse weather events, including as a result of climate change.

Our key facility and most 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 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, such adverse weather event, natural disaster or similar occurrence could have an adverse effect on our business, financial condition, or results of operations.

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

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

We and our partners may be subject to 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, 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. For example, the California Consumer Privacy Act (the “CCPA”) went into effect January 1, 2020. The CCPA, among other things, imposes new data privacy obligations on covered companies and provides expanded privacy rights to California residents, including the right to access, delete, and opt out of certain disclosures of their information. The CCPA provides for civil penalties for violations, as well as a private right of action with statutory damages for certain data breaches, which may increase the frequency and likelihood of data breach litigation. Although the law includes limited exceptions for health-related information, including clinical trial data, such exceptions may not apply to all of our operations and processing activities. Further, the California Privacy Rights Act (the “CPRA”) recently passed in California. The CPRA will impose additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. In addition, the CCPA has prompted a number of proposals for new federal and state privacy legislation that, if passed, could increase our potential liability, increase our compliance costs and adversely affect our business. If we fail to comply with applicable laws and regulations we could be subject to penalties or sanctions, including criminal penalties if we knowingly obtain or disclose individually identifiable health information from a covered entity in a manner that is not authorized or permitted by HIPAA or applicable state laws.

We are also or may become subject to rapidly evolving data protection laws, rules, and regulations in foreign jurisdictions. For example, the European Union 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 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) obligations to consider data protection as 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 the supervisory authority without undue delay (and no later than 72 hours where feasible). In addition, the EU GDPR prohibits the transfer of personal data from the European Economic Area (“EEA”) to the United States and other jurisdictions that the European Commission does not recognize as having “adequate” data protection laws unless a data transfer mechanism has been put in place. In July 2020, the Court of Justice of the European Union limited how organizations could lawfully transfer personal data from the EEA to the United States by invalidating the EU-US Privacy Shield for purposes of international transfers and imposing further restrictions on the use of standard contractual clauses (“SCCs”) including, a requirement for companies to carry out a transfer privacy impact assessment, 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 SCCs will need to be implemented to ensure an essentially equivalent level of data protection to that afforded in the EEA. The EU GDPR imposes substantial fines for breaches and violations (up to the greater of €20 million or 4% of our annual global revenue). The EU GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the EU GDPR. Relatedly, following the United Kingdom’s withdrawal from the EU (i.e., Brexit), and the expiry of the Brexit transition period, which ended on December 31, 2020, the EU GDPR has been implemented in the United Kingdom (as the “UK GDPR”). 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 who process personal data in relation to the offering of goods or services to individuals in the UK, or to monitor 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 global turnover. The above-described changes lead to additional costs and increase our overall risk exposure.

Compliance with U.S. and foreign data privacy and security laws, rules, and regulations could require us 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.

The COVID-19 pandemic has adversely affected our business and could have a material adverse effect on our liquidity, results of operations, financial condition or business, including our nonclinical and clinical development programs.

The outbreak of the novel strain of coronavirus SARS-CoV-2, which causes coronavirus disease (“COVID-19”), continues to be a global pandemic. While it is not possible at this time to estimate the overall impact that COVID-19 could have on our business, the continued rapid spread of COVID-19, the emergence of variant strains, and the measures taken by the governments and local authorities of affected countries and local jurisdictions, has disrupted our Phase 2 clinical trial for prasinezumab, has delayed initiating clinical trial sites for our Phase 3 clinical trial for birtamimab, and could disrupt and delay our planned clinical trials, our research and nonclinical studies, the manufacture or shipment of both drug substance and finished drug product for our drug candidates for preclinical testing and clinical trials and materially adversely impact our liquidity, results of operations, financial condition, or business, including the following:

- our Phase 2 clinical trial for prasinezumab has been disrupted and this and other clinical trials pursued by us and our collaboration partners may be further delayed or interrupted, including as a result of (i) interruptions of supply to clinical trial sites of drug candidate or other equipment or materials, (ii) inability or unwillingness of site investigators or other study personnel to travel to study sites, dispense drug product, or otherwise treat or monitor study participants or follow study protocols, or conduct necessary data collection or verification, (iii) inability or unwillingness of study participants to travel to clinical trial sites, receive infusions, or otherwise continue to participate in the study, (iv) diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials, or (v) interruptions in contracting with essential third-party vendors;
- initiation of clinical trial sites for our Phase 3 clinical trial for birtamimab has been delayed and we, or our collaboration partners, may be further delayed in or prevented from initiating new clinical trials of current or

prospective drug candidates because of (i) delays or difficulties in manufacturing drug product, (ii) delays or difficulties preparing regulatory submissions, (iii) delays or difficulties contracting with essential third-party vendors (such as contract research organizations), (iv) delays or difficulties enlisting site investigators or initiating clinical trial sites, (v) delays or difficulties recruiting or enrolling study participants, or (vi) delays or difficulties supplying drug product or other equipment or materials to clinical trial sites or other locations;

- we may experience delays or interruptions in our business operations due to our key personnel, or a significant number of our personnel, becoming infected with COVID-19 and therefore being unable to work, even remotely, for an extended period of time;
- interruption or delays in the operations of the FDA and comparable foreign regulatory agencies may impact review, inspection, and approval timelines for any of our development programs;
- the pandemic may adversely affect our collaboration partners, Roche, BMS, and/or Novo Nordisk, in ways that adversely impacts our collaborations with them;
- business development opportunities may become more limited or difficult to undertake;
- our costs may significantly increase to manage impacts to our business to complete our planned operations within our projected timelines;
- changes in local regulations as part of a response to COVID-19 may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or discontinuation of the clinical trials altogether;
- we may experience delays in necessary interactions with local regulators, ethics committees, and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees; or
- our liquidity needs may be adversely impacted by the economic effects of the pandemic on financial markets.

Any one or more of these risks 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.

In addition, the spread of COVID-19 has caused a broad impact globally, and may materially affect us economically. For example, if the subtenant to the office space that we subleased in South San Francisco, California defaults on its payment obligations, we will not receive sublease income to offset our lease payments to the landlord of the South San Francisco office space until such time as we are able to secure a new subtenant and enter into a new sublease agreement. The spread of COVID-19 has had a negative impact on the commercial real estate market and there can be no assurance that we would be able to re-sublet the space for the same rent that the current subtenant is obligated to pay us or at all.

While the potential economic impact brought by, and the duration of, COVID-19 may be difficult to assess or predict, a widespread pandemic could result in significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the market price of our ordinary shares.

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

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

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

There is no assurance that the results of the Phase 3 clinical trial for birtamimab, the Phase 2 clinical trial for prasinezumab, the Phase 2b clinical trial for prasinezumab, the Phase 2 clinical trial for NNC6019, the Phase 1 clinical trial for PRX005, and the Phase 1 clinical trial for PRX012 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 will encounter problems with the Phase 3 clinical trial for birtamimab, the Phase 2 clinical trial for prasinezumab, the Phase 2b clinical trial for prasinezumab, the Phase 2 clinical trial for NNC6019, the Phase 1 clinical trial for PRX005, the Phase 1 clinical trial for PRX012, 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 composite primary endpoint that is event-based;

- serious and unexpected drug-related side effects experienced by subjects in clinical trials; or
- failure of our third-party contractors and collaborators to meet their contractual obligations to us or otherwise meet their development or other objectives in a timely manner.

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

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

We are dependent upon Novo Nordisk with respect to further development of NNC6019, 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 at 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.

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 an NDA or a BLA to the FDA, a Marketing Authorization Application (“MAA”) to the EMA, or similar applications to comparable regulatory authorities;
- the FDA, the EMA, or comparable regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; or
- the approval policies or regulations of the FDA, the EMA, or comparable regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

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

Separately, in response to the COVID-19 pandemic, on March 10, 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities and products through April 2020, and on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, on July 10, 2020, the FDA announced its intention to resume certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. In May 2021, the FDA updated its guidance, first published in August 2020, clarifying how it intends to conduct inspections during the COVID-19 pandemic, including how it plans to determine which inspections are “mission critical.” The FDA intends to use this risk-based assessment system to identify the categories of regulatory activity that can occur within a given geographic area, ranging from mission critical inspections to resumption of all regulatory activities. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic, including providing guidance regarding the conduct of clinical trials. If global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, or impact reviews or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

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

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

We are and may choose to conduct international clinical trials in the future. The acceptance of study data by the FDA or other comparable foreign regulatory authority from clinical trials conducted outside of their respective jurisdictions may be subject to certain conditions. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (1) the data are applicable to the United States population and United States medical practice; (2) the trials are performed by clinical investigators of recognized competence; and (3) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any other comparable foreign regulatory authority will accept data from trials conducted outside of its applicable jurisdiction. If the FDA or any other comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our product candidates not receiving approval for commercialization in the applicable jurisdiction.

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

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

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

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

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

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

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

Both before and after regulatory approval to market a particular drug candidate, adverse event reporting, manufacturing, labeling, packaging, storage, distribution, advertising, promotion, record keeping, and reporting related to the product are subject to extensive, ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, as well as continued compliance with current good manufacturing practice (“cGMP”) requirements and current good clinical practice (“cGCP”) requirements for any clinical trials that we conduct. Any regulatory approvals that we receive for our drug candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the drug candidate. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or not previously observed in clinical trials, or problems with our third-party manufacturers or manufacturing processes, or failure

to comply with the regulatory requirements of the FDA, the EMA, or other comparable regulatory authorities could subject us to administrative or judicially imposed sanctions, including:

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

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

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

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

- regulatory authorities may withdraw their approval of the product;
- regulatory authorities may require the addition of labeling statements, such as contraindications, warnings, or precautions; or impose additional safety monitoring or reporting requirements;
- we may be required to change the way the product is administered, or to conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

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

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

Some of our research and development activities involve the controlled storage, use, and disposal of hazardous materials. We are subject to U.S. federal, state, local, and other countries' and jurisdictions' laws and regulations governing the use, manufacture, storage, handling, and disposal of these hazardous materials. Although we believe that our safety procedures for the handling and disposing of these materials comply with the standards prescribed by these laws and regulations, we cannot

eliminate the risk of accidental contamination or injury from these materials. In the event of an accident, state or federal authorities may curtail our use of these materials, and we could be liable for any civil damages that result, which may exceed our financial resources and may seriously harm our business. Because we believe that our laboratory and materials handling policies and practices sufficiently mitigate the likelihood of materials liability or third-party claims, we currently carry no insurance covering such claims. An accident could damage, or force us to shut down, our operations.

Risks Related to the Commercialization of Our Drug Candidates

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

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

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

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

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

The success of sales of prasinezumab in the U.S. will be dependent on the ability of Roche to successfully develop in collaboration with us, and launch and commercialize prasinezumab, if approved by the FDA, pursuant to the License Agreement we entered into in December 2013. Our collaboration with Roche is complex, particularly with respect to future U.S. commercialization of prasinezumab, with respect to financial provisions, allocations of responsibilities, cost estimates, and the respective rights of the parties in decision making. Accordingly, significant aspects of the development and commercialization of prasinezumab require Roche to execute its responsibilities under the arrangement, or require Roche's agreement or approval, prior to implementation, which could cause significant delays that may materially impact the potential success of prasinezumab in the U.S. In addition, Roche may under some circumstances independently develop products that compete with prasinezumab, or Roche may decide to not commit sufficient resources to the development, commercialization, marketing and distribution of prasinezumab. If we are not able to collaborate effectively with Roche on plans and efforts to develop and commercialize prasinezumab, our business could be materially adversely affected.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

In both U.S. and non-U.S. markets, our sales of any future products will depend in part upon the availability of reimbursement from third-party payers. Such third-party payers include government health programs such as Medicare, 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. Among the provisions of the ACA of importance to the pharmaceutical industry are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;

- an increase in the minimum rebates a manufacturer must pay under the U.S. Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- expansion of healthcare fraud and abuse laws, including the U.S. False Claims Act and the U.S. Anti-Kickback Statute, new government investigative powers and enhanced penalties for non-compliance;
- a new Medicare Part D coverage gap discount program, under which manufacturers must now agree to offer 70 percent point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- a licensure framework for follow-on biologic products;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements under the federal Open Payments program and its implementing regulations;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect in 2013 and will stay in effect through 2030, with the exception of a temporary suspension from May 1, 2020, through March 31, 2021, unless additional congressional action is taken. In 2013, the U.S. American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our drugs, if approved, and, accordingly, our financial operations.

Since its enactment, there have been judicial, executive, and Congressional challenges to certain aspects of the ACA. The U.S. Supreme Court is currently reviewing the constitutionality of the ACA in its entirety, although it is unclear how the Supreme Court will rule. It is also unclear how other efforts, if any, to challenge, repeal, or replace the ACA will impact the law. The ultimate content, timing, or effect of any healthcare reform legislation on the U.S. healthcare industry is unclear.

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

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

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

The research, development, and commercialization of new drugs is highly competitive. We will face competition with respect to all drug candidates we may develop or commercialize in the future from pharmaceutical and biotechnology companies worldwide. The key factors affecting the success of any approved product will be its indication, label, efficacy,

safety profile, drug interactions, method of administration, pricing, coverage, reimbursement, and level of promotional activity relative to those of competing drugs.

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

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

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

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

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

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

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

We believe that any of our drug candidates approved as a biologic product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our drug candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biologic products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

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

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

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

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

Birtamimab and PRX012 have been granted Fast Track Designation by the FDA for the treatment of AL amyloidosis and Alzheimer's disease, respectively. 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. Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering 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 or recommendation of an item or service reimbursable under 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;
- U.S. federal false claims laws, including the False Claims Act, 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 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 government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;

- 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. Physician Payment Sunshine Act, which requires applicable manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children’s Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services (“CMS”) information related to “payments or other transfers of value” made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by the physicians (as defined by statute) and their immediate family members. Effective January 1, 2022, these reporting obligations extended to include transfers of value made during the previous year to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists, and certified nurse midwives;
- state laws and regulations that apply to sales or marketing arrangements; apply to healthcare items or services reimbursed by non-governmental third-party payers, including private insurers; require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines; that restrict payments that may be made to healthcare providers; require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; 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.

On September 4, 2018, we received a subpoena from the U.S. Department of Justice requesting the production of documents relating to our NEOD001 development program. We completed the production of documents in July 2019. Since that time, the Department of Justice has not requested that we provide any additional information.

We cannot predict the outcome of this matter or whether any government agency will take further action. If further action is taken, it could divert the attention of management and require the devotion of a substantial amount of time and resources.

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.

To date, we believe our consultants, contract research organizations, and other third parties with which we are working have performed well; however, if these third parties do not successfully carry out their contractual duties, meet expected deadlines, or comply with applicable regulations, we 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. If any of these third-parties fail to perform these activities for us, nonclinical or clinical development of our drug candidates could 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 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 could incur significant additional costs and delays in identifying and qualifying any new third-party manufacturer, due to the technology transfer to such new manufacturer and because the FDA, the EMA, and other comparable regulatory authorities must approve any new manufacturer prior to manufacturing our drug candidates. Such approval would require successful technology transfer, comparability and other testing and compliance inspections. Transferring manufacturing to a new manufacturer could therefore interrupt supply, delay our clinical trials and any commercial launch, and/or increase our costs for

our drug candidates, any of which could have an adverse effect on our business, financial condition, results of operations, and/or growth prospects.

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

Roche, with whom we are collaborating on development of prasinezumab, manufactured clinical supplies for the Phase 2 and Phase 2b clinical trials for prasinezumab and is expected to do so for any subsequent clinical trials of prasinezumab. We are dependent on Roche to continue to manufacture these clinical supplies.

We are dependent on Novo Nordisk, and its third party manufacturers if applicable, to manufacture clinical supplies of NNC6019.

Catalent and Berkshire Sterile Manufacturing, LLC (“Berkshire”) are our third-party manufacturers of clinical supplies of PRX005. We are dependent on Catalent and Berkshire to manufacture these clinical supplies.

Catalent is our third-party manufacturer of clinical supplies of our drug candidate PRX012. We are dependent on Catalent to manufacture these clinical supplies.

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 NNC6019 (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. 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 the COVID-19 pandemic 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, 2022, are anticipated to expire on dates ranging from 2023 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, 2022, the resulting patents are projected to expire on dates ranging from 2025 to 2042. 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 may be breached, and we 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. Such claims 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 the impact of the COVID-19 pandemic on our business operations or 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 the COVID-19 pandemic 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 December 2021 Distribution Agreement), 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, 2022, the number of ordinary shares available for issuance pursuant to outstanding and future equity awards under our equity plans was 12,618,591.

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 may identify deficiencies and 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, 2022. 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 authority may challenge our structure and inter-group arrangements. Responding to or defending against challenges from taxing authorities could be expensive and time consuming, and could 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.

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

Under current law, we are treated as a foreign corporation for U.S. federal tax purposes. However, changes to the U.S. Internal Revenue Code, U.S. Treasury Regulations or other IRS guidance thereunder could adversely affect our status as a foreign corporation or otherwise affect our effective tax rate. For example, in 2017 the United States enacted tax reform that contained significant changes to corporate taxation, including a provision that requires capitalization and amortization of research and development costs over five years for tax years beginning after December 31, 2021. In addition, the Irish Government, Irish Revenue, U.S. Congress, the IRS, the Organization for Economic Co-operation and Development, and other governments and agencies in jurisdictions where we do business have recently focused on issues related to the taxation of multinational corporations, and specifically in the area of “base erosion and profit shifting,” such as where payments are made between affiliates from a jurisdiction with high tax rates to a jurisdiction with lower tax rates. As a result, 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 treaty with Ireland providing for the reciprocal recognition and enforcement of judgments in civil and commercial matters. 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 should not be subject to Irish stamp duty. Shareholders may also transfer their shares into or out of DTC without giving rise to Irish stamp duty provided that there is no change in the beneficial ownership of such shares and the transfer into or out of DTC is not effected in contemplation of a subsequent sale of such shares to a third party; in order to benefit from this exemption from Irish stamp duty, the seller must confirm to us that there is no change in the ultimate beneficial ownership of the shares as a result of the transfer and there is no agreement for the sale of the shares by the beneficial owner to a third party being contemplated.

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

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

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

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

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

Although we do not currently anticipate paying cash dividends, if we were to do so in the future, a dividend withholding tax (currently at a rate of 25%) may arise. A number of exemptions from 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 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 2. PROPERTIES

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

In Dublin, Ireland, we occupy approximately 700 square feet of office under a lease which expires in July 2023. In May 2022, the Company renewed the lease for another one year term starting August 2022.

In South San Francisco, California, we occupy approximately 82,000 square feet of office and laboratory space under a lease which expires in December 2023.

In October 2022, we entered into sublease with Arcus Biosciences, Inc. to sublease approximately 31,157 square feet of office and laboratory space located in Brisbane, California. The sublease expires on September 30, 2028, unless terminated earlier. As of the filing date, the term of such sublease has not commenced as we did not have the right to use or control physical access to such new facility.

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 5,275 shareholders of record of our ordinary shares as of February 17, 2023. 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).

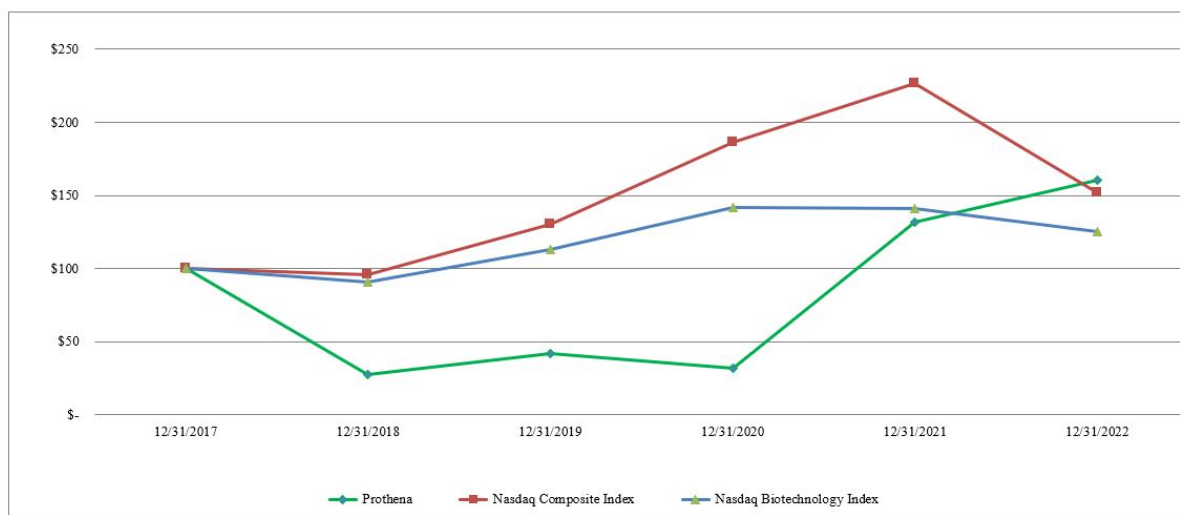
Securities Authorized for Issuance Under Equity Compensation Plans

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, 2017, through December 31, 2022, 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	12/31/2017	12/31/2018	12/31/2019	12/31/2020	12/31/2021	12/31/2022
Prothena Corporation plc	\$100	\$ 27	\$ 42	\$ 32	\$ 132	\$ 161
Nasdaq Composite Index	\$100	\$ 96	\$ 130	\$ 187	\$ 227	\$ 152
Nasdaq Biotechnology Index	\$100	\$ 91	\$ 113	\$ 142	\$ 141	\$ 126

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

Recent Sales of Unregistered Securities

None.

Use of Proceeds

None.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

Irish Law Matters

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

Irish Restrictions on Import and Export of Capital

Except as indicated below, there are no restrictions on non-residents of Ireland dealing in Irish domestic securities, which includes ordinary shares of Irish companies. Dividends and redemption proceeds also continue to be freely transferable to non-resident holders of such securities. The Irish Financial Transfers Act, 1992 (the “Transfers Act”) gives power to the Minister for Finance of Ireland to restrict financial transfers between Ireland and other countries and persons. Financial transfers are broadly

defined and include all transfers that would be movements of capital or payments within the meaning of the treaties governing the member states of the European Union. The acquisition or disposal of interests in shares issued by an Irish incorporated company and associated payments falls within this definition. In addition, dividends or payments on redemption or purchase of shares and payments on a liquidation of an Irish incorporated company would fall within this definition. At present, the Transfers Act prohibits financial transfers involving the late Slobodan Milosevic and associated persons, certain persons indicted by the International Criminal Tribunal for the former Yugoslavia, the late Osama bin Laden, Al-Qaida, the Taliban of Afghanistan, certain persons, entities, and activities in Burma (Myanmar), Belarus, Democratic Republic of Congo, Democratic People's Republic of Korea (North Korea), Iran, Iraq, Côte d'Ivoire, Lebanon, Liberia, Zimbabwe, Sudan, Somalia, Republic of Guinea, Afghanistan, Egypt, Eritrea, Libya, Syria, Tunisia, Ukraine, Russia, certain known terrorists and terrorist groups, and countries that harbor certain terrorist groups, without the prior permission of the Central Bank of Ireland.

Irish Taxes Applicable to U.S. Holders

Withholding Tax on Dividends

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

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

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

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

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

Income Tax on Dividends

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

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

Irish Tax on Capital Gains

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

Capital Acquisitions Tax

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

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

Stamp Duty

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

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

ITEM 6. [RESERVED]

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

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

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

Overview

Prothena is a late-stage clinical biotechnology company with expertise in protein dysregulation and a pipeline of investigational therapeutics with the potential to change the course of devastating neurodegenerative and rare peripheral amyloid diseases.

Fueled by our deep scientific expertise built over decades of research, we are advancing a pipeline of therapeutic candidates for a number of indications and novel targets for which our ability to integrate scientific insights around neurological dysfunction and the biology of misfolded proteins can be leveraged. Our wholly-owned programs include birtamimab for the potential treatment of AL amyloidosis, a portfolio of programs for the potential treatment of Alzheimer's disease including PRX012, which targets Amyloid beta (A β), and PRX123, a novel dual A β -tau vaccine. Our partnered programs include prasinezumab, in collaboration with Roche for the potential treatment of Parkinson's disease and other related synucleinopathies, and programs that target tau (PRX005), TDP-43, and an undisclosed target (PRX019) in collaboration with BMS for the potential treatment of Alzheimer's disease, ALS, and other neurodegenerative diseases. We are also entitled to certain potential milestone payments pursuant to our share purchase agreement with Novo Nordisk pertaining to our ATTR amyloidosis business.

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.

Contracts with Multiple Performance Obligations

Our License Agreement with Roche and our Collaboration Agreement with BMS contain multiple performance obligations. 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 Roche and BMS 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 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 Prothena) is included in the transaction price. Milestone payments that are not within our control, such as approvals from regulators or where attainment of the specified event is dependent on the development activities of a third party, are not considered probable of being achieved until those approvals are received or the specified event occurs. In general, we consider such milestone payments as variable consideration with constraint and therefore we recognize the revenue from such milestone payments as collaboration revenue at point in time when we can conclude it is probable that a significant revenue reversal will not occur in future periods.

Research and Development

We expense R&D costs as incurred. R&D expenses include, but are not limited to, salary and benefits, share-based compensation, clinical trial activities, drug development and manufacturing prior to FDA approval and third-party service fees, including clinical research organizations, investigative sites and contract manufacturing organizations. 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. The objective of our accrual policy is to match the recording of the expenses in our Consolidated Financial Statements to the actual services we have received and efforts expended. 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. 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 our 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.

The information contained in Note 2 to the Consolidated Financial Statements under the heading “Recent Accounting Pronouncements” is hereby incorporated by reference into this Part II, Item 7.

Results of Operations

Comparison of Years Ended December 31, 2022, 2021 and 2020

Revenue

	Year Ended December 31,			Percentage Change	
	2022	2021	2020	2022/2021	2021/2020
	(Dollars in thousands)				
Collaboration revenue	\$ 13,855	\$ 139,833	\$ 564	(90)%	24,693 %
Revenue from license and intellectual property	40,050	60,744	289	(34)%	20,919 %
Total revenue	<u>\$ 53,905</u>	<u>\$ 200,577</u>	<u>\$ 853</u>	(73)%	23,414 %

Total revenue was \$53.9 million, \$200.6 million, and \$0.9 million for the years ended December 31, 2022, 2021 and 2020, respectively.

Collaboration revenue includes revenue recognized under our Collaboration Agreement with BMS. For the year ended December 31, 2022, collaboration revenue recognized from BMS was \$13.9 million for US Development Services related to the Tau/PRX005 program. For the year ended December 31, 2021, collaboration revenue recognized from BMS was \$79.7 million of the total transaction consideration of \$104.9 million for the PRX005 US License and US Development Services, see Note 7, “Significant Agreements” to the Consolidated Financial Statements regarding the Collaboration Agreement with BMS for more information.

Collaboration revenue also includes milestone payments and reimbursements under our License Agreement with Roche. For the year ended December 31, 2021, collaboration revenue from Roche included a \$60.0 million clinical milestone recognized upon first patient dosed in the global Phase 2b for prasinezumab PADOVA study. For the years ended December 31, 2021 and 2020, collaboration revenue also included reimbursements under our License Agreement with Roche. See Note 7, “Significant Agreements” to the Consolidated Financial Statements regarding the Roche License Agreement for more information.

License and intellectual property revenue for the year ended December 31, 2022 included \$40.0 million in milestone payment from Novo Nordisk related to the continued advancement of NNC6019 (formerly PRX004) in a Phase 2 clinical study for the treatment of ATTR cardiomyopathy. For the year ended December 31, 2021, License and intellectual property revenue included \$60.7 million in revenue from the sale of intellectual property and related rights to the Company’s ATTR amyloidosis business and pipeline to Novo Nordisk. See Note 7, “Significant Agreements” to the Consolidated Financial Statements regarding the Novo Nordisk Share Purchase Agreement for more information. For the years ended December 31, 2022, 2021 and 2020, license revenue also included license fees recognized under a License Agreement entered into on March 1, 2020, between the Company’s wholly owned subsidiary, Prothena Biosciences Limited, and F. Hoffmann-La Roche Ltd. See Note 7, “Significant Agreements” to the Consolidated Financial Statements regarding the Roche License Agreement for more information.

Assuming no significant change in our business, we expect our 2023 revenue to decline over the prior year as our 2022 revenue was primarily comprised of nonrecurring intellectual property revenue.

Operating Expenses

	Year Ended December 31,			Percentage Change	
	2022	2021	2020	2022/2021	2021/2020
	(Dollars in thousands)				
Research and development	\$ 135,562	\$ 82,284	\$ 74,884	65 %	10 %
General and administrative	49,900	46,318	38,703	8 %	20 %
Total operating expenses	<u>\$ 185,462</u>	<u>\$ 128,602</u>	<u>\$ 113,587</u>	44 %	13 %

Total operating expenses consist of R&D expenses, general and administrative (“G&A”) expenses. Our operating expenses were \$185.5 million, \$128.6 million and \$113.6 million for the years ended December 31, 2022, 2021 and 2020, respectively.

Our research activities are aimed at developing new drug products. Our development activities involve the translation of our research into potential new drugs. Our R&D expenses primarily consist of personnel costs and related expenses, including share-based compensation and external costs associated with clinical activities and drug development related to our drug programs, including birtamimab, prasinezumab, PRX004 (through July 8, 2021), PRX005, PRX012, PRX123 and preclinical activities related to our discovery programs. Through May 28, 2021, pursuant to our License Agreement with Roche, we made payments to Roche for our share of the development expenses incurred by Roche related to the prasinezumab program, which is included in our R&D expenses. On May 28, 2021, we announced the exercise of our rights under the terms of the ongoing worldwide collaboration with Roche to receive potential U.S. commercial sales milestones and tiered royalties in lieu of a U.S. profit and loss share for prasinezumab in Parkinson’s disease.

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

Research and Development Expenses

Our R&D expense increased by \$53.3 million, or 65%, for the year ended December 31, 2022, compared to the prior year. The increase for year ended December 31, 2022, was primarily due to higher manufacturing expenses primary related to the birtamimab, PRX019, PRX012, and PRX123 programs, higher personnel expenses, higher clinical trial expenses primarily related to the PRX012 and birtamimab programs and higher R&D consulting and other expenses; offset in part by lower collaboration expenses related to the prasinezumab program with Roche as a result of the cost share opt-out exercised in May 2021 and lower manufacturing expense related to the NNC6019 program.

For the year ended December 31, 2021, our R&D expense increased by \$7.4 million, or 10%, compared to the prior year. The increase for year ended December 31, 2021, was primarily due to higher personnel expenses, higher clinical trial expenses primarily related to the birtamimab and PRX005 programs (offset in part by lower PRX004 clinical trial expense) and higher R&D consulting expenses; offset in part by lower collaboration expenses related to the prasinezumab program with Roche as a result of the cost share opt-out exercised in May 2021 and lower manufacturing expenses primary related to the PRX005 and birtamimab programs.

The following table sets forth the R&D expenses for our major programs (specifically, any program with successful first dosing in a Phase 1 clinical trial, which were birtamimab, prasinezumab, PRX003, NNC6019, PRX005, PRX012 and other R&D expenses for the years ended December 31, 2022, 2021 and 2020, and the cumulative amounts to date (in thousands):

	Year Ended December 31,			Cumulative to Date
	2022	2021	2020	
Birtamimab (NEOD001) ⁽¹⁾	\$ 49,312	\$ 30,785	\$ 13,113	\$ 403,486
PRX002/RG7935 ⁽²⁾	261	8,181	18,937	106,781
PRX003 ⁽³⁾	25	52	(209)	59,035
NNC6019 (PRX004) ⁽⁴⁾	1,038	3,800	11,354	79,800
PRX005 ⁽⁵⁾	14,444	12,617	13,571	47,300
PRX012 ⁽⁶⁾	41,990	13,748	5,655	63,003
Other R&D ⁽⁷⁾	28,492	13,101	12,463	
	<u>\$ 135,562</u>	<u>\$ 82,284</u>	<u>\$ 74,884</u>	

- ⁽¹⁾ Cumulative R&D costs to date for birtamimab include the costs incurred from the date when the program was separately tracked in preclinical development. Expenditures in the early discovery stage are not tracked by program and accordingly have been excluded from this cumulative amount.
- ⁽²⁾ Cumulative R&D costs to date for prasinezumab and related antibodies include the costs incurred from the date when the program was separately tracked in nonclinical development. Expenditures in the early discovery stage are not tracked by program and accordingly have been excluded from this cumulative amount. Through May 28, 2021, Prasinezumab costs include payments to Roche for our share of the development expenses incurred by Roche related to prasinezumab programs. For the years ended December 31, 2022, 2021 and 2020, respectively, nil, \$0.2 million and \$0.6 million of reimbursements from Roche for development services were recorded as part of collaboration revenue.
- ⁽³⁾ Cumulative R&D costs to date for PRX003 include the costs incurred from the date when the program was separately tracked in nonclinical development. Expenditures in the early discovery stage are not tracked by program and accordingly have been excluded from this cumulative amount. Based on the Phase 1b multiple ascending dose study results announced in September 2017, we announced that we will not advance PRX003 into mid-stage clinical development for psoriasis or psoriatic arthritis as previously planned.
- ⁽⁴⁾ Cumulative R&D costs to date for NNC6019 (PRX004) include the costs incurred from the date when the program was separately tracked in nonclinical development. Expenditures in the early discovery stage are not tracked by program and accordingly have been excluded from this cumulative amount. On July 8, 2021, we sold shares of one of our wholly-owned subsidiaries to Novo Nordisk. In connection with the transaction, Novo Nordisk acquired our ATTR amyloidosis business, including the clinical stage antibody NNC6019 (PRX004). Expenses incurred in 2022 relate to certain close out activities and transition services provided to Novo Nordisk.
- ⁽⁵⁾ Cumulative R&D costs to date for PRX005 include the costs incurred from the date when the program was separately tracked in nonclinical development. Expenditures in the early discovery stage are not tracked by program and accordingly have been excluded from this cumulative amount.
- ⁽⁶⁾ Cumulative R&D costs to date for PRX012 include the costs incurred from the date when the program was separately tracked in nonclinical development. Expenditures in the early discovery stage are not tracked by program and accordingly have been excluded from this cumulative amount.
- ⁽⁷⁾ Other R&D is comprised of preclinical development and discovery programs that have not progressed to first patient dosing in a Phase 1 clinical trial.

We expect our R&D expenses to increase in 2023 over the prior year, primarily due to anticipated higher personnel costs including share-based compensation and anticipated increase in spending for clinical trials and manufacturing related to our active clinical trials.

General and Administrative Expenses

Our G&A expenses increased by \$3.6 million, or 8%, for the year ended December 31, 2022, compared to the prior year. The increase for the year ended December 31, 2022, compared to the prior year, was primarily due to higher personnel expense, and higher consulting expense; offset in part by lower legal fees and lower expense for our director and officer insurance premium.

For the year ended December 31, 2021, our G&A expenses increased by \$7.6 million, or 20%, compared to the prior year. The increase for the year ended December 31, 2021, compared to the prior year, was primarily due to higher personnel expense, higher legal expenses, higher expense for our director and officer insurance premium and higher consulting expense.

We expect our G&A expenses to increase in 2023 compared to the prior year, primarily related to anticipated higher personnel costs including share-based compensation.

Other Income (Expense)

	Year Ended December 31,			Percentage Change	
	2022	2021	2020	2022/2021	2021/2020
	(Dollars in thousands)				
Interest income	\$ 6,349	\$ 42	\$ 1,369	15,017 %	(97)%
Other income (expense), net	(397)	(96)	(62)	314 %	55 %
Total other income (expense), net	\$ 5,952	\$ (54)	\$ 1,307	nm	nm

nm = not meaningful

Interest income increased by \$6.3 million, or 15,017%, for the year ended December 31, 2022, compared to the prior year, primarily due to higher interest income from our cash and money market accounts resulting from higher interest rates.

Interest income, decreased by \$1.3 million, or 97%, for the year ended December 31, 2021, compared to the prior year, primarily due to lower interest income from our cash and money market accounts resulting from lower interest rates.

Other income (expense), net for the years ended December 31, 2022, 2021 and 2020, was primarily foreign exchange gains (losses) from transactions with vendors denominated in Euros.

Provision for (benefit from) Income Taxes

	Year Ended December 31,			Percentage Change	
	2022	2021	2020	2022/2021	2021/2020
	(Dollars in thousands)				
Provision for (benefit from) income taxes	\$ (8,656)	\$ 4,946	\$ (283)	nm	nm

nm = not meaningful

The provision for (benefit from) income taxes were \$(8.7) million, \$4.9 million and \$(0.3) million for the years ended December 31, 2022, 2021 and 2020, respectively. The benefit from income taxes increased by \$13.6 million for the year ended December 31, 2022, compared to the same period in the prior year primarily due to an increase in deferred tax asset (DTA) of \$10.5 million related to Section 174 R&D Capitalization requirements, which became effective in 2022.

Whereas, for the year ended December 31, 2021, the provision for income taxes increased by \$5.2 million, compared to the same period of the prior year, primarily due to a decrease in deferred tax asset related to our February 12, 2021 option exchange program and a change in our share-based compensation 162(m) limitations associated with the increase in the number of covered employees under the American Rescue Plan Act.

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

Liquidity and Capital Resources

Overview

	December 31,	
	2022	2021
	(Dollars in thousands)	
Working capital	\$ 668,951	\$ 551,357
Cash and cash equivalents	\$ 710,406	\$ 579,094
Total assets	\$ 758,035	\$ 609,366
Total liabilities	\$ 135,993	\$ 143,324
Total shareholders' equity	\$ 622,042	\$ 466,042

Working capital was \$669.0 million as of December 31, 2022, an increase of \$117.6 million from working capital of \$551.4 million as of December 31, 2021. This increase in working capital during the year ended December 31, 2022, was primarily attributable to a higher cash and cash equivalents balance resulting from net proceeds of approximately \$172.6 million from our public offering in December 2022, \$51.0 million from our December 2021 Distribution Agreement, \$40.0 million development milestone payment from Novo Nordisk, and proceeds from stock option exercises of approximately \$17.8 million, partially offset by cash use of \$185.5 million for operating expenses (adjusted to exclude non-cash charges).

As of December 31, 2022, we had \$710.4 million in cash and cash equivalents. 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 the future in order to continue the research and development of our drug candidates. Additionally, in order to develop and obtain regulatory approval for our potential products 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, including pursuant to the December 2021 Distribution Agreement (See Note 8, "Shareholders' Equity" to the Consolidated Financial Statements for more information). We cannot assume that such additional financings will be available on acceptable terms, if at all, and such financings may only be available on terms dilutive to our shareholders.

In managing our liquidity needs in Ireland, we do not rely on unrepatriated earnings as a source of funds. As of December 31, 2022, \$204.2 million of our outstanding cash and cash equivalents related to U.S. operations are considered permanently reinvested. We do not intend to repatriate these funds. However, if these funds were repatriated back to Ireland, we would incur a withholding tax from the dividend distribution.

The adequacy of our cash resources depends on many assumptions, including assumptions with respect to our expenses. These assumptions may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with completing the development of our product candidates. Our future capital requirements will depend on numerous factors, including, without limitation, the timing of initiation, progress, results and costs of our clinical trials; the results of our research and nonclinical studies; the costs of clinical manufacturing and of establishing commercial manufacturing arrangements; the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims; the costs and timing of capital asset purchases; our ability to establish research collaborations, strategic collaborations, licensing or other arrangements; the costs to satisfy our obligations under current and potential future collaborations; the costs of any in-licensing transactions; and the timing, receipt, and amount of revenues or royalties, if any, from any approved drug candidates.

Our cash and cash equivalents may also be potentially supplemented in the future by proceeds from our collaboration partners 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 (formerly Celgene), 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 for the Years Ended December 31, 2022, 2021 and 2020

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

	2022	Year Ended December 31, 2021	2020
Net cash provided by (used in) operating activities	\$ (108,821)	\$ 92,605	\$ (80,362)
Net cash used in investing activities	(464)	(575)	(196)
Net cash provided by financing activities	241,457	190,332	215
Net increase (decrease) in cash, cash equivalents and restricted cash	<u>\$ 132,172</u>	<u>\$ 282,362</u>	<u>\$ (80,343)</u>

Cash Used in Operating Activities

Net cash used in operating activities was \$108.8 million for the year ended December 31, 2022, primarily due to the use of \$185.5 million for operating expense (adjusted to exclude non-cash charges of approximately \$26.9 million) and partially offset by a \$40.0 million development milestone payment from Novo Nordisk.

Net cash provided by operating activities was \$92.6 million for the year ended December 31, 2021, primarily due to the option exercise fee of \$80.0 million from BMS, milestone payment of \$60.0 million from Roche and upfront payment of \$60.0 million from Novo Nordisk offset in part by the use of \$128.6 million for operating expense (adjusted to exclude non-cash charges of approximately \$36.0 million).

Net cash used in operating activities was \$80.4 million for the year ended December 31, 2020, primarily due to use of \$113.6 million for operating expense (adjusted to exclude non-cash charges of approximately \$27.3 million).

Cash Used in Investing Activities

Net cash used in investing activities was \$0.5 million, \$0.6 million and \$0.2 million for the years ended December 31, 2022, 2021 and 2020, respectively. Net cash used in investing activities for the years ended December 31, 2022, 2021 and 2020 was primarily related to purchases of property and equipment.

Cash Provided by Financing Activities

Net cash provided by financing activities was \$241.5 million for the year ended December 31, 2022, primarily from net proceeds from issuances of ordinary shares pursuant to the December 2022 public offering of \$172.6 million, net proceeds from issuances of ordinary shares pursuant to the December 2021 Distribution Agreement of \$51.0 million, and proceeds from issuances of ordinary shares upon exercises of stock options of \$17.8 million.

Net cash provided by financing activities was \$190.3 million for the year ended December 31, 2021, primarily from net proceeds from issuance of ordinary shares pursuant to our May 2021 Distribution Agreement (as discussed below) of \$96.7 million, net proceeds from issuance of ordinary shares in public offering of \$78.0 million, and proceeds from issuances of ordinary shares upon exercises of stock options of \$15.5 million.

Net cash provided by financing activities was \$0.2 million and for the year ended December 31, 2020, which was proceeds from issuances of ordinary shares upon exercises of stock options.

Off-Balance Sheet Arrangements

At December 31, 2022, 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, 2022, consisted of minimum cash payments under operating leases of \$21.3 million, purchase obligations of \$11.5 million (of which \$5.6 million is included in accrued current liabilities), and contractual obligations under license agreements of \$0.4 million (of which \$29 thousand is included in accrued current

liabilities). Purchase obligations consist of non-cancelable purchase commitments to suppliers. Operating leases represent our future minimum rental commitments under our non-cancelable operating leases. For additional information regarding the timing for our contractual obligations See Note 6, “Commitments and Contingencies” to our Consolidated Financial Statements.

In March 2016, we entered into a noncancelable operating sublease to lease 128,751 square feet of office and laboratory space in South San Francisco, California. We are obligated to make lease payments totaling approximately \$39.2 million over the lease term. Of this obligation, approximately \$6.5 million remains outstanding as of December 31, 2022. We sub-sublease approximately 46,641 square feet of the office and laboratory in South San Francisco, California to Assembly Biosciences, Inc. See Note 6, “Commitments and Contingencies” to our Consolidated Financial Statements for additional information regarding sub-sublease rental income.

In June 2021, we entered into a lease agreement for office space in Dublin, Ireland, which commenced in August 2021 and had a term of one year. This lease has an automatic renewal clause, pursuant to which the agreement will be extended automatically for successive periods equal to the current term, unless cancelled by us. In May 2022, we renewed the lease for another one year term starting August 2022.

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 \$14.7 million remains outstanding as of December 31, 2022.

As of the filing date, the term of the sublease has not commenced as we did not have the right to use or control physical access to the facility, and therefore no accounting relating to the sublease has been recorded in the Balance Sheet as of December 31, 2022. We expect to have the right to use or control the access to the facility in the second half of 2023.

The following is a summary of our contractual obligations as of December 31, 2022 (in thousands):

	Total	2023	2024	2025	2026	2027	Thereafter
Operating leases ⁽¹⁾	\$ 21,332	\$ 6,624	\$ 2,707	\$ 3,051	\$ 3,158	\$ 3,269	\$ 2,523
Purchase obligations	11,467	11,382	85	—	—	—	—
Contractual obligations under license agreements	431	89	64	64	64	60	90
Total	<u>\$ 33,230</u>	<u>\$ 18,095</u>	<u>\$ 2,856</u>	<u>\$ 3,115</u>	<u>\$ 3,222</u>	<u>\$ 3,329</u>	<u>\$ 2,613</u>

⁽¹⁾ See Note 6, “Commitments and Contingencies” 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 2023 net cash used in operating and investing activities to be approximately \$213 million to \$229 million.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Foreign Currency Risk

Our business is primarily conducted in U.S. dollars except for our agreements with contract manufacturers for drug supplies which are denominated in Euros. We recorded a loss on foreign currency exchange rate differences of approximately \$397,000, \$96,000, and \$62,000 during the years ended December 31, 2022, 2021 and 2020, 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 continue to 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. We may invest any surplus funds in accordance with a policy approved by our board of directors which will specify the categories, allocations, and ratings of securities we may consider for investment. The primary objectives of our investment policy are to preserve principal and maintain proper liquidity to meet our operating requirements. Our investment policy also specifies credit quality standards for our investments and limits the amount of credit exposure to any single issue, issuer or type of investment.

Credit Risk

Financial instruments that potentially subject us to concentration of credit risk consist of cash and cash equivalents and accounts receivable. We place our cash and cash equivalents with high credit quality financial institutions and pursuant to our investment policy, we limit the amount of credit exposure with any one financial institution. Deposits held with banks may exceed the amount of insurance provided on such deposits. 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, 2022 and 2021, the related consolidated statements of operations, cash flows, and shareholders' equity for each of the years in the three-year period ended December 31, 2022, 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, 2022, 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, 2022 and 2021, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2022, 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, 2022 based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's consolidated financial statements and an opinion on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of a critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Evaluation of Accrued Research and Development Costs

As discussed in Note 2 to the consolidated financial statements, research and development costs are expensed by the Company as incurred. As of December 31, 2022, the Company recognized accrued research and development costs of \$10.8 million. Costs for certain development activities, such as clinical trials and contract manufacturing, are recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, or information provided to the Company by its vendors, including clinical research organizations, investigative sites, and contract manufacturing organizations, on their actual costs incurred. 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, trial contract, or manufacturing contract. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the consolidated financial statements as prepaid or accrued research and development.

We identified the evaluation of accrued research and development costs relating to clinical research organizations, investigative sites, and contract manufacturing organizations as a critical audit matter. 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. Complex and subjective auditor judgment was involved in evaluating the status of the clinical trials and progress of manufacturing activities used to determine accrued research and development costs.

The following are the primary procedures we performed to address this critical audit matter. We evaluated the design and tested the operating effectiveness of certain internal controls related to accrued research and development costs. This included a control related to the development of the key assumptions listed above. For a sample of accrued research and development costs, we agreed the amount, duration and any key terms to the underlying contract. We examined underlying documentation and third-party evidence from clinical research organizations and contract manufacturing organizations and compared them to the assumptions and inputs that are described above. We assessed the Company's estimate of costs incurred as of December 31, 2022, which included examining invoices received after December 31, 2022, but prior to the issuance of the Company's consolidated financial statements. In addition, we inquired of the individuals who are responsible for monitoring and tracking the status of the clinical trials and contract manufacturing to understand the progress of the activities.

/s/ KPMG LLP

We have served as the Company's auditor since 2012

San Francisco, California
February 28, 2023

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

	December 31,	
	2022	2021
Assets		
Current assets:		
Cash and cash equivalents	\$ 710,406	\$ 579,094
Prepaid expenses and other current assets	8,692	5,715
Total current assets	719,098	584,809
Non-current assets:		
Property and equipment, net	1,731	2,012
Operating lease right-of-use assets	6,277	12,123
Deferred tax assets	18,204	7,071
Restricted cash, non-current	2,212	1,352
Other non-current assets	10,513	1,999
Total non-current assets	38,937	24,557
Total assets	\$ 758,035	\$ 609,366
Liabilities and Shareholders' Equity		
Current liabilities:		
Accounts payable	\$ 9,270	\$ 3,691
Accrued research and development	10,794	6,351
Deferred revenue, current	11,442	7,657
Lease liability, current	6,473	5,940
Other current liabilities	12,168	9,813
Total current liabilities	50,147	33,452
Non-current liabilities:		
Deferred revenue, non-current	85,293	102,933
Lease liability, non-current	—	6,386
Other liabilities	553	553
Total non-current liabilities	85,846	109,872
Total liabilities	135,993	143,324
Commitments and contingencies (Note 6)		
Shareholders' equity:		
Euro deferred shares, €22 nominal value:	—	—
Authorized shares — 10,000 at December 31, 2022 and 2021		
Issued and outstanding shares — none at December 31, 2022 and 2021		
Ordinary shares, \$0.01 par value:	521	466
Authorized shares — 100,000,000 at December 31, 2022 and 2021		
Issued and outstanding shares — 52,103,608 and 46,660,294 at December 31, 2022 and 2021, respectively		
Additional paid-in capital	1,454,524	1,181,630
Accumulated deficit	(833,003)	(716,054)
Total shareholders' equity	622,042	466,042
Total liabilities and shareholders' equity	\$ 758,035	\$ 609,366

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,		
	2022	2021	2020
Collaboration revenue	\$ 13,855	\$ 139,833	\$ 564
Revenue from license and intellectual property	40,050	60,744	289
Total revenue	53,905	200,577	853
Operating expenses:			
Research and development	135,562	82,284	74,884
General and administrative	49,900	46,318	38,703
Total operating expenses	185,462	128,602	113,587
Income (loss) from operations	(131,557)	71,975	(112,734)
Other income (expense):			
Interest income	6,349	42	1,369
Other expense, net	(397)	(96)	(62)
Total other income (expense), net	5,952	(54)	1,307
Income (loss) before income taxes	(125,605)	71,921	(111,427)
Provision for (benefit from) income taxes	(8,656)	4,946	(283)
Net income (loss)	\$ (116,949)	\$ 66,975	\$ (111,144)
Basic net income (loss) per ordinary share	\$ (2.47)	\$ 1.51	\$ (2.78)
Diluted net income (loss) per ordinary share	\$ (2.47)	\$ 1.38	\$ (2.78)
Shares used to compute basic net income (loss) per share	47,369	44,228	39,915
Shares used to compute diluted net income (loss) per share	47,369	48,464	39,915

See accompanying Notes to Consolidated Financial Statements.

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

	2022	Year Ended December 31, 2021	2020
Operating activities			
Net income (loss)	\$ (116,949)	\$ 66,975	\$ (111,144)
Adjustments to reconcile net income (loss) to cash provided by (used in) operating activities:			
Depreciation and amortization	744	1,115	1,514
Share-based compensation	31,322	24,658	22,014
Deferred income taxes	(11,133)	4,573	(1,688)
Reduction in the carrying amount of right-of-use assets	5,997	5,688	5,463
Loss on disposal of fixed assets	1	—	—
Changes in operating assets and liabilities:			
Prepaid and other assets	(10,809)	(4,748)	852
Deferred revenue	(13,855)	348	—
Accounts payable, accruals and other liabilities	11,865	(492)	7,728
Operating lease liabilities	(6,004)	(5,512)	(5,101)
Net cash provided by (used in) operating activities	(108,821)	92,605	(80,362)
Investing activities			
Purchases of property and equipment	(464)	(575)	(196)
Net cash used in investing activities	(464)	(575)	(196)
Financing activities			
Proceeds from issuance of ordinary shares in public offering, net	172,583	78,049	—
Proceeds from issuance of ordinary shares in at-the market offering, net	51,033	96,739	—
Proceeds from issuance of ordinary shares upon exercise of stock options	17,841	15,544	215
Net cash provided by financing activities	241,457	190,332	215
Net increase (decrease) in cash, cash equivalents and restricted cash	132,172	282,362	(80,343)
Cash, cash equivalents and restricted cash, beginning of the year	580,446	298,084	378,427
Cash, cash equivalents and restricted cash, end of the period	\$ 712,618	\$ 580,446	\$ 298,084
Supplemental disclosures of cash flow information			
Cash paid for income taxes, net	\$ 2,659	\$ 580	\$ 1,367
Supplemental disclosures of non-cash investing and financing activities			
Receivable from option exercises	\$ 62	\$ 13	\$ —
Right-of-use assets obtained in exchange for lease obligations	\$ 151	\$ —	\$ —
At-the market offering costs included in accounts payable and accrued liabilities	\$ 13	\$ —	\$ —
Public offering costs included in accounts payable and accrued liabilities	\$ 220	\$ —	\$ —

See accompanying Notes to Consolidated Financial Statements.

The following table provides a reconciliation of cash, cash equivalents and restricted cash reported within the statement of financial position that sum to the total of the same such amounts shown in the Consolidated Statements of Cash Flows.

	Year Ended December 31,		
	2022	2021	2020
Cash and cash equivalents	\$ 710,406	\$ 579,094	\$ 295,380
Restricted cash, current	—	—	1,352
Restricted cash, non-current	2,212	1,352	1,352
Total cash, cash equivalents and restricted cash, end of the period	<u>\$ 712,618</u>	<u>\$ 580,446</u>	<u>\$ 298,084</u>

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, 2019	39,898,561	\$ 399	\$ 944,407	\$ (671,885)	\$ 272,921
Share-based compensation	—	—	22,014	—	22,014
Issuance of ordinary shares upon exercise of stock options	22,852	—	215	—	215
Net loss	—	—	—	(111,144)	(111,144)
Balances at December 31, 2020	39,921,413	399	966,636	(783,029)	184,006
Share-based compensation	—	—	24,658	—	24,658
Issuance of ordinary shares upon exercise of stock options	1,073,707	11	15,546	—	15,557
Issuance of ordinary shares in public offering, net of issuance costs of \$5.5 million	4,025,000	40	78,009	—	78,049
Issuance of ordinary shares under the at-the-market offering program, net of issuance costs of \$3.2 million	1,640,174	16	96,781	—	96,797
Net income	—	—	—	66,975	66,975
Balances at December 31, 2021	46,660,294	466	1,181,630	(716,054)	466,042
Share-based compensation	—	—	31,322	—	31,322
Issuance of ordinary shares upon exercise of stock options	1,282,086	14	17,876	—	17,890
Issuance of ordinary shares in public offering, net of issuance costs of \$11.3 million	3,250,000	32	172,331	—	172,363
Issuance of ordinary shares under the at-the-market offering program, net of issuance costs of \$1.7 million	911,228	9	51,365	—	51,374
Net loss	—	—	—	(116,949)	(116,949)
Balances at December 31, 2022	52,103,608	\$ 521	\$ 1,454,524	\$ (833,003)	\$ 622,042

See accompanying Notes to Consolidated Financial Statements.

Notes to the Consolidated Financial Statements

1. Organization

Description of Business

Prothena Corporation plc (“Prothena” or the “Company”) is a late-stage clinical biotechnology company with expertise in protein dysregulation and a pipeline of investigational therapeutics with the potential to change the course of devastating neurodegenerative and rare peripheral amyloid diseases.

Fueled by its deep scientific expertise built over decades of research, the Company is advancing a pipeline of therapeutic candidates for a number of indications and novel targets for which its ability to integrate scientific insights around neurological dysfunction and the biology of misfolded proteins can be leveraged. The Company’s wholly-owned programs include birtamimab for the potential treatment of AL amyloidosis, and a portfolio of programs for the potential treatment of Alzheimer’s disease including PRX012, which targets Amyloid beta (A β), and PRX123, a novel dual A β -tau vaccine. The Company’s partnered programs include prasinezumab, in collaboration with Roche for the potential treatment of Parkinson’s disease and other related synucleinopathies, and programs that target tau (PRX005), TDP-43, and an undisclosed target (PRX019) in collaboration with Bristol Myers Squibb (BMS) for the potential treatment of Alzheimer’s disease, amyotrophic lateral sclerosis (ALS), and other neurodegenerative diseases. The Company is also entitled to certain potential milestone payments pursuant to the Company’s share purchase agreement with Novo Nordisk pertaining to the Company’s ATTR amyloidosis business.

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, 2022, the Company had an accumulated deficit of \$833.0 million and cash and cash equivalents of \$710.4 million.

Based on the Company’s business plans, management believes that the Company’s cash and cash equivalents at December 31, 2022, 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. The Company expects to continue to finance future cash needs that exceed its cash from operating activities primarily through its current cash and cash equivalents, its collaborations with Roche and BMS, its agreement with Novo Nordisk, and, to the extent necessary, through proceeds from public or private equity or debt financings, loans and other collaborative agreements with corporate partners or other arrangements.

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. (“GAAP”) and with the instructions for Form 10-K and Regulations S-X statements. 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. These Consolidated Financial Statements include the accounts of the Company and its consolidated subsidiaries. All intercompany balances and transactions have been eliminated in consolidation. Certain amounts in the Consolidated Financial Statements have been reclassified to conform to the current year presentation. These reclassifications have not changed the results of operations of prior periods.

Use of Estimates

The preparation of the Consolidated Financial Statements in conformity with GAAP requires management 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, share-based compensation, research and development expenses and leases. 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 and Cash Equivalents

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.

Restricted Cash

Cash accounts that are restricted to withdrawal or usage are presented as restricted cash. As of December 31, 2022, the Company had \$2.2 million of restricted cash held by a bank in certificates of deposit as collateral to standby letters of credit under certain operating leases. See Note 6, "Commitments and Contingencies" for additional information regarding our operating lease.

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 improvements and betterments 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, plant and equipment are as follows:

	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

Long-lived assets are reviewed 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 circumstances require that a long-lived asset be tested for possible impairment, the Company compares the undiscounted cash flows expected to be generated by the asset to the carrying amount of the asset. If the carrying amount of the long-lived asset is not recoverable on an undiscounted cash flow basis, an impairment 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, 2022, 2021 and 2020.

Leases

At the inception, the Company determines if an arrangement is a lease. If so, the Company evaluates the lease agreement to determine whether the lease is an operating or capital 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.

Operating Leases

Operating leases are included in the operating lease right-of-use assets, lease liability, current and lease liability, non-current in the Company's Consolidated Balance Sheets. Operating lease right-of-use 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 right-of-use assets and liabilities are recognized at the lease commencement date based on the present value of minimum 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 right-of-use assets also include any lease prepayments made and exclude lease incentives including rent abatements and/or concessions and rent holidays. Tenant improvements made by the Company as a lessee in which they are deemed to be owned by the lessor is viewed as lease prepayments by the Company and included in the operating lease right-of-use assets. Lease expense is recognized on a straight-line basis over the expected lease term. For lease agreements entered after the adoption of ASC 842 that include lease and non-lease components, such components are generally accounted separately.

Revenue Recognition

The Company's collaboration revenue includes revenue recognized for milestone payments and reimbursements under the Company's License Agreement with Roche as well as revenue recognized under the Company's Collaboration Agreement with BMS. 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.

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.

For contracts that contain multiple performance obligations, such as the Company's License Agreement with Roche and the Collaboration Agreement with BMS, 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 Roche and BMS 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, Roche and BMS). 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.

Profit Share Revenue

For agreements, with profit sharing arrangements, the Company will record its share of the pre-tax commercial profit as collaboration revenue when the profit sharing can be reasonably estimated and that a significant revenue reversal will not occur in future periods.

Royalty Revenue

The Company will recognize revenue from royalties based on licensees' sales of the Company's products or products using the Company's technologies. Royalties are recognized as earned in accordance with the contract terms when royalties from licensees can be reasonably estimated and that a significant revenue reversal will not occur in future periods. There were no royalties earned during the years ended December 31, 2022, 2021 and 2020.

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.

Incremental Costs to Obtain or Fulfill a Contract

For costs to obtain a contract, the Company will capitalize such amounts if they are incremental and expected to be recovered. Sales commissions directly related to obtaining new contracts will be capitalized unless the amortization period is one year or less, at which these costs will be recorded within selling and general administrative expenses. As of December 31, 2022, the Company does not have such costs capitalized in its Consolidated Balance Sheet.

Research and Development

Research and development costs are expensed as incurred. Such costs 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. 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. 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. 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. 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.

Acquired In-Process Research and Development Expense

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 expensed as research and development provided that the drug has not achieved regulatory approval for marketing and, absent obtaining such approval, has no alternative future use.

Loss Contingencies

Loss contingencies, including claims and legal actions arising in the ordinary course of business, are recorded as liabilities when the likelihood of loss is probable and an amount or range of loss can be reasonably estimated. The Company's accruals for losses are based on management's judgment of all possible outcomes and their financial effect, the probability of

losses, and where applicable, the consideration of opinions of the Company's legal counsel. The Company's accounting policy for legal costs related to loss contingencies is to accrue for the probable fees that can be reasonably estimated and expensed as incurred. Additionally, the Company records insurance recovery receivable from third party insurers when recovery has been determined to be probable.

Share-based Compensation

Share-based payment awards, including stock options and restricted stock units (RSUs), are measured at fair value as of the grant date and share-based compensation expense is recognized on a straight-line basis over the requisite service period for each award. To determine the fair value of stock options, 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 proper assumptions used in these models. The assumptions used include the risk-free interest rate, expected term, expected volatility and expected dividend yield. The fair value of RSUs is based on the closing market price of the Company's ordinary shares on the date of grant. Further, 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. Forfeitures are estimated based on historical experience. If actual forfeitures differ from estimates at the time of grant they will be revised in subsequent periods. The Company uses its historical volatility for the Company's stock to estimate expected volatility. If factors change and different assumptions are employed in determining the fair value of share-based awards, the share-based compensation expense recorded in future periods may differ significantly from what was recorded in the current period (see Note 9, "Share-Based Compensation" for further information).

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 stock options are exercised.

Income Taxes

The Company files its own U.S. and foreign income tax returns and income taxes are presented in the Consolidated Financial Statements using the asset and liability method prescribed by the accounting guidance for income taxes. Deferred tax assets ("DTAs") and liabilities are determined based on the difference between the financial statement and tax basis of assets and liabilities using the enacted tax rates projected to be in effect for the year in which the differences are expected to reverse. Net deferred tax assets are recorded to the extent the Company believes that these assets will more likely than not be realized. In making such determination, all available positive and negative evidence is considered, including scheduled reversals of deferred tax liabilities, recent cumulative earnings/losses by taxing jurisdiction, projected future taxable income, tax planning strategies and recent financial operations. Actual operating results in future years could differ from our current assumptions, judgments and estimates.

The Company's significant tax jurisdictions are Ireland and the United States. Estimates are required in determining the Company's provision for income taxes. Some of these estimates are based on management's interpretations of jurisdiction-specific tax laws or regulations. Various internal and external factors may have favorable or unfavorable effects on the future effective income tax rate of the business. These factors include, but are not limited to, changes in tax laws, regulations and/or rates, changing interpretations of existing tax laws or regulations, changes in estimates of prior years' items, past and future levels of R&D spending, the impact of accounting for share-based compensation, and changes in overall levels of income before taxes.

The Company did not recognize certain tax benefits from uncertain tax positions within the provision for income taxes. The tax benefit from an uncertain tax position is recognized only if it is more likely than not the tax position will be sustained on examination by the taxing authorities, based on the technical merits of the position. The tax benefits recognized in the financial statements from such positions are then measured based on the largest benefit that has a greater than 50% likelihood of being realized upon settlement. Changes in recognition or measurement are reflected in the period in which the change in judgment occurs. Interest and penalties related to unrecognized tax benefits are accounted for in income tax expense.

Net Income (Loss) per Ordinary Share

Basic net income (loss) per ordinary share is calculated by dividing net income (loss) by the weighted-average number of ordinary shares outstanding during the period. Shares used in diluted net income per ordinary share would include the dilutive effect of ordinary shares potentially issuable upon the exercise of stock options outstanding. However, potentially issuable ordinary shares are 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, 2022 and 2020, and therefore diluted net loss per share is equal to basic net

loss per share. During the year ended December 31, 2021, diluted net income per ordinary share is computed by giving effect to all dilutive potential ordinary shares including options.

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.

Segment and Concentration of Risks

The Company operates in one segment. The Company's chief operating decision maker (the "CODM"), its Chief Executive Officer, manages the Company's operations on a consolidated basis for purposes of allocating resources. When evaluating the Company's financial performance, the CODM reviews all financial information on a consolidated basis.

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 may exceed the amount of insurance provided on such deposits. 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 denominated in Euros. The Company recorded a loss on foreign currency exchange rate differences of approximately \$397,000, \$96,000 and \$62,000 during the years ended December 31, 2022, 2021 and 2020, respectively. If the Company increases its business activities that require the use of foreign currencies, it may be exposed to losses if the Euro and other such currencies continue to strengthen against the U.S. dollar.

As of December 31, 2022, and 2021, \$1.7 million and \$2.0 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.

Recent Accounting Pronouncements

The Company has evaluated all recently issued or enacted accounting pronouncements and has determined that all such pronouncements either do not apply or their impact is insignificant to the consolidated financial statements.

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 — Observable inputs such as quoted prices (unadjusted) for identical assets or liabilities in active markets.

Level 2 — Include other inputs that are based upon quoted prices for similar instruments in active markets, quoted prices for identical or similar instruments in markets that are not active, and model-based valuation techniques for which all significant inputs are observable in the market or can be derived from observable market data. Where applicable, these models project future cash flows and discount the future amounts to a present value using market-based observable inputs including interest rate curves, foreign exchange rates, and credit ratings.

Level 3 — 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 of certain financial instruments, such as cash equivalents, accounts receivable, accounts payable and accrued liabilities, approximate fair value due to their relatively short maturities, and low market interest rates, if applicable.

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 \$599.1 million and \$480.5 million in money market funds included in cash and cash equivalents at December 31, 2022, and 2021, respectively.

4. Composition of Certain Balance Sheet Items

Prepaid and Other Current Assets

Prepaid and other current assets consisted of the following (in thousands):

	December 31,	
	2022	2021
Prepaid R&D expenses	\$ 5,325	\$ 3,859
Prepaid G&A expenses	1,597	1,077
Receivable from stock option exercises in-transit	62	13
Other	1,708	766
Prepaid and other current assets	<u>\$ 8,692</u>	<u>\$ 5,715</u>

Property and Equipment, net

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

	December 31,	
	2022	2021
Machinery and equipment	\$ 9,901	\$ 9,758
Leasehold improvements	1,498	1,393
Purchased computer software	1,500	1,322
	<u>12,899</u>	<u>12,473</u>
Less: accumulated depreciation and amortization	(11,168)	(10,461)
Property and equipment, net	<u>\$ 1,731</u>	<u>\$ 2,012</u>

Depreciation expense was \$0.7 million, \$1.1 million, and \$1.5 million for the years ended December 31, 2022, 2021 and 2020, respectively.

Other Current Liabilities

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

	December 31,	
	2022	2021
Payroll and related expenses	\$ 11,060	\$ 8,644
Professional services	605	764
Other	503	405
Other current liabilities	<u>\$ 12,168</u>	<u>\$ 9,813</u>

5. 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. Shares used in diluted net income per ordinary share would include the dilutive effect of ordinary shares potentially issuable upon the exercise of stock options outstanding. However, potentially issuable ordinary shares are 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, 2022 and 2020, and therefore diluted net loss per share is equal to basic net loss per share. During the year ended December 31, 2021, diluted net income per ordinary share is computed by giving effect to all dilutive potential ordinary shares including options.

Net income (loss) per ordinary share was determined as follows (in thousands, except per share amounts):

	2022	Year Ended December 31, 2021	2020
Numerator:			
Net income (loss)	\$ (116,949)	\$ 66,975	\$ (111,144)
Denominator:			
Weighted-average ordinary shares outstanding used in per share calculations - basic	47,369	44,228	39,915
Dilutive stock options outstanding	—	4,236	—
Weighted-average ordinary shares outstanding used in per share calculations - diluted	47,369	48,464	39,915
Net income (loss) per share:			
Basic net income (loss) per ordinary share	\$ (2.47)	\$ 1.51	\$ (2.78)
Diluted net income (loss) per ordinary share	\$ (2.47)	\$ 1.38	\$ (2.78)

The equivalent ordinary shares not included in diluted net income (loss) per share because their effect would be anti-dilutive are as follows (in thousands):

	2022	Year Ended December 31, 2021	2020
Stock options to purchase ordinary shares	9,480	382	8,745
Restricted Stock Units (RSU)	23	—	—
Total	9,503	382	8,745

6. Commitments and Contingencies

Lease Commitments

The Company currently has three leases relating to its facilities in South San Francisco and Brisbane, California, and Dublin, Ireland.

Current South San Francisco Facility

The Company has a noncancelable operating sublease (the "Lease") covering 128,751 square feet of office and laboratory space in South San Francisco, California, U.S. (the "Current SSF Facility"). The Lease includes a free rent period and escalating rent payments and has a remaining lease term of 1 year that expires on December 31, 2023, unless terminated earlier. The Company's obligation to pay rent commenced on August 1, 2016.

Total operating lease cost was \$6.3 million, \$6.3 million and \$6.3 million for the years ended December 31, 2022, 2021 and 2020, respectively. Total cash paid against the operating lease liability was \$6.3 million, \$6.2 million and \$6.0 million for the years ended December 31, 2022, 2021 and 2020, respectively.

The discount rate used to determine the lease liability was 4.25%.

The Company obtained a standby letter of credit in April 2016 in the initial amount of \$4.1 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 Lease 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 Company not cured within the applicable cure period. This standby letter of credit is collateralized by a certificate of deposit of the same amount which is classified as restricted cash. The Company was entitled to a \$1.4 million reduction in the face amount of the standby letter of credit on the third anniversary of the contractual rent commencement, which was received in 2019, and another \$1.4 million on the fifth anniversary of the contractual rent commencement, which was received in September 2021. As a condition to the reduction of the standby letter of credit amount, no uncured default by the Company shall then exist under the Lease. As of December 31, 2022, none of the remaining standby letter of credit amount of \$1.4 million has been used.

Sub-Sublease of Current SSF Facility

On July 18, 2018, the Company entered into a Sub-Sublease Agreement (the "Sub-Sublease") with Assembly Biosciences, Inc. (the "Sub-Subtenant") to sub-lease approximately 46,641 square feet of office and laboratory space of the Current SSF Facility to the Sub-Subtenant. The Sub-Sublease is considered an operating lease under ASC 842. For the years ended December 31, 2022, 2021, and 2020, the Company recorded \$2.9 million, \$2.9 million and \$2.9 million, respectively, of sub-lease rental income as an offset to its operating expenses.

The Sub-Sublease provides for initial annual base rent for the complete Sub-Subleased Premises of approximately \$2.7 million, with increases of approximately 3.5% in annual base rent on September 1, 2019, and each anniversary thereof. The Sub-Sublease rental income excludes reimbursements for executory costs received from the Sub-Subtenant. The Sub-Sublease became effective on September 24, 2018, and has a term of 5.2 years which terminates on December 15, 2023. The Sub-Sublease will terminate if the Lease or the corresponding master lease terminates. The Company or the Sub-Subtenant may elect, subject to limitations set forth in the Sub-Sublease, to terminate the Sub-Sublease following a material casualty or condemnation affecting the Subleased Premises. The Company may terminate the Sub-Sublease following an event of default, which is defined in the Sub-Sublease to include, among other things, non-payment of amounts owing by the Sub-Subtenant under the Sub-Sublease.

The Company is required under the Lease to pay to the sublandlord 50% of that portion of the cash sums and other economic consideration received from the Sub-Subtenant that exceeds the base rent paid by the Company to the sublandlord after deducting certain of the Company's costs.

Dublin

In June 2021, the Company entered into a new lease agreement for new office space in Dublin, Ireland, which commenced in August 2021 and has a term of one year. This lease has an automatic renewal clause, pursuant to which the agreement will be extended automatically for successive periods equal to the current term, unless the agreement is cancelled by the Company. In May 2022, the Company renewed the lease for another one year term starting August 2022.

New Brisbane Facility

On October 28, 2022, Prothena Biosciences Inc, a wholly owned subsidiary of the Company, entered into a noncancelable operating sublease (the "New Sublease") to sublease approximately 31,157 square feet of office and laboratory space located in Brisbane, California (the "New Facility") with Arcus Biosciences, Inc., (the "Sublandlord"). The New Sublease became effective on October 28, 2022. The New Sublease provides that the Company's obligation to pay rent shall commence 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 is due upon execution of the New 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 New Sublease further provides that the Company is obligated to pay to the Sublandlord certain costs, including taxes and operating expenses. The Company has the option to expand the sublease to include additional space by providing written notice prior to April 30, 2023. Additionally, 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.

The Company is entitled to an improvement allowance of up to \$9.3 million, to be used for costs incurred by the Company to construct certain improvements to the New Facility and to prepare for the Company's occupancy of the New Facility.

In conjunction with the New 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 New 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, 2022, none of the standby letter of credit amount of \$0.9 million has been used.

As of December 31, 2022, the term of the New Sublease has not commenced as the Company did not have the right to use or control physical access to the New Facility, and therefore no right-of-use asset and lease liability relating to the New Sublease has been recorded in the Balance Sheet as of December 31, 2022.

Future minimum payments under the above-described noncancelable operating leases, including a reconciliation to the lease liabilities recognized in the Consolidated Balance Sheets, and future minimum rentals to be received under the Sub-Sublease as of December 31, 2022, are as follows (in thousands):

Year Ended December 31,	Operating Leases	Sub-Sublease Rental
2023	6,624	3,019
2024	2,707	—
2025	3,051	—
2026	3,158	—
2027	3,269	—
Thereafter	2,523	—
Total	\$ 21,332	\$ 3,019
Less: Present value adjustment	(151)	
Lease commitments on New Sublease that has not yet commenced	(14,708)	
Lease liability	\$ 6,473	

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, 2022, and 2021.

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, 2022, the Company had non-cancelable purchase commitments to suppliers for \$11.5 million of which \$5.6 million is included in accrued current liabilities, and contractual obligations under license agreements of \$0.4 million of which \$29 thousand is included in accrued current liabilities. The following is a summary of the Company's non-cancelable purchase commitments and contractual obligations as of December 31, 2022 (in thousands):

	Total	2023	2024	2025	2026	2027	Thereafter
Purchase Obligations ⁽¹⁾	\$ 11,467	\$ 11,382	\$ 85	\$ —	\$ —	\$ —	\$ —
Contractual obligations under license agreements	431	89	64	64	64	60	90
Total	\$ 11,898	\$ 11,471	\$ 149	\$ 64	\$ 64	\$ 60	\$ 90

⁽¹⁾ Purchase obligations consist of non-cancelable purchase commitments to suppliers and contract research organizations.

Legal Proceedings

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

7. Significant Agreements

Roche License Agreement

In December 2013, the Company through its wholly owned subsidiary Prothena Biosciences Limited and Prothena Biosciences Inc entered into a License, Development, and Commercialization Agreement (the "License Agreement") with F. Hoffmann-La Roche Ltd. and Hoffmann-La Roche Inc. (together, "Roche") to develop and commercialize certain antibodies that target α -synuclein, including prasinezumab, which are referred to collectively as "Licensed Products." Upon the effectiveness of the License Agreement in January 2014, the Company granted to Roche an exclusive, worldwide license to develop, make, have made, use, sell, offer to sell, import and export the Licensed Products. The Company retained certain rights to conduct development of the Licensed Products and an option to co-promote prasinezumab in the U.S. During the term of the License Agreement, the Company and Roche will work exclusively with each other to research and develop antibody products targeting alpha-synuclein (or α -synuclein) potentially including incorporation of Roche's proprietary Brain Shuttle™ technology to potentially increase delivery of therapeutic antibodies to the brain. The License Agreement provided for Roche making an upfront payment to the Company of \$30.0 million, which was received in February 2014; making a clinical milestone payment of \$15.0 million upon initiation of the Phase 1 study 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 study 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 filed an Investigational New Drug Application ("IND") with the FDA for prasinezumab and subsequently initiated a Phase 1 study in 2014. Following the Phase 1 studies, Roche became primarily responsible for developing, obtaining and maintaining regulatory approval for and commercializing Licensed Products. Roche also became responsible for the clinical and commercial manufacture and supply of Licensed Products.

In addition, the Company has an option under the License Agreement to co-promote prasinezumab in the U.S. in the Parkinson's disease indication. If the Company exercises such option, it may also elect to co-promote additional Licensed Products in the U.S. approved for Parkinson's disease. Outside the U.S., Roche will have responsibility for developing and commercializing the Licensed Products. Roche bears all costs that are specifically related to obtaining or maintaining regulatory approval outside the U.S. and will pay the Company a variable royalty based on annual net sales of the Licensed Products outside the U.S.

The License Agreement continues on a country-by-country basis until the expiration of all payment obligations under the License Agreement. The License Agreement may also be terminated (i) by Roche at will after the first anniversary of the

effective date of the License Agreement, either in its entirety or on a Licensed Product-by-Licensed Product basis, upon 90 days' prior written notice to the Company prior to first commercial sale and 180 days' prior written notice to Prothena after first commercial sale, (ii) by either party, either in its entirety or on a Licensed Product-by-Licensed Product or region-by-region basis, upon written notice in connection with a material breach uncured 90 days after initial written notice, and (iii) by either party, in its entirety, upon insolvency of the other party. The License Agreement may be terminated by either party on a patent-by-patent and country-by-country basis if the other party challenges a given patent in a given country. The Company's rights to co-develop Licensed Products under the License Agreement will terminate if the Company commences certain studies for certain types of competitive products. The Company's rights to co-promote Licensed Products under the License Agreement will terminate if the Company commences a Phase 3 study for such competitive products.

The License Agreement cannot be assigned by either party without the prior written consent of the other party, except to an affiliate of such party or in the event of a merger or acquisition of such party, subject to certain conditions. The License Agreement also includes customary provisions regarding, among other things, confidentiality, intellectual property ownership, patent prosecution, enforcement and defense, representations and warranties, indemnification, insurance, and arbitration and dispute resolution.

Collaboration Accounting

The License Agreement was evaluated under ASC 808, Collaborative Agreements. At the outset of the License Agreement, the Company concluded that it did not qualify as a collaboration under ASC 808 because the Company does not share significant risks due to the net profit and loss split (under which Roche incurs substantially more of the costs of the collaboration) and because of the Company's opt-out provision. The Company believes that Roche will be the principal in future sales transactions with third parties as Roche will be the primary obligor bearing inventory and credit risk. The Company will record its share of pre-tax commercial profit generated from the collaboration as collaboration revenue once the Company can conclude it is probable that a significant revenue reversal will not occur in future periods. Prior to commercialization of a Licensed Product, the Company's portion of the expenses related to the License Agreement reflected on its income statement will be limited to R&D expenses. After commercialization, if the Company opts in to co-detail commercialization, expenses related to commercial capabilities, including expenses related to the establishment of a field sales force and other activities to support the Company's commercialization efforts, will be recorded as sales, general and administrative ("SG&A") expense and will be factored into the computation of the profit and loss share. The Company will record the receivable related to commercialization activities as collaboration revenue once the Company can conclude it is probable that a significant revenue reversal will not occur in future periods.

Performance Obligations

The License Agreement was evaluated under ASC 606. The License Agreement includes the following distinct performance obligations: (1) the Company's grant of an exclusive royalty bearing license, with the right to sublicense to develop and commercialize certain antibodies that target α -synuclein, including prasinezumab, and the initial know how transfer which was delivered at the effective date (the "Royalty Bearing License"); (2) the Company's obligation to supply clinical material as requested by Roche for a period up to twelve months (the "Clinical Product Supply Obligation"); (3) the Company's obligation to provide manufacturing related services to Roche for a period up to twelve months (the "Supply Services Obligation"); (4) the Company's obligation to prepare and file the IND (the "IND Obligation"); and (5) the Company's obligation to provide development activities under the development plan during Phase 1 clinical trials (the "Development Services Obligation"). Revenue allocated to the above performance obligations under the License Agreement are recognized when the Company has satisfied its obligations either at a point in time or over a period of time.

The Company concluded that the Royalty Bearing License and the Clinical Product Supply Obligation were satisfied at a point in time. The Royalty Bearing License is considered to be a functional intellectual property, in which the revenue would be recognized at the point in time since (a) the Company concluded that the license to Roche has a significant stand-alone functionality, (b) the Company does not expect the functionality of the intellectual property to be substantially changed during the license period as a result of activities of Prothena, and (c) Prothena's activities transfer a good or service to Roche. The Clinical Product Supply Obligation does not meet criteria for over time recognition; as such, the revenue related to such performance obligation was recognized at the point in time at which Roche obtained control of manufactured supplies, which occurred during the first quarter of 2014.

The Company concluded that the Supply Services Obligation, the IND Obligation and the Development Services Obligation were satisfied over time. The Company utilized an input method measure of progress by basing the recognition period on the efforts or inputs towards satisfying the performance obligation (i.e. costs incurred and the time elapsed to

complete the related performance obligations). The Company determined that such input method provides an appropriate measure of progress toward complete satisfaction of such performance obligations.

As of December 31, 2022, and December 31, 2021, there were no remaining performance obligations under 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.

Significant Payment Terms

Payments for development services are due within 45 days after receiving an invoice from the Company. Variable considerations related to clinical and regulatory milestone payments are constrained due to high likelihood of a revenue reversal. The payment term for all milestone payments are due within 45 days after the achievement of the relevant milestone and receipt by Roche of an invoice for such an amount from the Company.

According to ASC 606-10-32-17, a significant financing component does not exist if a substantial amount of the consideration promised by the customer is variable, and the amount or timing of that consideration varies on the basis of the occurrence or nonoccurrence of a future event that is not substantially within the control of the customer or the entity. Since a “substantial amount of the consideration” promised by Roche to the Company is variable (i.e., is in the form of either milestone payments or sales-based royalties) and the amount of such variable consideration varies based upon the occurrence or nonoccurrence of future events that are not within the control of either Roche or the Company (i.e., are largely subject to regulatory approval), the License Agreement does not have a significant financing component.

Post Contract Deliverables

Any development services provided by the Company after performance of the Development Service Obligation are not considered a contractual performance obligation under the License Agreement, since the License Agreement does not require the Company to provide any development services after completion of the Development Service Obligation. However, the collaboration’s Joint Steering Committee approved continued funding for additional development services to be provided by the Company (the “Additional Development Services”). Under the License Agreement the Company recognizes the reimbursements for Additional Development Services as collaboration revenue as earned.

Revenue and Expense Recognition

No collaboration revenue from Roche was recognized for the year ended December 31, 2022 as compared to \$60.2 million and \$0.6 million for the years ended December 31, 2021 and 2020, respectively. For the year ended December 31, 2021 collaboration revenue from Roche included a \$60.0 million clinical milestone recognized upon first patient dosed in the PADOVA study. Through May 28, 2021, cost sharing payments to Roche were recorded as R&D expenses. The Company recognized nil in R&D expenses for payments made to Roche during the year ended December 31, 2022, as compared to \$7.2 million and \$17.4 million for the years ended December 31, 2021 and 2020, respectively. The Company had accounts receivable from Roche of nil at December 31, 2022, and 2021, respectively.

Milestone Accounting

Under the License Agreement, only if the U.S. and or global options are exercised, the Company is eligible to receive milestone payments upon the achievement of development, regulatory and various first commercial sales milestones. Milestone payments are evaluated under ASC Topic 606. Factors considered in this determination included scientific and regulatory risk that must be overcome to achieve each milestone, the level of effort and investment required to achieve the milestone, and the monetary value attributed to the milestone. Accordingly, the Company estimates payments in the transaction price based on the most likely approach, which considers the single most likely amount in a range of possible amounts related to the achievement of these milestones. Additionally, milestone payments are included in the transaction price only when the Company can conclude it is probable that a significant revenue reversal will not occur in future periods when the milestone is achieved.

The Company excludes the milestone payments and royalties in the initial transaction price calculation because such payments are considered to be variable considerations with constraint. Such milestone payments and royalties will be recognized as revenue once the Company can conclude it is probable that a significant revenue reversal will not occur in future periods.

The clinical and regulatory milestones under the License Agreement after the point at which the Company could opt out are considered to be variable considerations with constraint due to the fact that active participation in the development activities

that generate the milestones is not required under the License Agreement, and the Company can opt out of these activities. There are no refunds or claw-back provisions and the milestones are uncertain of occurrence even after the Company has opted out. Based on this determination, these milestones will be recognized when the Company can conclude it is probable that a significant revenue reversal will not occur in future periods.

Collaboration Agreement with Bristol Myers Squibb

Overview

On March 20, 2018, the Company, through its wholly owned subsidiary Prothena Biosciences Limited (“PBL”), entered into a Master Collaboration Agreement (the “Collaboration Agreement”) with Celgene Switzerland LLC (“Celgene”), a subsidiary of Celgene Corporation (which was acquired by Bristol Myers Squibb (“BMS”) in November 2019), pursuant to which Prothena granted to Celgene a right to elect in its sole discretion to exclusively license rights both in the U.S. (the “US Rights”) and on a global basis (the “Global Rights”), with respect to the Company’s programs to develop and commercialize antibodies targeting tau, TDP-43 and an undisclosed target (the “Collaboration Targets”). For each such program, BMS may exercise its US Rights at the IND filing, and if it so exercises such US Rights would also have a right to expand the license to Global Rights. If BMS exercises its US Rights for a program, then following the first to occur of (a) completion by the Company, in its discretion and at its cost, of Phase 1 clinical trials for such program or (b) the date on which BMS elects to assume responsibility for completing such Phase 1 clinical trials (at its cost), BMS would have decision making authority over development activities and all regulatory, manufacturing and commercialization activities in the U.S. As discussed below, BMS exercised its US Rights for the tau/PRX005 Collaboration Target and on July 30, 2021, PBL entered into a U.S. License Agreement granting BMS the exclusive license to develop, manufacture and commercialize antibody products in the United States targeting tau (the “Tau US License Agreement”).

The Collaboration Agreement provided for Celgene making an upfront payment to the Company of \$100.0 million which was received in April 2018, plus future potential license exercise payments and regulatory and commercial milestones for each program under the Collaboration Agreement, as well as royalties on net sales of any resulting marketed products. In connection with the Collaboration Agreement, the Company and Celgene entered into a Share Subscription Agreement on March 20, 2018, under which Celgene subscribed to 1,174,536 of the Company’s ordinary shares for a price of \$42.57 per share, for a total of approximately \$50.0 million.

BMS US and Global Rights and Licenses

On a program-by-program basis, beginning on the effective date of the Collaboration Agreement and ending on the date that the IND Option term expires for such program (which generally occurs sixty days after the date on which the Company delivers to BMS the first complete data package for an IND that was filed for a lead candidate from the relevant program), BMS may elect in its sole discretion to exercise its US Rights to receive an exclusive license to develop, manufacture and commercialize antibodies targeting the applicable Collaboration Target in the U.S. (the “US License”). If BMS exercises its US Rights for a collaboration program, it is obligated to pay the Company an exercise fee of approximately \$80.0 million per program. Thereafter, following the first to occur of (a) completion by the Company, in its discretion and at its cost, of Phase 1 clinical trials for such program or (b) BMS’s election to assume responsibility to complete such Phase 1 clinical trials (at its cost), BMS would have the sole right to develop, manufacture and commercialize antibody products targeting the relevant Collaboration Target for such program (the “Collaboration Products”) in the U.S.

On a program-by-program basis, following completion of a Phase 1 clinical trial for a collaboration program for which BMS has previously exercised its US Rights, BMS may elect in its sole discretion to exercise its Global Rights with respect to such collaboration program to receive a worldwide, exclusive license to develop, manufacture and commercialize antibodies targeting the applicable Collaboration Target (the “Global License”). If BMS exercises its Global Rights, BMS would be obligated to pay the Company an additional exercise fee of \$55.0 million for such collaboration program. The Global Rights would then replace the US Rights for that collaboration program, and BMS would have decision making authority over developing, obtaining and maintaining regulatory approval for, manufacturing and commercializing the Collaboration Products worldwide.

After BMS’s exercise of Global Rights for a collaboration program, the Company is eligible to receive up to \$562.5 million in regulatory and commercial milestones per program. Following an exercise by BMS of either US Rights or Global Rights for such collaboration program, the Company will also be eligible to receive tiered royalties on net sales of Collaboration Products ranging from high single digit to high teen percentages, on a weighted average basis depending on the achievement of certain net sales thresholds. Such exercise fees, milestones and royalty payments are subject to certain reductions as specified in the Collaboration Agreement, the agreement for US Rights and the agreement for Global Rights.

BMS will continue to pay royalties on a Collaboration Product-by-Collaboration Product and country-by-country basis, until the latest of (i) expiration of certain patents covering the Collaboration Product, (ii) expiration of all regulatory exclusivity for the Collaboration Product, and (iii) an agreed period of time after the first commercial sale of the Collaboration Product in the applicable country (the “Royalty Term”).

Term and Termination

The research term under the Collaboration Agreement continues for a period of six years, which BMS may extend for up to two additional 12-month periods by paying an extension fee of \$10.0 million per extension period. The term of the Collaboration Agreement continues until the last to occur of the following: (i) expiration of the research term; (ii) expiration of all US Rights terms; and (iii) expiration of all Global Rights terms.

The term of any US License or Global License would continue on a Licensed Product-by-Licensed Product and country-by-country basis until the expiration of all Royalty Terms under such agreement.

The Collaboration Agreement may be terminated (i) by either party on a program-by-program basis if the other party remains in material breach of the Collaboration Agreement following a cure period to remedy the material breach, (ii) by BMS at will on a program-by-program basis or in its entirety, (iii) by either party, in its entirety, upon insolvency of the other party, or (iv) by the Company, in its entirety, if BMS challenges a patent licensed by the Company to BMS under the Collaboration Agreement.

Share Subscription Agreement

Pursuant to the terms of the Collaboration Agreement, the Company entered into a Share Subscription Agreement (the “SSA”) with Celgene, pursuant to which the Company issued, and Celgene subscribed for, 1,174,536 of the Company’s ordinary shares (the “Shares”) for an aggregate subscription price of approximately \$50.0 million, pursuant to the terms and conditions thereof.

Under the SSA, BMS (formerly Celgene) is subject to certain transfer restrictions. In addition, BMS will be entitled to request the registration of the Shares with the SEC on Form S-3ASR or Form S-3 following termination of the transfer restrictions if the Shares cannot be resold without restriction pursuant to Rule 144 promulgated under the U.S. Securities Act of 1933, as amended.

Collaboration Accounting

The Collaboration Agreement was evaluated under ASC 808, Collaborative Agreements. At the outset of the Collaboration Agreement, the Company concluded that it does not qualify as a collaboration under ASC 808 because the Company does not share significant risks due to economics of the collaboration.

Performance Obligations

The Company assessed the Collaboration Agreement and concluded that it represented a contract with a customer within the scope of ASC 606. Per ASC 606, a performance obligation is defined as a promise to transfer a good or service or a series of distinct goods or services. At inception of the Collaboration Agreement, the Company is not obligated to transfer the US License or Global License to BMS unless BMS exercises its US Rights or Global Rights, respectively, and the Company is not obligated to perform development activities under the development plan during preclinical and Phase 1 clinical trials including the regulatory filing of the IND.

The discovery, preclinical and clinical development activities performed by the Company are to be performed at the Company’s discretion and are not promised goods or services and therefore are not considered performance obligations under ASC 606, unless and until the Company agrees to perform the Phase 1 clinical studies (after the IND option exercise) that are determined to be performance obligations at the time the option is exercised. Per the terms of the Collaboration Agreement, the Company may conduct discovery activities to characterize, identify and generate antibodies to become collaboration candidates that target such Collaboration Target, and thereafter may pre-clinically develop collaboration candidates to identify lead candidates that target such Collaboration Target and file an IND with the U.S. Food and Drug Administration (the “FDA”) for a Phase 1 clinical trial for such lead candidates. In the event the Company agrees to be involved in a Phase 1 clinical study, the Company will further evaluate whether any such promise represents a performance obligation at the time the option is

exercised. If it is concluded that the Company has obligated itself to an additional performance obligation besides the license granted at IND option exercise, then the effects of the changes in the arrangement will be evaluated under the modification guidance of ASC 606.

The Company is not obligated to perform manufacturing activities. Per the terms of the Collaboration Agreement, to the extent that the Company, at its discretion, conducts a program, the Company shall be responsible for the manufacture of collaboration candidates and collaboration products for use in such program, as well as the associated costs. Delivery of manufactured compound (clinical product supply) is not deemed a performance obligation under ASC 606 as the Company is not obligated to transfer supply of collaboration product to BMS unless BMS exercises its right to participate in the Phase 1 development.

Compensation for the Company's provision of inventory supply, to the extent requested by BMS would be paid to the Company by BMS at a reasonable stand-alone selling price for such supply. Given that (i) there is substantial uncertainty about the development of the programs, (ii) the pricing for the inventory is at its standalone selling price and (iii) the manufacturing services require the entity to transfer additional goods or services that are incremental to the goods and services provided prior to the resolution of the contingency, the Company's supply of product is not a material right. Therefore, the inventory supply is not considered a performance obligation unless and until, requested by BMS.

In addition to the grant of the US License after BMS exercises its US Rights for a program, BMS is entitled to receive certain ancillary development services from the Company, such as technology transfer assistance, regulatory support, safety data reporting activities and transition supply, if requested by BMS.

In addition to the grant of the Global License after BMS exercises the Global Rights for a program, BMS is entitled to receive certain ancillary development services from the Company, such as ongoing clinical trial support upon request by BMS, transition supply, if requested by BMS, and regulatory support for coordination of pharmacovigilance matters.

The Company evaluated the potential obligations to transfer the US Licenses and Global Licenses and performance of the ancillary development services subsequent to exercise of the US Rights and Global Rights, if the options are exercised by BMS, under ASC 606-10-55-42 and 55-43 to determine whether the US Rights or the Global Rights provided BMS a "material right" and concluded that BMS's options to exercise its US Rights and Global Rights represented "material rights" to BMS that it would not have received without entering into the Agreement.

There are a total of six options including US Rights and Global Rights to acquire a US License and a Global License, respectively, and rights to request certain development services (following exercise of the US Rights and Global Rights, respectively) for each of the three programs. Per ASC 606, the US Rights and Global Rights are material rights and therefore are performance obligations. The goods and services underlying the options are not accounted for as separate performance obligations, but rather become performance obligations, if and when, an option is exercised.

US License Agreement for the Tau/PRX005 Collaboration Target

On July 30, 2021, the Company entered into the Tau US License Agreement. The Tau US License Agreement includes an upfront payment of \$80.0 million and the Company will be eligible to receive regulatory and sales milestones up to \$465.0 million upon achievement of certain developmental events, including regulatory approval, of a tau Collaboration Product, and on BMS achieving certain annual net sales thresholds in the United States. The Company also will be 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 achieving of certain net sales thresholds. Such exercise fees, milestones, and royalty payments are subject to certain reductions as specified in the agreement.

The Tau US License Agreement includes the following distinct performance obligations: (1) the delivery of the US License for tau/PRX005 Collaboration Target ("Tau US License Obligation"); and (2) the Company's obligation to provide development activities under the development plan during Phase 1 clinical trials (the "Tau US Development Services Obligation"). Revenue allocated to the Tau US License Obligation is recognized when the Company has satisfied its obligation at a point in time, while the revenue allocated to the Tau US Development Services Obligation are recognized over time using an input-based model.

Transaction Price

According to ASC 606-10-32-2, the transaction price is the amount of consideration to which an entity expects to be entitled in exchange for transferring promised goods or services to a customer, excluding amounts collected on behalf of third parties (for example, some sales taxes). The consideration promised in a contract with a customer may include fixed amounts, variable amounts, or both. Factors considered in the determination of the transaction price included, among other things, estimated selling price of the license and costs for clinical supply and development costs.

At the inception of the Collaboration Agreement, the Company did not transfer any goods or services to BMS (formerly Celgene) that are material. Accordingly, the Company has concluded that the initial transaction price will be recognized as a contract liability and will be deferred until the Company transfers control of goods or services to BMS (which would be when BMS exercises the US Right or Global Right and receives control of the US License or Global License for at least one of the programs), or when the IND Option term expires if BMS does not exercise the US Right (which is generally sixty days after the date on which the Company delivers to BMS the first complete data package for an IND that was filed for a lead candidate from the relevant program), or when the Phase 1 Option term expires if BMS does not exercise the Global Right (which is generally ninety days after the date on which the Company delivers to BMS the first complete data package for a Phase 1 clinical trial for a lead candidate from the relevant program) or at the termination of the Collaboration Agreement, whichever occurs first. At such point that the Company transfers control of goods or services to BMS, or when the option expires, the Company will recognize revenue as a continuation of the original contract. Under this approach, the Company will treat the consideration allocated to the material right as an addition to the consideration for the goods or services underlying the contract option.

At inception of the Collaboration Agreement, the Company estimated the standalone selling price for each performance obligation (i.e., the US Rights and Global Rights by program). The estimate of standalone selling price for the US Rights and Global Rights by program was based on the adjusted market assessment approach using a discounted cash flow model. The key assumptions used in the discounted cash flow model included the market opportunity for commercialization of each program in the U.S. or globally depending on the license, the probability of successfully developing and commercializing a given program target, the estimated remaining development costs for the respective program, the estimated time to commercialization of the drug for that program and a discount rate.

The initial transaction price under the Collaboration Agreement, pursuant to ASC 606, was \$110.2 million, including the \$100.0 million upfront payment and \$10.2 million premium on the ordinary shares purchased under the SSA. The Company expects that the initial transaction price will be allocated across the US Rights and Global Rights for each program in a range of approximately \$15-\$25 million and \$10-\$18 million, respectively.

The Company did not include the option fees in the initial transaction price because such fees are contingent on the options to the US Rights and the Global Rights being exercised. Upon the exercise of the US Rights and the Global Rights for a program, the Company will have the obligation to deliver the US License and Global License and provide certain ancillary development services if requested by BMS, subsequent to its exercise of the US Rights and Global Rights, respectively, for such program. The Company will include the option fees in the transaction price at the point in time a material right is exercised and the Company transfers control of the goods and services to BMS. In addition, the Company did not include in the initial transaction price certain clinical and regulatory milestone payments since they relate to licenses for which BMS has not yet exercised its option to obtain and these variable considerations are constrained due to the likelihood of a significant revenue reversal.

Upon entering into the Tau US License Agreement, the Company granted BMS a US License for the tau/PRX005 Collaboration Target, which transferred control of such underlying US License to BMS. Following execution of the Tau US License Agreement, BMS paid the Company an \$80.0 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 US License for tau/PRX005. The Company used the original allocated consideration for the US Right for tau/PRX005 of \$24.9 million (computed at the inception of the contract) plus the \$80.0 million option exercise fee to arrive at the total transaction price of approximately \$104.9 million. This total transaction price was further allocated using the relative sales price method between the Tau US License Obligation and the Tau US Development Services Obligation.

The best estimate of selling price for the US License for tau/PRX005 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 tau/PRX005, the probability of successfully developing/commercializing PRX005, the remaining development costs for tau/PRX005, and the estimated time to commercialization of tau/PRX005. Based on the relative selling price method, the amount that the Company allocated to the performance obligations

is as follows: \$77.5 million to the license to be recognized concurrent with the delivery of the license; and \$27.5 million as development services to be recognized based on percentage completion over the service period estimated to be from 2021-2024.

Significant Payment Terms

The upfront payment of \$100.0 million was due within ten business days after the effective date of the Collaboration Agreement and was received in April 2018, while all option fees and milestone payments are due within 30 days after the achievement of the relevant milestone by BMS or receipt by BMS of an invoice for such an amount from the Company.

The Collaboration Agreement does not have a significant financing component since a substantial amount of consideration promised by BMS to the Company is variable and the amount of such variable consideration varies based upon the occurrence or non-occurrence of future events that are not within the control of either BMS or the Company. Variable considerations related to clinical and regulatory milestone payments and option fees are constrained due to the likelihood of a significant revenue reversal.

Revenue and Expense Recognition

For the year ended December 31, 2022, collaboration revenue from BMS recognized based on an input-based model included \$13.9 million for Tau US Development Services Obligation recognized as collaboration revenue. For the years ended December 31, 2021, collaboration revenue included \$77.5 million in US License revenue and \$2.2 million for Tau US Development Services Obligation for a total of \$79.7 million in collaboration revenue. As of December 31, 2022, the aggregate amount of the transaction price allocated to the performance obligations that are unsatisfied was \$11.4 million. The Company had no accounts receivable from BMS at December 31, 2022, and December 31, 2021, respectively.

Deferred Revenue

The deferred revenue balance at the beginning of the fiscal year was \$110.6 million of which \$13.9 million was recognized as revenue related to the Tau US Development Services Obligation performed during the year ended December 31, 2022. As of December 31, 2022, the deferred revenue balance was \$96.7 million, of which \$11.4 million was current and the balance of \$85.3 million was long term deferred revenue. The deferred revenue balance as of December 31, 2022, includes amounts deferred related to outstanding US Rights and Global Rights of \$85.3 million and unsatisfied performance obligations for the US Rights for the tau/PRX005 program of \$11.4 million.

Milestone and Royalties Accounting

The Company is eligible to receive milestone payments of up to \$90.0 million per program upon the achievement of certain specified regulatory milestones and milestone payments of up to \$375.0 million per program upon the achievement of certain specified commercial sales milestones under the US License for such program. The Company is also eligible to receive milestone payments of up to \$187.5 million per program upon the achievement of certain specified regulatory milestones and milestone payments of up to \$375.0 million per program upon the achievement of certain specified commercial sale milestones under the Global License for such program. Milestone payments are evaluated under ASC Topic 606. Factors considered in this determination included scientific and regulatory risk that must be overcome to achieve each milestone, the level of effort and investment required to achieve the milestone, and the monetary value attributed to the milestone. Accordingly, the Company estimates payments in the transaction price based on the most likely approach, which considers the single most likely amount in a range of possible amounts related to the achievement of these milestones. Additionally, milestone payments are included in the transaction price only when the Company can conclude it is probable that a significant revenue reversal will not occur in future periods.

The Company excluded the milestone payments and royalties in the initial transaction price because such payments are considered to be variable considerations with constraint. Such milestone payments and royalties will be recognized as revenue at a point in time when the Company can conclude it is probable that a significant revenue reversal will not occur in future periods.

The Company did not achieve any clinical and regulatory milestones under the Collaboration Agreement during the years ended December 31, 2022 and 2021.

Novo Nordisk Share Purchase Agreement

On July 8, 2021, the Company together with its wholly owned subsidiary, Prothena Biosciences Limited (“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 consists 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 NNC6019 (formerly PRX004) or a derivative thereof in ATTR amyloidosis, PBL is entitled to receive certain milestone payments based on specified development and commercial milestones. The development and commercialization milestone payments will be discounted if the milestone events are achieved with respect to other indications. Should Novo Nordisk achieve specified thresholds of worldwide, annual net sales of the milestone products, regardless of indication, PBL will also be entitled to receive specified one-time net sales milestone payments. All milestone payments attributable to an achieved milestone will be paid to PBL, subject to Novo Nordisk’s offset right for indemnity claims or unpaid amounts in respect of any purchase price adjustment.

The upfront payment of \$60.0 million was accounted for as revenue for the year ended December 31, 2021. In addition to the upfront payment, Novo Nordisk agreed to pay for certain out of pocket expenses under the Transition Services Agreement, which netted to \$0.7 million after closing adjustments related to the sale of the ATTR amyloidosis business and pipeline.

Contingent Consideration /Milestone Accounting

In December 2022, the Company received a \$40.0 million development milestone payment related to the continued advancement of NNC6019 in a Phase 2 clinical study for the treatment of ATTR cardiomyopathy. This amount was accounted for as revenue from license and intellectual property for the year ended December 31, 2022.

The Company is eligible to receive additional development and sales milestone payments from Novo Nordisk totaling up to \$1.13 billion upon achievement of certain specified development and commercial sales milestones under the share purchase agreement.

The Company excluded the milestone payments in the initial transaction price because such payments are considered to be variable considerations with constraint. Such milestone payments will be recognized as revenue at a point in time when the Company can conclude it is probable that a significant revenue reversal will not occur in future periods.

Revenue Recognition

Total revenue recognized related to the transaction during the year ended December 31, 2022 and 2021 was \$40.0 million and \$60.7 million, respectively. The Company had no accounts receivable from Novo Nordisk as of December 31, 2022 and 2021, respectively.

8. Shareholders' Equity

Ordinary Shares

As of December 31, 2022, the Company had 100,000,000 ordinary shares authorized for issuance with a par value of \$0.01 per ordinary share and 52,103,608 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.

Euro Deferred Shares

As of December 31, 2022, 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, 2022. 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.

March 2021 Offering

In March 2021, the Company completed an underwritten public offering of an aggregate of 4,025,000 of its ordinary shares at a public offering price of \$20.75 per ordinary share. The Company received aggregate net proceeds of approximately \$78.0 million, after deducting the underwriting discount and offering costs.

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.

At-the-Market Offerings

In May 2021, the Company entered into an Equity Distribution Agreement (the “May 2021 Distribution Agreement”), pursuant to which the Company could issue and sell, from time to time, shares of the Company's ordinary shares. In connection with entering into the May 2021 Distribution Agreement, on May 28, 2021, the Company filed with the SEC a prospectus supplement relating to the offer, issuance and sale of up to \$100.0 million of the Company's ordinary shares pursuant to the May 2021 Distribution Agreement. For the year ended December 31, 2021, the Company issued 1,640,174 ordinary shares pursuant to the May 2021 Distribution Agreement, for total gross proceeds of approximately \$100.0 million before deducting underwriting discounts, commissions, and other offering expenses payable by the Company of \$3.2 million. The May 2021 Distribution Agreement was no longer effective as of December 23, 2021.

In December 2021, the Company entered into an Equity Distribution Agreement (the “December 2021 Distribution Agreement”), pursuant to which the Company may 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 pursuant to the December 2021 Distribution Agreement. For the year ended December 31, 2022, the Company sold and issued 911,228 ordinary shares, pursuant to the December 2021 Distribution Agreement, for total gross proceeds of approximately \$53.1 million before deducting underwriting discounts, commissions, and other offering expenses payable by the Company of \$1.7 million.

The issuance and sale of the Company's ordinary shares pursuant to the May 2021 Distribution Agreement and the December 2021 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 ISOs, NQSOs, SARs, 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 2022, 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, 2022, the number of ordinary shares authorized under the 2018 LTIP was 12,614,183. Upon adoption of the 2018 LTIP, no new awards are permitted under the 2012 LTIP.

As of December 31, 2022, the number of ordinary shares authorized under the 2020 EIIP was 1,470,000 and 70,000 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 granted 2,309,436, 3,530,477 (1,372,587 of which were replacement options granted pursuant to the Option Exchange, as discussed below) and 2,108,950 options during the years ended December 31, 2022, 2021 and 2020, respectively, in aggregate under its equity plans. The Company's option awards generally vest over four years, while RSUs vest over two years. As of December 31, 2022, 3,104,093 ordinary shares remained available for grant under its equity plans, 23,000 RSUs were outstanding and unvested, and options to purchase 9,479,998 ordinary shares in aggregate under the Company's equity plans were outstanding with a weighted-average exercise price of approximately \$23.16 per share.

2020 Option Exchange Program

On May 19, 2020, the Company's shareholders approved a proposal to allow for a one-time option exchange program (the "Option Exchange") designed to give its employees, including our named executive officers, and non-employee directors of the Company, who are employed by or providing services to the Company through the completion of the Option Exchange, the opportunity to exchange eligible options for new replacement options with an exercise price equal to the fair market value of the Company's ordinary shares on the date the replacement options are granted. Any new replacement options would be subject to a new initial one-year vesting period from the replacement option grant date and after such initial one-year vesting period would vest in substantially equal installments on the remaining original vesting dates of each exchanged option. Additionally, any new replacement options would have a term equal to the remaining term of the applicable exchanged option.

On November 9, 2020, the Company commenced the Option Exchange which closed on February 12, 2021. Options to purchase approximately 2.1 million ordinary shares were exchanged for options to purchase approximately 1.4 million ordinary shares with an exercise price of \$22.85 per share. Options were eligible to exchange if they had an exercise price equal to or greater than \$17.63 per share, were granted prior to April 23, 2018, under the 2012 LTIP, and were held by an eligible participant. No incremental share-based compensation expense was recognized for the Option Exchange.

Share-based Compensation Expense

The Company estimates the fair value of share-based compensation on the date of grant using an option-pricing model. The Company uses the Black-Scholes model to value share-based compensation, excluding RSUs, which the Company values using the fair market value of its ordinary shares on the date of grant. The Black-Scholes option-pricing model determines the fair value of share-based payment awards based on the share price on the date of grant and is affected by assumptions regarding a number of complex and subjective variables. These variables include, but are not limited to, the Company's share price, volatility over the expected life of the awards and actual and projected employee stock option exercise behaviors. The simplified method has been used to estimate the expected life of all options. The Company uses its historical volatility for the Company's stock to estimate expected volatility starting January 1, 2018. Although the fair value of share options granted by the Company is estimated by the Black-Scholes model, the estimated fair value may not be indicative of the fair value observed in a willing buyer and seller market transaction.

As share-based compensation expense recognized in the Consolidated Financial Statements is based on awards ultimately expected to vest, it has been reduced for estimated forfeitures. Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from estimates. Forfeitures were estimated based on estimated future turnover and historical experience. The estimated forfeiture rate as of December 31, 2022 was 8%. Changes in our estimates and assumptions relating to forfeitures may cause us to realize material changes in stock-based compensation expense in the future.

Share-based compensation expense will continue to have an adverse impact on the Company's results of operations, although it will have no impact on its overall financial position. The amount of unearned share-based compensation currently estimated to be expensed from now through the year 2026 related to unvested stock options at December 31, 2022, is \$70.0 million. The weighted-average period over which the unearned share-based compensation related to stock options is expected to be recognized is 2.58 years.

Share-based compensation expense recorded in these Consolidated Financial Statements for the years ended December 31, 2022, 2021 and 2020, respectively, was based on awards granted under the 2012 LTIP, the 2018 LTIP, and the 2020 EIIP.

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

	Year Ended December 31,		
	2022	2021	2020
Research and development	\$ 14,805	\$ 9,514	\$ 8,214
General and administrative	16,517	15,144	13,800
Total share-based compensation expense	<u>\$ 31,322</u>	<u>\$ 24,658</u>	<u>\$ 22,014</u>

The Company recognized tax benefits from share-based awards of \$5.8 million, \$4.7 million, and \$4.3 million for the years ended December 31, 2022, 2021 and 2020, respectively.

With the exception of the options granted pursuant to the Option Exchange, the fair value of the options granted to employees and non-employee directors during the years ended December 31, 2022, 2021 and 2020, respectively was estimated as of the grant date using the Black-Scholes option-pricing model assuming the weighted-average assumptions listed in the following table:

	Year Ended December 31,		
	2022	2021	2020
Expected volatility	82.4 %	81.7 %	80.9 %
Risk-free interest rate	2.2 %	1.0 %	0.9 %
Expected dividend yield	— %	— %	— %
Expected life (in years)	6.0	6.0	6.0
Weighted average grant date fair value	\$23.43	\$21.39	\$8.12

The fair value of employee stock options is being 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 significant management judgment to determine.

The following table summarizes the Company's stock option activity during the year ended December 31, 2022:

	Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2021	8,684,322	\$ 19.20	6.98	\$ 269,182
Granted	2,309,436	33.13		
Exercised	(1,282,086)	13.95		
Forfeited	(231,674)	25.20		
Expired	—	—		
Outstanding at December 31, 2022	<u>9,479,998</u>	\$ 23.16	6.82	\$ 354,856
Vested and expected to vest at December 31, 2022	9,129,523	\$ 22.80	6.74	\$ 344,875
Vested at December 31, 2022	5,639,807	\$ 18.40	5.59	\$ 236,928

The total intrinsic value of options exercised was \$49.2 million, \$33.9 million and \$0.1 million during the years ended December 31, 2022, 2021 and 2020, 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, 2022:

	Number of Units	Weighted Average Grant-Date Fair Value	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2021	—	\$ —		
Units Granted	23,000	60.89		
Units Vested	—	—		
Units Forfeited	—	—		
Outstanding at December 31, 2022	<u>23,000</u>	\$ 60.89	1.67	\$ 1,386

In 2022, the Company granted RSUs covering an equal number of Prothena's ordinary shares to employees with a weighted-average grant date fair value of \$60.89. The fair value of RSUs was determined on the date of grant based on the market price of the Company's ordinary shares as of that date. The fair value of the RSUs is recognized as an expense on a straight-line basis over the vesting period of each RSU. Upon the vesting of the RSUs, a portion of the shares vested are sold by the employee to satisfy employee withholding tax requirements (sell-to-cover). The total fair value of shares vested during the year ended December 31, 2022 was nil. As of December 31, 2022, total compensation cost not yet recognized related to unvested RSUs was \$1.3 million, which is expected to be recognized over a weighted-average period of 1.92 years. RSUs settle into ordinary shares upon vesting.

The following table summarizes information about the Company's options outstanding as of December 31, 2022:

Range of Exercise Prices	Options Outstanding			Options Exercisable		
	Number of Options	Weighted - Average Remaining Contractual Life (Years)	Weighted Average Exercise Price	Number of Options	Weighted Average Exercise Price	
\$ 6.41 \$ 11.33	955,935	6.50	\$ 10.35	697,556	\$ 10.18	
11.37 12.72	954,497	6.90	12.18	651,056	12.16	
12.76 13.53	613,160	5.71	13.53	584,708	13.53	
15.04 15.04	1,504,734	5.21	15.04	1,504,734	15.04	
16.43 22.60	983,805	7.93	22.22	462,880	21.80	
22.85 22.85	1,141,705	3.87	22.85	1,141,705	22.85	
23.97 29.81	1,023,350	7.76	26.63	361,931	26.72	
30.63 30.63	58,750	9.10	30.63	—	—	
32.45 32.45	1,422,825	9.12	32.45	—	—	
33.10 70.81	821,237	8.33	53.49	235,237	52.66	
<u>\$ 6.41 \$ 70.81</u>	<u>9,479,998</u>	<u>6.82</u>	<u>\$23.16</u>	<u>5,639,807</u>	<u>\$ 18.40</u>	

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,		
	2022	2021	2020
Ireland	\$ (119,571)	\$ 65,456	\$ (116,981)
Switzerland	—	—	8
U.S.	(6,034)	6,465	5,546
Income (loss) before provision for income taxes	<u>\$ (125,605)</u>	<u>\$ 71,921</u>	<u>\$ (111,427)</u>

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

	Year Ended December 31,		
	2022	2021	2020
Current:			
U.S. Federal	\$ 2,422	\$ 356	\$ 1,402
U.S. State	55	16	2
Switzerland	—	—	1
Ireland	—	—	—
Total current provision	<u>\$ 2,477</u>	<u>\$ 372</u>	<u>\$ 1,405</u>
Deferred:			
U.S. Federal	\$ (11,039)	\$ 4,581	\$ (1,688)
U.S. State	(94)	(7)	—
Switzerland	—	—	—
Ireland	—	—	—
Total deferred benefit	<u>\$ (11,133)</u>	<u>\$ 4,574</u>	<u>\$ (1,688)</u>
Provision for (benefit from) income taxes	<u>\$ (8,656)</u>	<u>\$ 4,946</u>	<u>\$ (283)</u>

The Company recorded a net tax shortfall (windfall) of \$(3.2) million, \$(2.3) million, and \$1.0 million for the years ended December 31, 2022, 2021 and 2020, respectively, all of which were recorded as part of its income tax provision in the Consolidated Statements of Operations.

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

	Year Ended December 31,		
	2022	2021	2020
Taxes at the Irish statutory tax rate of 12.5%	\$ (15,700)	\$ 8,990	\$ (13,928)
Income tax at rates other than applicable statutory rate	(2,338)	(398)	(3,402)
Change in valuation allowance	22,681	4,108	16,266
Share-based payments	518	5,173	3,409
Tax credits	(8,949)	(5,355)	(2,786)
Income not subject to tax	(5,000)	(7,587)	—
Other	132	15	158
Provision for (benefit from) income taxes	<u>\$ (8,656)</u>	<u>\$ 4,946</u>	<u>\$ (283)</u>

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, 2022, and 2021 are as follows (in thousands):

	December 31,	
	2022	2021
Deferred tax assets:		
Net operating loss carryforwards	\$ 136,487	\$ 115,424
Tax credits	23,193	17,552
Lease liability	1,398	2,670
Accruals and other	1,587	1,017
Capitalized R&D	10,544	—
Share-based compensation	7,628	7,114
Gross deferred tax assets	180,837	143,777
Valuation allowance	(161,098)	(133,845)
Net deferred tax assets	19,739	9,932
Deferred tax liability:		
Operating lease right-of-use assets	(1,355)	(2,626)
Fixed Assets	(180)	(235)
Net deferred tax assets	\$ 18,204	\$ 7,071

The Company's deferred tax assets ("DTA") are composed primarily of its Irish subsidiaries' net operating loss carryforwards, state net operating loss carryforwards available to reduce future taxable income of the Company's U.S. subsidiaries, federal and California tax credit carryforwards, share-based compensation, capitalized R&D, and other temporary differences. The Company maintains a valuation allowance against certain U.S. federal and state and Irish deferred tax assets. Each reporting period, the Company evaluates the need for a valuation allowance on its deferred tax assets by jurisdiction.

For the year ended December 31, 2022, the Company recorded an increase in DTA of \$11.1 million, primarily due to Section 174 R&D Capitalization requirements of \$10.5 million, which became effective in 2022. For the year ended December 31, 2021, the Company recorded a reduction in DTA of \$4.6 million, primarily due to changes in the Company's 162(m) limitations of \$3.5 million as a result of the Company's option exchange program that closed on February 12, 2021, which was considered a material modification from a tax perspective, and a \$1.0 million DTA reduction related to the American Rescue Plan Act, which expanded the list of covered employees.

Recognition of deferred tax assets is appropriate when realization of such assets is more likely than not. Based upon the weight of available evidence, especially the uncertainties surrounding the realization of deferred tax assets through future taxable income, the Company believes it is not yet more likely than not that certain deferred tax assets will be fully realizable. Accordingly, the Company has provided a valuation allowance of \$161.1 million against its deferred tax assets as of December 31, 2022, primarily in relation to deferred tax assets arising from tax credits and net operating losses. The deferred tax assets recognized net of the valuation allowance, \$18.2 million as of December 31, 2022, consisted predominantly of U.S. federal temporary differences. Due to expected future U.S. operating income, the Company expects to realize such deferred tax assets. The net increase of \$27.3 million in the valuation allowance during the year ended December 31, 2022, was primarily due to Irish net operating losses.

As of December 31, 2022, certain of the Company's Irish entities had trading loss carryovers of \$956.9 million and non-trading loss carryovers of \$32.9 million, each of which can be carried forward indefinitely. Trading losses are available against income from the same trade/trades while non-trading losses (excess management expenses) are available against future investment income in the company in which they arise. In addition, as of December 31, 2022, the Company had state net operating loss carryforwards of approximately \$97.7 million, which are available to reduce future taxable income, if any, for the Company's U.S. subsidiary. If not utilized, the state net operating loss carryforward begins expiring in 2032.

The Company also has federal and California research and development credit carryforwards of \$17.8 million and \$17.0 million, respectively, at December 31, 2022. 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 2038 if not utilized. The California tax credits can be carried forward indefinitely.

Cumulative unremitted earnings of the Company's U.S. subsidiaries total approximately \$143.3 million at December 31, 2022. The Company's U.S. subsidiaries' cash balances at December 31, 2022, are committed for its working capital needs. No provision for income tax in Ireland has been recognized on undistributed earnings of the Company's U.S. subsidiaries as the Company considers the U.S. earnings to be indefinitely reinvested.

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

	<u>2022</u>	<u>2021</u>
Gross Unrecognized Tax Benefits at January 1	\$ 8,329	\$ 7,252
Additions for tax positions taken in the current year	2,243	1,342
Additions for tax positions taken in the prior year	992	—
Reductions for tax positions taken in the prior year	—	(265)
Gross Unrecognized Tax Benefits at December 31	<u>\$ 11,564</u>	<u>\$ 8,329</u>

If recognized, none of the Company's unrecognized tax benefits as of December 31, 2022, would reduce its annual effective tax rate, primarily due to corresponding adjustments to its deferred tax valuation allowance. As of December 31, 2022, the Company has not recorded a liability for potential interest or penalties. The Company also does not expect its unrecognized tax benefits to change significantly over the next 12 months.

The tax years 2013 to 2022 remain subject to examination by the U.S. taxing authorities and the tax years 2017 to 2022 remain subject to examination by the Irish taxing authorities as of December 31, 2022.

11. Employee Retirement Plan

In the U.S., the Company provides a qualified retirement plan under section 401(k) of the Internal Revenue Code (the "IRC") under which participants may contribute up to 100% of their eligible compensation, subject to maximum deferral limits specified by the IRC. In addition, the Company contributes 3% of each participating employee's eligible compensation, subject to limits specified by the IRC, on a quarterly basis. Further, the Company may make an annual discretionary matching and/or profit-sharing contribution as determined solely by the Company. The Company recorded total expense for matching contributions of \$1.3 million, \$0.9 million and \$0.6 million for the years ended December 31, 2022, 2021 and 2020, respectively.

In Europe, the Company recorded total expense for employer contribution of \$133,000, \$73,000 and \$32,000 in the years ended December 31, 2022, 2021 and 2020, respectively. In Ireland, the Company operates a defined contribution plan in which it contributes up to 7.5% of an employee's eligible earnings.

12. Subsequent Event

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 \$21.0 million proceeds from the exercise, net of underwriting discount but before deducting any offering costs.

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, 2022, 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, 2022, 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, 2022, our internal control over financial reporting was effective. The effectiveness of our internal control over financial reporting as of December 31, 2022, 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, 2022, 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

None.

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 16, 2023 (our “Proxy Statement”).

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

Except for the information about our executive officers and Code of Conduct 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	54	President and Chief Executive Officer, Director	2016
Hideki Garren	59	Chief Medical Officer	2021
Carol D. Karp	70	Chief Regulatory Officer	2016
Michael J. Malecek	57	Chief Legal Officer and Company Secretary	2019
Tran B. Nguyen	49	Chief Financial Officer	2013
		Chief Strategy Officer	2021
Brandon S. Smith	48	Chief Operating Officer	2021
Karin L. Walker	59	Chief Accounting Officer	2013
Wagner M. Zago	50	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.: Senior Vice President of Pharmacological Sciences (from 2011 to 2012) and Vice President, Pharmacology (from 2009 to 2011); and while in those positions, he also served as Head of Nonclinical Research for Janssen Alzheimer Immunotherapy R&D. From 2001 to 2009, Dr. Kinney was Senior Director, Head of Central Pharmacology and acting lead for Bioanalytics & Pathology at the Merck Research Laboratories, where he contributed to the strategic direction and oversight of drug discovery activities and led a number of non-clinical discovery and clinical development programs targeted for the treatment of neurodegenerative and psychiatric conditions. Dr. Kinney also held positions at Bristol Myers Squibb and was an Assistant Professor at the Emory University School of Medicine, Department of Psychiatry and Behavioral Sciences. He earned his BA from Bloomsburg University and his MA and PhD from Florida Atlantic University.

Hideki Garren, M.D., Ph.D., has served as our Chief Medical Officer since April 2021. Prior to joining Prothena, between 2013 and 2021, Dr. Garren was with F. Hoffmann-La Roche Ltd. (Roche) & Genentech Inc. and most recently served as Vice President, Global Head of Neuroimmunology with responsibility for leading Roche’s Neuroimmunology franchise team. Prior to Roche, between 2011 and 2013, Dr. Garren held the role of Executive Director, Translational Medicine Expert in Neuroscience with Novartis Pharma. Dr. Garren also served as Co-Founder, Executive Vice President, Chief Scientific Officer, and Chief Operating Officer of Bayhill Therapeutics, Inc., a company he started in 2002 based on a technology platform he co-invented while at Stanford University. He serves as a director of Coya Therapeutics, Inc. (a publicly traded biotechnology company). Dr. Garren earned his Bachelor of Science from the California Institute of Technology and his MD and PhD from the University of California, Los Angeles (UCLA). He completed his internship in internal medicine at UCLA, and his residency in neurology and fellowship in neuroimmunology at Stanford University.

Carol D. Karp has served as our Chief Regulatory Officer since 2016. Prior to joining Prothena, she was an independent regulatory consultant to biotechnology and pharmaceutical companies. From 2013 to 2014, Ms. Karp was Senior Vice President, Regulatory Affairs and Compliance at Esperion Therapeutics, Inc., and from 2010 to 2013, she was Vice President,

Head of Global Regulatory Affairs, Pharmacovigilance & Risk Management at Janssen Alzheimer Immunotherapy, a Johnson & Johnson Company. Previously, Ms. Karp held senior regulatory positions at CV Therapeutics, Inc., PowderJect Technologies, VIVUS, Inc., Cygnus, Inc., and Janssen Pharmaceutica. She earned her BA in Biology from the University of Rochester, where she is Vice Chair of the Board of Trustees.

Michael J. Malecek has served as our Chief Legal Officer since 2019. Prior to joining Prothena in 2019, he was Vice President, Deputy General Counsel, Intellectual Property and Litigation of Snowflake (a data warehouse company) from 2018. From 2010 to 2018, he was a Partner at Arnold & Porter Kaye Scholer LLP. From 2008 to 2010, Mr. Malecek was Partner at Dewey & LeBoeuf, LLP. From 2002-2008, 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 20 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. Mr. Nguyen serves as a director of Rain Oncology Inc. (a publicly traded biotechnology company). 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.

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 serves on the board of Cylcacec Pharmaceutical Inc. (a publicly traded clinical-stage oncology company) and served on the board of 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 <http://ir.prothena.com/corporate-governance>. We will provide to any person without charge, upon request, a copy of that Code of Conduct; such a request may be made by sending it to our Company Secretary, 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 <http://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.

ITEM 11. EXECUTIVE COMPENSATION

The information appearing in our Proxy Statement under the following headings is incorporated herein by reference:

- 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	
2.1	Demerger Agreement, dated as of November 8, 2012, between Elan Corporation, plc and Prothena Corporation plc	10/A	001-35676	11/30/2012	2.1
2.2(a)	Amended and Restated Intellectual Property License and Contribution Agreement, dated as of December 20, 2012, by and among Neotope Biosciences Limited, Elan Pharma International Limited, and Elan Pharmaceuticals, Inc.	8-K	001-35676	12/21/2012	2.1
2.2(b)	Amendment Number One to the Amended and Restated Intellectual Property License and Contribution Agreement, effective as of December 20, 2012, among Neotope Biosciences Limited, Elan Pharma International Limited, Elan Pharmaceuticals, LLC, Elan Corporation, plc, and Crimagua Limited	S-1/A	333-191218	9/30/2013	2.2(b)
2.3	Intellectual Property License and Conveyance Agreement, dated as of December 20, 2012, among Neotope Biosciences Limited, Elan Pharma International Limited and Elan Pharmaceuticals, Inc.	8-K	001-35676	12/21/2012	2.2
3.1	Amended and Restated Memorandum and Articles of Association (Constitution) of Prothena Corporation plc	8-K	001-35676	5/25/2016	3.1
4.1	Amended and Restated Memorandum and Articles of Association (Constitution) of Prothena Corporation plc	8-K	001-35676	5/25/2016	3.1
4.2	Description of Registrant's Securities				X
10.1(a)	Tax Matters Agreement, dated as of December 20, 2012, between Elan Corporation, plc and Prothena Corporation plc	8-K	001-35676	12/21/2012	10.1
10.1(b)	Amendment No. 1 to Tax Matters Agreement, dated as of June 25, 2013, between Elan Corporation, plc and Prothena Corporation plc	10-Q	001-35676	8/13/2013	10.2
10.2	License Agreement, dated as of December 31, 2008, between the University of Tennessee Research Foundation and Elan Pharmaceuticals, Inc.	10/A	001-35676	11/30/2012	10.14
10.3(a)†	License Agreement, dated as of November 4, 2013, between The Regents of the University of California and Neotope Biosciences Limited	10-Q/A	001-35676	8/17/2018	10.1(a)
10.3(b)†	License Agreement Amendment Number One, dated as of January 15, 2014, to License Agreement dated as of November 4, 2013, between The Regents of the University of California and Neotope Biosciences Limited	10-Q/A	001-35676	8/17/2018	10.1(b)
10.4†	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
10.5+	Amendment to License, Development, and Commercialization Agreement, entered into on October 1, 2019, among Prothena Biosciences Limited, Prothena Biosciences Inc, F. Hoffman-La Roche Ltd and Hoffman-La Roche Inc.	10-K	001-35676	3/3/2020	10.6

Exhibit No.	Description	Previously Filed				Filed Herewith
		Form	File No.	Filing Date	Exhibit	
10.6+	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	
10.7(a)	Understanding Related to License, Development, and Commercialization Agreement, dated as of March 1, 2020, among Prothena Biosciences Limited, Prothena Biosciences Inc, F. Hoffman-La Roche Ltd and Hoffman-La Roche Inc.	10-Q	001-35676	5/6/2020	10.4(a)	
10.7(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)	
10.8†	Master Collaboration Agreement, dated as of March 20, 2018, between Prothena Biosciences Limited and Celgene Switzerland LLC	10-Q/A	001-35676	8/17/2018	10.3	
10.9+	Share Subscription Agreement, dated as of March 20, 2018, between Celgene Switzerland LLC and Prothena Corporation plc	10-Q	001-35676	5/9/2018	10.4	
10.10+	U.S. License Agreement, dated as of July 30, 2021, as amended on August 12, 2021 and September 8, 2021, by and between Prothena Biosciences Limited and Celgene Switzerland LLC	10-Q	001-35676	11/4/2021	10.5	
10.11+	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	
10.12†	Master Process Development and Clinical Supply Agreement, dated as of June 23, 2010, as amended August 1, 2011, among Elan Pharma International Limited, Neotope Biosciences Limited and Boehringer Ingelheim Pharma GmbH & Co. KG	10-Q	001-35676	8/13/2013	10.3	
10.13(a)	Sublease, dated as of March 22, 2016, between Prothena Biosciences Inc and Amgen Inc.	10-Q	001-35676	5/4/2016	10.2(a)	
10.13(b)	Consent to Sublease Agreement, dated as of March 28, 2016, among Prothena Biosciences Inc, Amgen Inc. and HCP BTC, LLC	10-Q	001-35676	5/4/2016	10.2(b)	
10.14(a)	Sub-Sublease, dated as of July 18, 2018, between Prothena Biosciences Inc and Assembly Biosciences, Inc.	10-Q	001-35676	11/6/2018	10.2(a)	
10.14(b)	Consent to Sub-Sublease, dated as of September 19, 2018, among Prothena Biosciences Inc, Assembly Biosciences, Inc., Amgen Inc. and HCP BTC, LLC	10-Q	001-35676	11/6/2018	10.2(b)	
10.15(a)	Sublease, dated as of October 28, 2022, by and between Arcus Biosciences, Inc. and Prothena Biosciences Inc.					X
10.15(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.					X
10.16#	Prothena Corporation plc Amended and Restated 2012 Long Term Incentive Plan	8-K	001-35676	5/23/2017	10.1	

Exhibit No.	Description	Previously Filed				Filed Herewith
		Form	File No.	Filing Date	Exhibit	
10.17#	Prothena Corporation plc 2018 Long Term Incentive Plan	8-K	001-35676	5/18/2018	10.1	
10.18#	First Amendment to the Prothena Corporation plc 2018 Long Term Incentive Plan	8-K	001-35676	5/22/2020	10.1	
10.19#	Second Amendment to the Prothena Corporation plc 2018 Long Term Incentive Plan	8-K	001-35676	5/21/2021	10.1	
10.20#	Third Amendment to the Prothena Corporation plc 2018 Long Term Incentive Plan	8-K	001-35676	5/20/2022	10.1	
10.21#	Prothena Corporation plc 2020 Employment Inducement Incentive Plan	10-Q	001-35676	5/6/2020	10.2	
10.22#	First through Thirteenth Amendments to the Prothena Corporation plc 2020 Employment Inducement Incentive Plan					X
10.23#	Prothena Corporation plc Amended and Restated Incentive Compensation Plan	10-Q	001-35676	5/9/2017	10.1	
10.24#	Prothena Biosciences Inc Amended and Restated Severance Plan	8-K	001-35676	12/15/2015	10.1	
10.25#	Form of Deed of Indemnification between Prothena Corporation plc and its Directors and Officers	8-K	001-35676	12/11/2014	10.1	
10.26#	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	
10.27#	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	
10.28#	Form of Option Award Agreement between Prothena Corporation plc and its Named Executive Officers under the Prothena Corporation plc 2012 Long Term Incentive Plan (used beginning January 29, 2013 until February 4, 2014)	S-8	333-196572	6/6/2014	99.3	
10.29#	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	
10.30#	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	
10.31 #	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	
10.32#	Offer letter, dated March 20, 2013, between Prothena Biosciences Inc and Tran B. Nguyen	8-K	001-35676	3/28/2013	10.1	
10.33#	Employment Agreement, dated September 30, 2016, between Prothena Biosciences Inc and Gene G. Kinney	8-K	001-35676	11/4/2016	10.1	

Exhibit No.	Description	Previously Filed				Filed Herewith
		Form	File No.	Filing Date	Exhibit	
10.34#	Offer letter, dated April 19, 2013, between Prothena Biosciences Inc and Karin L. Walker	8-K	001-35676	5/22/2013	10.1	
10.35#	Offer letter, dated December 5, 2016, between Prothena Biosciences Inc and Carol D. Karp	10-K	001-35676	2/27/2017	10.28	
10.36#	Promotion letter, dated June 9, 2017, between Prothena Biosciences Inc and Wagner M. Zago	10-Q	001-35676	8/9/2017	10.3	
10.37#	Promotion letter, dated December 11, 2018, between Prothena Biosciences Inc and Radhika Tripuraneni	10-K	001-35676	3/15/2019	10.35	
10.38#	Offer letter, dated June 4, 2019, between Prothena Biosciences Inc and Michael J. Malecek	10-Q	001-35676	8/6/2019	10.1	
10.39#	Offer Letter, dated February 18, 2020, between Prothena Biosciences Inc and Brandon S. Smith	10-Q	001-35676	5/6/2020	10.1	
10.40#	Offer Letter, dated March 18, 2021, between Prothena Biosciences Inc and Hideki Garren	10-Q	001-35676	5/11/2021	10.1	
10.41#	Consulting Agreement, dated October 1, 2022, between Prothena Biosciences Inc and Dennis J. Selkoe	10-Q	001-35676	11/3/2022	10.4	
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
101.INS	The instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document					X
101.SCH	Inline XBRL Taxonomy Extension Schema Document					X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document					X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document					X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document					X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document					X

Exhibit No.	Description	Previously Filed			Filed Herewith
		Form	File No.	Filing Date	
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)				X

* *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 28, 2023

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
<u>/s/ Gene G. Kinney</u> Gene G. Kinney, Ph.D.	President and Chief Executive Officer (Principal Executive Officer) and Director	February 28, 2023
<u>/s/ Tran B. Nguyen</u> Tran B. Nguyen	Chief Strategy Officer and Chief Financial Officer (Principal Financial Officer)	February 28, 2023
<u>/s/ Karin L. Walker</u> Karin L. Walker	Chief Accounting Officer (Principal Accounting Officer)	February 28, 2023
<u>/s/ Lars G. Ekman</u> Lars G. Ekman, M.D., Ph.D.	Chairman of the Board	February 28, 2023
<u>/s/ Paula K. Cobb</u> Paula K. Cobb	Director	February 28, 2023
<u>/s/ Richard T. Collier</u> Richard T. Collier	Director	February 28, 2023
<u>/s/ Shane M. Cooke</u> Shane M. Cooke	Director	February 28, 2023
<u>/s/ K. Anders O. Härfstrand</u> K. Anders O. Härfstrand, M.D., Ph.D.	Director	February 28, 2023
<u>/s/ Helen S. Kim</u> Helen S. Kim	Director	February 28, 2023
<u>/s/ Oleg Nodelman</u> Oleg Nodelman	Director	February 28, 2023
<u>/s/ Sanjiv K. Patel</u> Sanjiv K. Patel, MBBS	Director	February 28, 2023
<u>/s/ Dennis J. Selkoe</u> Dennis J. Selkoe, M.D.	Director	February 28, 2023

DESCRIPTION OF REGISTRANT'S SECURITIES

This description is summarized from, and qualified in its entirety by reference to, our Amended and Restated Memorandum and Articles of Association (our "Constitution"), each of which are incorporated by reference as exhibits to the Annual Report on Form 10-K of which this exhibit is a part. In this exhibit, unless the context otherwise requires, references to "we," "us," "our," "Company," or "Prothena" refer to Prothena Corporation plc.

The following description of our ordinary shares and Euro Deferred Shares is a summary. This summary does not purport to be complete and is qualified in its entirety by reference to the Irish Companies Act 2014 (the "Companies Act"), and the complete text of our Constitution. You should read those laws and documents carefully.

For the avoidance of any doubt, the ordinary shares are the subject of this registration statement. The Euro Deferred Shares are not listed on any stock exchange and are not the subject of any registration.

Capital Structure***Issued Share Capital***

As of December 31, 2022, our issued share capital was 52,103,608 ordinary shares. We have no Euro Deferred Shares in issue. Our ordinary shares are listed on the Nasdaq Global Select Market ("Nasdaq"), under the symbol "PRTA."

Authorized Share Capital

The authorized share capital of the Company is \$1,000,000 and €220,000 consisting of 100,000,000 ordinary shares with a par value of \$0.01 per share and 10,000 Euro Deferred Shares with a par value of €22 per share. The authorized share capital may be increased or reduced by a resolution approved by a simple majority of the votes cast at a general meeting of our shareholders at which a quorum is present (referred to under Irish law as an "ordinary resolution"). The shares comprising our authorized share capital may be divided into shares of such nominal value as the resolution shall prescribe. As a matter of Irish law, our board of directors (our "Board"), may issue new ordinary shares or Euro Deferred Shares without shareholder approval once authorized to do so by our Constitution or by an ordinary resolution adopted by the shareholders at a general meeting. The authorization may be granted for a maximum period of five years, at which point it must be renewed by the shareholders by an ordinary resolution.

Our Board is authorized pursuant to an ordinary resolution passed by shareholders at our annual general meeting held on May 17, 2022, to issue new ordinary shares for cash without shareholder approval up to an aggregate nominal amount equal to the authorized but unissued share capital of the Company as at May 17, 2022, for a period of five years from the date of the passing of the resolution. As a result, our shareholders must renew this authorization by an ordinary resolution no later than May 17, 2027.

The rights and restrictions to which our ordinary shares and Euro Deferred Shares are subject are prescribed in our Constitution. We may, by ordinary resolution and without obtaining any vote or consent of the holders of any class or series of shares, unless expressly provided by the terms of that class or series of shares, provide from time to time for the issuance of other classes or series of shares and to establish the characteristics of each class or series, including the number of shares, designations, relative voting rights, dividend rights, liquidation and other rights, redemption, repurchase or exchange rights and any other preferences and relative, participating, optional or other rights and limitations not inconsistent with applicable law.

Irish law does not recognize fractional shares held of record. Accordingly, our Constitution does not provide for the issuance of fractional shares of the Company, and the official Irish share register of the Company will not reflect any fractional shares. Whenever as a result of an issuance, alteration, reorganization, consolidation, division, or subdivision of the share capital of the Company would result in any shareholder becoming entitled to fractions of a share, no such fractions shall be issued or delivered to any shareholder. All such fractions of a share will be aggregated into whole shares and sold in the open market at prevailing market prices and the aggregate cash

proceeds from such sale (net of tax, commissions, costs and other expenses) shall be distributed on a pro rata basis, rounding down to the nearest cent, to each shareholder who would otherwise have been entitled to receive fractions of a share.

Preemption Rights, Share Warrants and Share Options

Under Irish law, certain statutory preemption rights apply automatically in favor of shareholders where shares are to be issued for cash. However, as permitted by Irish law, we have opted out of these preemption rights by way of special resolution (a “special resolution” requires the approval of not less than 75% of the votes of our shareholders cast at a general meeting at which a quorum is present) passed at our annual general meeting on May 17, 2022. Irish law requires this opt-out to be renewed every five years by a special resolution. As a result, our shareholders must renew this opt-out authorization by a special resolution no later than May 17, 2027.

If the opt-out is not renewed, shares issued for cash must be offered to existing shareholders of the Company on a *pro rata* basis to their existing shareholding before the shares may be issued to any new shareholders. The statutory preemption rights do not apply (i) where shares are issued for non-cash consideration (such as in a share-for-share acquisition), (ii) to the issue of non-equity shares (that is, shares that have the right to participate only up to a specified amount in any income or capital distribution) or (iii) where shares are issued pursuant to an employee share option or similar equity plan.

Our Constitution provides that, subject to any shareholder approval requirement under any laws, regulations or the rules of any stock exchange to which we are subject, our Board is authorized, from time to time, in its discretion, to grant such persons, for such periods and upon such terms as it deems advisable, options to purchase such number of shares of any class or classes or of any series of any class as our Board may deem advisable, and to cause warrants or other appropriate instruments evidencing such options to be issued. The Companies Act provides that directors may issue share warrants or options without shareholder approval once authorized to do so by a company’s constitution or an ordinary resolution of shareholders. We are subject to the rules of Nasdaq and the U.S. Internal Revenue Code of 1986, as amended, which require shareholder approval of certain equity plans and share issuances. Our Board may issue shares upon exercise of warrants or options without shareholder approval or authorization (up to the relevant authorized share capital limit).

Dividends

Under Irish law, dividends and distributions may only be made from distributable reserves. Distributable reserves generally means accumulated, realized profits, so far as not previously utilized by distribution or capitalization, less accumulated, realized losses, so far as not previously written off in a reduction or re-organization of capital duly made. In addition, no distribution or dividend may be made unless our net assets 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 the undenominated capital (effectively the share premium and capital redemption reserve) and the amount by which our accumulated unrealized profits, so far as not previously utilized by any capitalization, exceed the Company’s 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 the Company. 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 Companies Act, 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).

Our Constitution authorizes our Board to declare dividends without shareholder approval to the extent they appear justified by profits lawfully available for distribution. Our Board may also recommend a dividend to be approved and declared by the shareholders at a general meeting. Our Board may direct that the payment be made by distribution of assets, shares or cash, and no dividend issued may exceed the amount recommended by the directors.

Dividends may be declared and paid in the form of cash or non-cash assets and may be paid in dollars or any other currency.

Our Board may deduct from any dividend payable to any shareholder any amounts payable by such shareholder to the Company in relation to the shares of the Company.

The Board may also authorize the Company to issue shares with preferred rights to participate in dividends declared by the Company from time to time, as determined by ordinary resolution. The holders of preferred shares may, depending on their terms, rank senior to our ordinary shares in terms of dividend rights and or be entitled to claim arrears of a declared dividend out of subsequently declared dividends in priority to ordinary shareholders.

Bonus Shares

Under our Constitution, our Board may resolve to capitalize any amount credited to any reserve available for distribution or the share premium account or other of our undistributable reserves for issuance and distribution to shareholders as fully paid up bonus shares on the same basis of entitlement as would apply in respect of a dividend distribution.

Share Repurchases, Redemptions and Conversions

Overview

Our Constitution provides that any ordinary share that we have agreed to acquire shall be deemed to be a redeemable share. Accordingly, for Irish law purposes, the repurchase of ordinary shares by us may technically be effected as a redemption of those shares as described below under “Description of Share Capital—Repurchases and Redemptions by Prothena.” If our Constitution did not contain such provision, repurchases by us would be subject to many of the same rules that apply to purchases of our ordinary shares by subsidiaries described below under “Description of Share Capital—Purchases by Subsidiaries of Prothena,” including the shareholder approval requirements described below, and the requirement that any overseas market purchases be effected on a recognized stock exchange, which, for purposes of the Companies Act, includes Nasdaq. Neither Irish law nor any of our constituent documents places limitations on the right of non-resident or foreign owners to vote or hold our ordinary shares. Except where otherwise noted, references in this Prospectus Supplement to repurchasing or buying back our ordinary shares refer to the redemption of ordinary shares by us or the purchase of our ordinary shares by one of our subsidiaries, in each case in accordance with our Constitution and Irish company law as described below.

Repurchases and Redemptions by Prothena

Under Irish law, a company may issue redeemable shares and redeem them out of distributable reserves or the proceeds of a new issue of shares for that purpose. Please see also “Description of Share Capital—Dividends.” We may only issue redeemable shares if the nominal value of the issued share capital that is not redeemable is not less than 10% of the nominal value of our total issued share capital. All redeemable shares must also be fully-paid and the terms of redemption of the shares must provide for payment on redemption. Redeemable shares may, upon redemption, be cancelled or held in treasury. Based on the provisions of our Constitution, shareholder approval will not be required to redeem our shares.

We may also be given an additional general authority for overseas market purchases of our ordinary shares by way of ordinary resolution, which would take effect on the same terms and be subject to the same conditions as applicable to purchases by our subsidiaries as described below.

Repurchased and redeemed shares may be cancelled or held as treasury shares. The nominal value of treasury shares held by us at any time must not exceed 10% of the nominal value of our issued share capital. We may not exercise any voting rights in respect of any shares held as treasury shares. Treasury shares may be cancelled by us or re-issued subject to certain conditions.

Purchases by Subsidiaries of Prothena

Under Irish law, an Irish or non-Irish subsidiary of the Company may purchase our shares by way of an: (i) overseas market purchase; or (ii) off-market purchase. For one of our subsidiaries to make overseas market purchases of our ordinary shares, our shareholders must provide general authorization for such purchase by way of ordinary resolution. However, as long as this general authority has been granted, no specific shareholder authority for a particular overseas market purchase by a subsidiary of our ordinary shares is required. For a purchase by one of our subsidiaries off-market, the proposed purchase contract must be authorized by special resolution of our shareholders before the contract is entered into. The person whose ordinary shares are to be bought back cannot vote in favor of the special resolution and from the date of the notice of the meeting at which the resolution approving the contract is proposed, the purchase contract must be on display or must be available for inspection by our shareholders at our registered office.

In order for one of our subsidiaries to make overseas market purchases of our shares, such shares must be purchased on a recognized stock exchange. Nasdaq, on which our ordinary shares are listed, is specified as a recognized stock exchange for this purpose in accordance with Irish law.

The number of shares held by our subsidiaries at any time will count as treasury shares and will be included in any calculation of the permitted treasury share threshold of 10% of the nominal value of our issued share capital. While a subsidiary holds our shares, it cannot exercise any voting rights in respect of those shares. The acquisition of our ordinary shares by a subsidiary must be funded out of distributable reserves of the subsidiary.

Lien on Shares, Calls on Shares and Forfeiture of Shares

Our Constitution provides that we have a first and paramount lien on every share that is not a fully paid up share for all amounts payable at a fixed time or called in respect of that share. Subject to the terms of their allotment, directors may call for any unpaid amounts in respect of any shares to be paid, and if payment is not made, the shares may be forfeited. These provisions are standard inclusions in the constitution of an Irish public company limited by shares such as Prothena and are only applicable to our shares that have not been fully paid up. Irish stamp duty may be payable in respect of transfers of our ordinary shares at the rate of 1%.

Consolidation and Division; Subdivision

Under our Constitution, we may, by ordinary resolution, consolidate and divide all or any of our share capital into shares of larger nominal value than our existing shares or subdivide our shares into smaller amounts than are fixed by our Constitution.

Reduction of Share Capital

We may, by ordinary resolution, reduce our authorized share capital in any way. We also may, by special resolution and subject to confirmation by the Irish High Court, reduce or cancel our issued share capital in any manner permitted by the Companies Act.

Annual Meetings of Shareholders

Under Irish company law, we are required to hold annual general meetings at intervals of no more than 15 months from the previous annual general meeting, provided that an annual general meeting is held in each calendar year following the first annual general meeting and no more than nine months after our fiscal year-end. Subject to compliance with the Companies Act, any of our annual general meetings may be held outside Ireland. Notice of an annual general meeting must be given to all of our shareholders and to our auditors. Our Constitution provides for a minimum notice period of 21 days' notice, which is the minimum permitted by the Companies Act.

The only matters which must, as a matter of Irish company law, be transacted at the Company's annual general meeting are the consideration of the statutory financial statements, report of the directors and the report of the auditors on those statements and that report, the review by the shareholders of the Company's affairs, the election and re-election of directors in accordance with our Constitution, the declaration of a dividend (if any), the

appointment or reappointment of the auditors and the fixing of the auditor's remuneration (or delegation of same). If no resolution is made in respect of the reappointment of an existing auditor at an annual general meeting, the existing auditor will be deemed to have continued in office.

Extraordinary General Meetings of Shareholders

Extraordinary general meetings of the Company may be convened by (i) our Board, (ii) on requisition of our shareholders holding not less than 10% of the paid up share capital of our carrying voting rights, (iii) on requisition of our auditors, or (iv) in exceptional cases, by order of the Irish High Court. Extraordinary general meetings are generally held for the purpose of approving shareholder resolutions as may be required from time to time. At any extraordinary general meeting only such business shall be conducted as is set forth in the notice thereof.

Notice of an extraordinary general meeting must be given to all of our shareholders and to our auditors. Under Irish law and our Constitution, the minimum notice periods are 21 days' notice in writing for an extraordinary general meeting to approve a special resolution and 14 days' notice in writing for any other extraordinary general meeting.

In the case of an extraordinary general meeting convened by the requisition of our shareholders under part (ii) above, the proposed purpose of the meeting must be set out in the requisition notice. Upon receipt of any such valid requisition notice, our Board has 21 days to convene a meeting of our shareholders to vote on the matters set out in the requisition notice. This meeting must be held within two months of the receipt of the requisition notice. If our Board does not convene the meeting within such 21-day period, the requisitioning shareholders, or any of them representing more than one half of the total voting rights of all of them, may themselves convene a meeting, which meeting must be held within three months of our receipt of the requisition notice.

If our Board becomes aware that our net assets are not greater than half of the amount of our called-up share capital, it must convene an extraordinary general meeting of our shareholders not later than 28 days from the date that they learn of this fact to consider how to address the situation.

Quorum for General Meetings

Our Constitution provides that no business shall be transacted at any general meeting unless a quorum is present. One or more of our shareholders present in person or by proxy holding not less than one-half of our issued and outstanding shares entitled to vote at the meeting in question constitute a quorum.

Voting

Our Constitution provides that our Board or chairman may determine the manner in which the poll is to be taken and the manner in which the votes are to be counted.

Each Company shareholder is entitled to one vote for each ordinary share that he or she holds as of the record date for the meeting. Voting rights may be exercised by shareholders registered in our share register as of the record date for the meeting or by a duly appointed proxy, which proxy need not be a Company shareholder. Where interests in shares are held by a nominee trust company, such company may exercise the rights of the beneficial holders on their behalf as their proxy. All proxies must be appointed in the manner prescribed by our Constitution, which permit shareholders to notify us of their proxy appointments electronically in such manner as may be approved by our Board.

In accordance with our Constitution, we may from time to time be authorized by ordinary resolution to issue preferred shares. These preferred shares may have such voting rights as may be specified in the terms of such preferred shares (e.g., they may carry more votes per share than ordinary shares or may entitle their holders to a class vote on such matters as may be specified in the terms of the preferred shares). Treasury shares or our shares that are held by our subsidiaries are not entitled to be voted at general meetings of shareholders.

Irish law requires special resolutions of our shareholders at a general meeting to approve certain matters. Examples of matters requiring special resolutions include:

- amending our Constitution;
- approving a change of name of Prothena;
- authorizing the entering into of a guarantee or provision of security in connection with a loan, quasi loan or credit transaction to a director or connected person;
- opting out of preemption rights on the issuance of new shares;
- re-registration of Prothena from a public limited company to a private company;
- variation of class rights attaching to classes of shares (where the Constitution does not provide otherwise);
- purchase of our shares off-market;
- reduction of issued share capital;
- sanctioning a compromise/scheme of arrangement with creditors or shareholders;
- resolving that we be wound up by the Irish courts;
- resolving in favor of a shareholders' voluntary winding-up; and
- setting the re-issue price of treasury shares.

Variation of Rights Attaching to a Class or Series of Shares

Under our Constitution and the Companies Act, any variation of class rights attaching to our issued shares must be approved by a special resolution of our shareholders of the affected class or with the consent in writing of the holders of three-quarters of all the votes of that class of shares.

The provisions of our Constitution relating to general meetings apply to general meetings of the holders of any class of our shares except that the necessary quorum is determined in reference to the shares of the holders of the class. Accordingly, for general meetings of holders of a particular class of our shares, a quorum consists of the holders present in person or by proxy representing at least one-half of the issued shares of the class.

Record Date

Our Board may from time to time fix a record date for the purposes of determining the rights of shareholders to notice of and/or to vote at any general meeting of the Company. The record date shall not precede the date upon which the resolution fixing the record date is adopted and may not be more than 90 days nor less than 10 days before the date of such meeting. If no record date is fixed by the Board, the record date for determining shareholders entitled to notice of, or to vote at, a meeting shall be the date immediately preceding the date on which notice of the meeting is deemed given under the Constitution.

The Board may also set a record date to determine the identity of the shareholders entitled to receive payment of any dividend or for any other proper purpose. The record date shall not precede the date upon which the resolution fixing the record date is adopted and the record date shall not be more than ninety days prior to such action. If no record date is fixed, the record date for determining shareholders for such purpose shall be the date on which the Board adopts the resolution relating to the payment of any dividend.

Advance Notice Provisions

Under Irish law, there is no general right for a shareholder to put items on the agenda of an annual general meeting of the Company, other than as set out in the Constitution. Our Constitution permits shareholders to nominate persons for election to the Board at general meetings called for the purpose of electing directors once they

comply with certain requirements set out in the Constitution. Under our Constitution, in addition to any other applicable requirements, for director nominations to be properly brought before a general meeting by a shareholder, such shareholder must have given timely notice thereof in writing to our corporate secretary.

To be timely for an annual general meeting, a shareholder's notice to our secretary as to the nominations to be brought before the meeting must be delivered to our registered office not less than 90 days nor more than 150 days prior to the first anniversary of the notice convening our annual general meeting for the prior year. In the event that the date of the annual general meeting is changed by more than 30 days from the first anniversary date of the prior year's annual general meeting, notice by the member must be delivered not earlier than 150 days prior to such annual general meeting and not later than the later of (a) 90 days prior to the day of the contemplated annual general meeting or (b) ten days after the day on which public announcement of the date of the contemplated annual general meeting is first made.

To be timely for nominations of a director at an extraordinary general meeting, notice must be delivered not more than 150 days prior to the date of such extraordinary general meeting and not later than 90 days prior to such extraordinary general meeting or 10 days after the day on which public announcement is first made of the date of the general meeting and of the nominees proposed by the Board to be elected at such meeting.

For nominations to the Board, the notice must include all information about the director nominee that is required to be disclosed by SEC rules regarding the solicitation of proxies for the election of directors pursuant to Regulation 14A under the Exchange Act. The notice also must include information about the shareholder and the shareholder's holdings of our shares. The chairman of the meeting shall have the power and duty to determine whether any proposed nomination was made or proposed in accordance with these provisions (as set out in our Constitution), and if any proposed nomination is not in compliance with these provisions, to declare that such nomination is defective and shall be disregarded.

Shareholders' Suits

In Ireland, the decision to institute proceedings on behalf of a company is generally taken by the company's board of directors. In certain limited circumstances, a shareholder may be entitled to bring a derivative action on our behalf. The central question at issue in deciding whether a minority shareholder may be permitted to bring a derivative action is whether, unless the action is brought, a wrong committed against us would otherwise go unredressed. The cause of action may be against a director, another person or both.

A shareholder may also bring proceedings against us in his or her own name where the shareholder's rights as such have been infringed or where our affairs are being conducted, or the powers of the board of directors are being exercised, in a manner oppressive to any shareholder or shareholders or in disregard of their interests as shareholders. Oppression connotes conduct that is burdensome, harsh or wrong. This is an Irish statutory remedy under Section 212 of the Companies Act and the court can grant any order it sees fit, including providing for the purchase or transfer of the shares of any shareholder.

Inspection of Books and Records

Under Irish law, shareholders have the right to: (i) receive a copy of our Constitution; (ii) inspect and obtain copies of the minutes of our general meetings and resolutions; (iii) inspect and receive a copy of the register of shareholders, register of directors and secretaries, register of directors' interests; (iv) inspect copies of directors' service contracts; (v) inspect copies of instruments creating charge; (vi) receive copies of the statutory financial statements and directors' and auditors' reports which have previously been sent to shareholders prior to an annual general meeting; and (vii) receive copies of the statutory financial statements and directors' and auditors' reports of any of our subsidiaries which have previously been sent to the shareholders of the subsidiaries prior to an annual general meeting for the preceding ten years. Our auditors also have the right of access, at all reasonable times, to the accounting records of the Company. The auditors' report must be circulated to the shareholders with our financial statements prepared in accordance with Irish law 21 days (not including the day of mailing or the day of the meeting) before the annual general meeting and must be laid before the shareholders at our annual general meeting.

Acquisitions

The Company may be acquired in a number of ways, including:

- a court-approved scheme of arrangement under the Companies Act. A scheme of arrangement with shareholders requires a court order from the Irish High Court and the approval of a majority in number representing 75% in value of each class of shareholders present and voting in person or by proxy at a meeting called to approve the scheme;
- through a tender or takeover offer by a third party for all of our shares. Where the holders of 80% or more of our shares have accepted an offer for their shares in Prothena, the remaining shareholders may also be statutorily required to transfer their shares. If the bidder does not exercise its “squeeze out” right, then the non-accepting shareholders also have a statutory right to require the bidder to acquire their shares on the same terms; and
- by way of a merger with a company incorporated in the European Economic Area (“EEA”) under the EU Cross-Border Mergers Directive (EU) 2017/1132 or with another Irish company under the Companies Act. Such a merger must be approved by a special resolution. Shareholders also may be entitled to have their shares acquired for cash. See the section entitled “Description of Share Capital – Appraisal Rights.”

Irish law does not generally require shareholder approval for a sale, lease or exchange of all or substantially all of a company’s property and assets.

Appraisal Rights

Generally, under Irish law, shareholders of an Irish company do not have statutory appraisal rights. If we are being merged as the transferor company with another EEA company under the EU Cross-Border Mergers Directive (EU) 2017/1132 as implemented in Ireland by the European Communities (“Cross-Border Mergers”) Regulations 2008 (as amended) or if we are being merged with another Irish company under the Irish Companies Act, (i) any of our shareholders who voted against the special resolution approving the merger or (ii) if 90% of our shares are held by the successor company, any other of our shareholders, may be entitled to require that the successor company acquire its shares for cash.

Disclosure of Interests in Shares

Under the Companies Act, our shareholders must notify us if, as a result of a transaction, the shareholder will become interested in three percent or more of the Prothena voting shares, or if as a result of a transaction a shareholder who was interested in more than three percent of Prothena voting shares ceases to be so interested. Where a shareholder is interested in more than three percent of Prothena voting shares, the shareholder must notify us of any alteration of his or her interest that brings his or her total holding through the nearest whole percentage number, whether an increase or a reduction. The relevant percentage figure is calculated by reference to the aggregate nominal value of the voting shares in which the shareholder is interested as a proportion of the entire nominal value of our issued share capital (or any such class of share capital in issue). Where the percentage level of the shareholder’s interest does not amount to a whole percentage, this figure may be rounded down to the next whole number. We must be notified within five business days of the transaction or alteration of the shareholder’s interests that gave rise to the notification requirement. If a shareholder fails to comply with these notification requirements, the shareholder’s rights in respect of any our shares it holds will not be enforceable, either directly or indirectly. However, such person may apply to the court to have the rights attaching to such shares reinstated.

In addition to these disclosure requirements, we, under the Companies Act, may, by notice in writing, require a person whom we know or have reasonable cause to believe to be, or at any time during the three years immediately preceding the date on which such notice is issued to have been, interested in shares comprised in our relevant share capital: (i) to indicate whether or not it is the case; and (ii) where such person holds or has during that time held an interest in our shares, to provide additional information, including the person’s own past or present

interests in our shares. If the recipient of the notice fails to respond within the reasonable time period specified in the notice, we may apply to court for an order directing that the affected shares be subject to certain restrictions, as prescribed by the Companies Act, as follows:

- any transfer of those shares or, in the case of unissued shares, any transfer of the right to be issued with shares and any issue of shares, shall be void;
- no voting rights shall be exercisable in respect of those shares;
- no further shares shall be issued in right of those shares or in pursuance of any offer made to the holder of those shares; and
- no payment shall be made of any sums due from Prothena on those shares, whether in respect of capital or otherwise.

The court may also order that shares subject to any of these restrictions be sold with the restrictions terminating upon the completion of the sale.

In the event we are in an offer period pursuant to the Irish Takeover Rules (as defined below), accelerated disclosure provisions apply for persons holding an interest in our securities of one percent or more.

Anti-Takeover Provisions

Shareholder Rights Plans and Share Issuances

Irish law does not expressly authorize or prohibit companies from issuing share purchase rights or adopting a shareholder rights plan as an anti-takeover measure; there is no directly relevant case law on this issue. We do not currently have a rights plan in place.

Our Constitution expressly authorizes our Board to adopt a shareholder rights plan, subject to applicable law, including the Irish Takeover Rules and Substantial Acquisition Rules described below and the requirement for shareholder authorization for the issue of shares described above.

Subject to the Irish Takeover Rules described below, our Board also has power to issue any of our authorized and unissued shares on such terms and conditions as it may determine, and any such action should be taken in the best interests of the Prothena. It is possible, however, that the terms and conditions of any issue of shares could discourage a takeover or other transaction that holders of some or a majority of the ordinary shares believe to be in their best interests or in which holders might receive a premium for their shares over the then market price of the shares.

Irish Takeover Rules and Substantial Acquisition Rules

A transaction in which a third party seeks to acquire 30% or more of Prothena voting rights and any other acquisitions of our securities are governed by the Irish Takeover Panel Act 1997 and the Irish Takeover Rules made thereunder, which are referred to in this Prospectus Supplement as the “Irish Takeover Rules,” and are regulated by the Irish Takeover Panel. The “General Principles” of the Irish Takeover Rules and certain important aspects of the Irish Takeover Rules are described below.

General Principles

The Irish Takeover Rules are built on the following General Principles which will apply to any transaction regulated by the Irish Takeover Panel:

- in the event of an offer, all holders of securities of the target company must be afforded equivalent treatment and, if a person acquires control of a company, the other holders of securities must be protected;

- the holders of securities in the target company must have sufficient time and information to enable them to reach a properly informed decision on the offer; where it advises the holders of securities, the board of directors of the target company must give its views on the effects of the implementation of the offer on employment, employment conditions and the locations of the target company's place of business;
- a target company's board of directors must act in the interests of the company as a whole and must not deny the holders of securities the opportunity to decide on the merits of the offer;
- false markets must not be created in the securities of the target company, the bidder or any other company concerned by the offer in such a way that the rise or fall of the prices of the securities becomes artificial and the normal functioning of the markets is distorted;
- a bidder can only announce an offer after ensuring that he or she can fulfill in full any cash consideration, if such is offered, and after taking all reasonable measures to secure the implementation of any other type of consideration;
- a target company may not be hindered in the conduct of its affairs for longer than is reasonable by an offer for its securities; and
- a "substantial acquisition" of securities (whether such acquisition is to be effected by one transaction or a series of transactions) shall take place only at an acceptable speed and shall be subject to adequate and timely disclosure.

Mandatory Bid

Under certain circumstances, a person who acquires our shares, or other voting securities, may be required under the Irish Takeover Rules to make a mandatory cash offer for remaining outstanding Prothena voting securities at a price not less than the highest price paid for the securities by the acquiror, or any parties acting in concert with the acquiror, during the previous 12 months. This mandatory bid requirement is triggered if an acquisition of securities would increase the aggregate holding of an acquiror, including the holdings of any parties acting in concert with the acquiror, to securities representing 30% or more of Prothena voting rights, unless the Irish Takeover Panel otherwise consents. An acquisition of securities by a person holding, together with its concert parties, securities representing between 30% and 50% of Prothena voting rights would also trigger the mandatory bid requirement if, after giving effect to the acquisition, the percentage of the voting rights held by that person (together with its concert parties) would increase by 0.05% within a 12-month period. Any person (excluding any parties acting in concert with the holder) holding securities representing more than 50% of the voting rights of a company is not subject to these mandatory offer requirements in purchasing additional securities.

Voluntary Bid; Requirements to Make a Cash Offer and Minimum Price Requirements

If a person makes a voluntary offer to acquire our outstanding ordinary shares, the offer price must not be less than the highest price paid for our ordinary shares by the bidder or its concert parties during the three-month period prior to the commencement of the offer period. The Irish Takeover Panel has the power to extend the "look back" period to 12 months if the Irish Takeover Panel, taking into account the General Principles, believes it is appropriate to do so.

If the bidder or any of its concert parties has acquired our ordinary shares (i) during the period of 12 months prior to the commencement of the offer period that represent more than 10% of our total ordinary shares or (ii) at any time after the commencement of the offer period, the offer must be in cash (or accompanied by a full cash alternative) and the price per our ordinary shares must not be less than the highest price paid by the bidder or its concert parties during, in the case of (i), the 12-month period prior to the commencement of the offer period or, in the case of (ii), the offer period. The Irish Takeover Panel may apply this rule to a bidder who, together with its concert parties, has acquired less than 10% of our total ordinary shares in the 12-month period prior to the commencement of the offer period if the Irish Takeover Panel, taking into account the General Principles, considers

it just and proper to do so. An offer period will generally commence from the date of the first announcement of the offer or proposed offer.

Substantial Acquisition Rules

The Irish Takeover Rules also contain rules governing substantial acquisitions of shares and other voting securities which restrict the speed at which a person may increase his or her holding of shares and rights over shares to an aggregate of between 15% and 30% of the Prothena voting rights. Except in certain circumstances, an acquisition or series of acquisitions of shares or rights over shares representing 10% or more of the Prothena voting rights is prohibited, if such acquisition(s), when aggregated with shares or rights already held, would result in the acquirer holding 15% or more but less than 30% of the Prothena voting rights and such acquisitions are made within a period of seven days. These rules also require accelerated disclosure of acquisitions of shares or rights over shares relating to such holdings.

Frustrating Action

Under the Irish Takeover Rules, our Board is not permitted to take any action that might frustrate an offer for our 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 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. Exceptions to this prohibition are available where:

- the action is approved by our shareholders at a general meeting; or
- the Irish Takeover Panel has given its consent, where:
- it is satisfied the action would not constitute frustrating action;
- our shareholders holding more than 50% of the voting rights state in writing that they approve the proposed action and would vote in favor of it at a general meeting;
- the action is taken in accordance with a contract entered into prior to the announcement of the offer (or any earlier time at which our Board considered the offer to be imminent); or
- the decision to take such action was made before the announcement of the offer and either has been at least partially implemented or is in the ordinary course of business.

Certain other provisions of Irish law or our Constitution may be considered to have antitakeover effects, including advance notice requirements for director nominations, as well as those described under the following captions: “Description of Share Capital—Capital Structure—Authorized Share Capital” (regarding issuance of preferred shares), “Description of Share Capital—Preemption Rights, Share Warrants and Share Options,” “Description of Share Capital—Disclosure of Interests in Shares” and “Description of Share Capital—Corporate Governance.”

Corporate Governance

Our Constitution allocates authority over the day-to-day management of Prothena to our Board. Our Board may then delegate the management of Prothena to committees of the Board (consisting of one or more members of the Board) or executives, but regardless, our Board remains responsible, as a matter of Irish law, for the proper management of the affairs of Prothena. Committees may meet and adjourn as they determine proper. A vote at any committee meeting will be determined by a majority of votes of the members present.

The Board has a standing audit committee, a standing compensation committee and a standing nominating and corporate governance committee, with each committee comprised solely of independent directors, as prescribed

by the Nasdaq listing standards and SEC rules and regulations. We have adopted corporate governance guidelines, as well as a code of conduct and other compliance policies.

The Companies Act provides for a minimum of two directors. Our Constitution provides that the Board may determine the size of the Board from time to time.

Our Constitution provides that at least one-third of the directors serving on the Board shall come up for re-election at a given annual general meeting, and that directors must come up for re-election at the third annual general meeting subsequent to their appointment or reappointment to the Board. Except as otherwise provided by law, vacancies on the Board may be filled only by ordinary resolution or the affirmative vote of a majority of the remaining directors. A director elected by the Board to fill a vacancy shall serve until the subsequent annual general meeting. At each annual general meeting of shareholders, the successors to directors whose terms will then expire will be elected to serve from the time of election and qualification until the third subsequent annual general meeting of shareholders.

Under the Companies Act and notwithstanding anything contained in our Constitution or in any agreement between us and a director, the shareholders may, by an ordinary resolution, remove a director from office before the expiration of his or her term at a meeting held on no less than 28 days' notice and at which the director is entitled to be heard. The power of removal is without prejudice to any claim for damages for breach of contract (e.g., employment contract) that the director may have against us in respect of his removal.

Our Constitution provides that the Board may fill any vacancy occurring on the Board. If the Board fills a vacancy, the director's term expires at the next annual general meeting. A vacancy on the Board created by the removal of a director may be filled by the shareholders at the meeting at which such director is removed and, in the absence of such election or appointment, the remaining directors may fill the vacancy.

Legal Name; Formation; Fiscal Year; Registered Office

Prothena Corporation plc was formed under the laws of Ireland on September 26, 2012 as a private limited company, under the name "Neotope Corporation Limited" (registration number 518146), and reregistered as a public limited company and changed its name to "Neotope Corporation plc" on October 25, 2012. On November 1, 2012, our shareholders resolved, by way of special resolution, to change the name of the company to "Prothena Corporation plc," and this was approved by the Irish Registrar of Companies on November 7, 2012. Our fiscal year ends on December 31 and our registered address is 77 Sir John Rogerson's Quay, Block C, Grand Canal Docklands, Dublin 2, D02 VK60, Ireland.

Duration; Dissolution; Rights upon Liquidation

Our duration is unlimited. We may be dissolved and wound up at any time by way of a shareholders' voluntary winding up or a creditors' winding up. In the case of a shareholders' voluntary winding up, a special resolution of shareholders is required. We may also be dissolved by way of court order on the application of a creditor, or by the Companies Registration Office as an enforcement measure where we have failed to file certain returns.

If our Constitution contains no specific provisions in respect of a dissolution or winding up, then, subject to the priorities of any creditors, the assets will be distributed to our shareholders in proportion to the paid-up nominal value of the shares held. Our Constitution provides that our ordinary shareholders are entitled to participate *pro rata* in a winding up.

Uncertificated Shares

Holders of our ordinary shares that hold their ordinary shares electronically have the right to require us to issue certificates for their shares.

Stock Exchange Listing

Our ordinary shares are listed on the Nasdaq Global Select Market under the symbol “PRTA.”

No Sinking Fund

Our ordinary shares have no sinking fund provisions.

Transfer and Registration of Shares

The transfer agent for our ordinary shares is Computershare Trust Company, N.A. Its address is 250 Royall Street, Canton, MA 02021. An Irish based affiliate of the transfer agent, Computershare Investor Services (Ireland) Limited, maintains our share register, registration in which is determinative of ownership of our ordinary shares. This affiliate provides an inspection facility in Ireland for inspection and copying of our register in accordance with the Companies Act. A shareholder who holds shares beneficially is not the holder of record of such shares. Instead, the depository (for example, Cede & Co. as nominee for DTC) or other nominee is the holder of record of those shares. Accordingly, a transfer of shares from a person who holds such shares beneficially to a person who also holds such shares beneficially through a depository or other nominee will not be registered in our official share register, as the depository or other nominee will remain the record holder of any such shares.

A written instrument of transfer is required under Irish law in order to register on our official share register any transfer of shares (i) from a person who holds such shares directly to any other person, (ii) from a person who holds such shares beneficially to a person who holds such shares directly, or (iii) from a person who holds such shares beneficially to another person who holds such shares beneficially where the transfer involves a change in the depository or other nominee that is the record owner of the transferred shares. An instrument of transfer is also required for a shareholder who directly holds shares to transfer those shares into his or her own broker account (or vice versa). Such instruments of transfer may give rise to Irish stamp duty, which must be paid prior to registration of the transfer on our official Irish share register. However, a shareholder who directly holds shares may transfer those shares into his or her own broker account (or vice versa) without giving rise to Irish stamp duty provided there is no change in the ultimate beneficial ownership of the shares as a result of the transfer and the transfer is not made in contemplation of a sale of the shares.

Any transfer of our ordinary shares that is subject to Irish stamp duty will not be registered in the name of the buyer unless an instrument of transfer is duly stamped and provided to the transfer agent. We, in our absolute discretion and insofar as the Companies Act or any other applicable law permit, may provide that one of our subsidiaries will, pay Irish stamp duty arising on a transfer of our ordinary shares on behalf of the transferee of such ordinary shares. If stamp duty resulting from the transfer of our ordinary shares which would otherwise be payable by the transferee is paid by us or any of our subsidiaries on behalf of the transferee, then in those circumstances, we will, on our behalf or on behalf of our subsidiary (as the case may be), be entitled to (i) seek reimbursement of the stamp duty from the transferee, (ii) set-off the stamp duty against any dividends payable to the transferee of those ordinary shares and (iii) claim a first and permanent lien on our ordinary shares on which stamp duty has been paid by us or our subsidiary for the amount of stamp duty paid. Our lien shall extend to all dividends paid on those ordinary shares. Parties to a share transfer may assume that any stamp duty arising in respect of a transaction in our ordinary shares has been paid unless one or both of such parties is otherwise notified by us or the transfer agent.

Our Constitution delegates to any director, the secretary or any of our assistant secretaries duly appointed (or such other person as may be appointed by the secretary for this purpose) the authority, on our behalf, to execute an instrument of transfer on behalf of a transferring party.

The directors may suspend registration of transfers from time to time, not exceeding 30 days in aggregate each year.

SUBLEASE

THIS SUBLEASE (this “Sublease”) is dated for reference purposes as of October 28, 2022 (the “Effective Date”), and is made by and between Arcus Biosciences, Inc., a Delaware corporation (“Sublessor”), and Prothena Biosciences Inc, a Delaware corporation (“Sublessee”). Sublessor and Sublessee hereby agree as follows:

1. Recitals: This Sublease is made with reference to the fact that HCP LS Brisbane, LLC, as landlord (“Master Lessor”), and Sublessor, as tenant, entered into that certain lease, dated as of December 30, 2020 (the “Master Lease”), with respect to premises consisting of approximately 109,237 rentable square feet of space, located at 1800 Sierra Point Parkway, Brisbane, California (the “Premises”). A copy of the Master Lease is attached hereto as Exhibit A. Capitalized terms used but not defined in this Sublease shall have the meanings ascribed to such terms in the Master Lease.

2. Premises: Sublessor hereby subleases to Sublessee, and Sublessee hereby subleases from Sublessor, a portion of the Premises consisting of approximately 31,157 rentable square feet of space located on the first floor of the Premises (hereinafter, the “Subleased Premises”) and Sublessee shall have the exclusive right to the use of certain storage space as described in Section 6.6 of the Master Lease, as incorporated herein, for the purposes as provided therein. The Subleased Premises are more particularly described on Exhibit B attached hereto. Except to the extent that the square footage of the Premises is adjusted under the Master Lease, the square footage of the Subleased Premises shall be as set forth in this paragraph, notwithstanding any remeasurement. In connection with its use of the Subleased Premises, Sublessee shall also have the non-exclusive right to use the Common Areas and, subject to Sublessor’s reasonable, non-discriminatory rules and regulations delivered from time to time to Sublessee, the portions of the Premises noted as “Shared Areas” on Exhibit B (the “Shared Areas”).

3. Term:

A. Term. The term (the “Term”) of this Sublease shall be for the period commencing on July 1, 2023 (the “Commencement Date”) and ending on September 30, 2028 (the “Expiration Date”), unless this Sublease is sooner terminated pursuant to its terms or the Master Lease sooner terminates or this Sublease is extended pursuant to its terms. For the avoidance of doubt, the Subleased Premises shall be deemed delivered and early access provided when Sublessor provides Sublessee keys or other means of access thereto, and the conditions in Paragraph 3(B)(i) have been satisfied. In the event Sublessee properly exercises the Extension Option in this Sublease for the Option Term (as hereinafter defined), the Term shall include the Option Term.

B. Early Possession. Sublessor shall permit Sublessee to enter the Subleased Premises commencing upon execution of this Sublease by Sublessor and Sublessee solely for the purpose of (x) planning construction of any Initial Alterations (as hereinafter defined), (y) conducting move coordination, and (z) constructing the Initial Alterations, and not for the purpose of conducting business therein, provided (i) Master Lessor’s consent to this Sublease has been received in substantially the form attached hereto as Exhibit E or other form executed by both Sublessor and Sublessee, which consent includes Master Lessor’s approval of Sublessee’s completion of the Environmental Questionnaire set forth in Exhibit E of the Master Lease, which approved Environmental Questionnaire shall be the Environmental Questionnaire for purposes of this Sublease (the “Master Lessor Consent”), (ii) Sublessee has delivered to Sublessor the Security Deposit and seventh month’s Base Rent as required under Paragraph 4, and (iii) Sublessee has delivered to Sublessor evidence of all insurance required under this Sublease (“Possession Date”). Such occupancy shall be subject to all of the provisions of this Sublease, except for the obligation to pay Base Rent or Direct Expenses (defined below) and shall not advance the Expiration Date of this Sublease.

4. Rent:

A. Base Rent. Sublessee shall pay to Sublessor as base rent for the Subleased Premises for each month during the Term the following amounts per month (“Base Rent”).

<u>Months</u>	<u>Base Rent</u>
1-12	\$241,466.75
13-24	\$249,918.09
25-36	\$258,665.22
37-48	\$267,718.50
49-60	\$277,088.65
61-63	\$286,786.75

*So long as Sublessee is not in default under this Sublease after expiration of any applicable cure period, Base Rent for the first six (6) full calendar months of the Term shall be abated.

Base Rent and Additional Rent, as defined in Paragraph 4(B) below, shall be paid on or before the first (1st) day of each month. Base Rent and Additional Rent for any period during the Term hereof which is for less than one (1) month of the Term shall be a pro rata portion of the monthly installment based on a thirty (30) day month. Base Rent and Additional Rent shall be payable without notice or demand and without any deduction, offset, or abatement, in lawful money of the United States of America except as expressly provided herein. Base Rent and Additional Rent shall be paid directly to Sublessor at 3928 Point Eden Way, Hayward, CA 94545, Attention: Finance/Accounts Receivable, or such other address as may be designated in writing by Sublessor, or pursuant to ACH instructions provided by Sublessor.

B. Additional Rent. All monies other than Base Rent required to be paid by Sublessor under the Master Lease as to the Subleased Premises, including, without limitation, any amounts payable by Sublessor to Master Lessor as “Direct Expenses” (as defined in Section 4.2.2 of the Master Lease), shall be paid by Sublessee hereunder as and when such amounts are due under the Master Lease, as incorporated herein. Sublessee shall also pay to Sublessor its pro rata share based on the square footage of the Subleased Premises to the square footage of the Premises (31,157/109,237) (“Pro Rata Share”), within thirty (30) days of request by Sublessor (but no earlier than the due date under the Master Lease), of the cost of utilities (to the extent that such utilities are not separately metered or sub-metered to the Subleased Premises, in which case Sublessee shall pay only the separately metered or sub-metered amounts), under Section 6.2 of the Master Lease, as incorporated herein. Sublessee shall also pay to Sublessor, within thirty (30) days of request by Sublessor, Sublessee’s Pro Rata Share of Sublessor’s actual out-of-pocket costs of performing any repairs or maintenance or providing other services that benefit the Subleased Premises or Shared Areas (such as maintenance of any systems therein and providing janitorial service and utilities to the shared lobby), and shall pay the entire cost of such amounts to the extent supplied solely or disproportionately to Sublessee or due to the misuse or excess use or negligence, willful misconduct or violation of this Sublease by Sublessee or its agent, employee or contractor. For the avoidance of doubt, Sublessee shall be responsible for the entire cost of operating the air handlers serving the labs in the Subleased Premises. Sublessee shall also pay any gross receipts or rent tax payable with respect to this Sublease and all costs directly incurred by or at the request of Sublessee with respect to its use of the Subleased Premises or Shared Areas. All such amounts shall be deemed additional rent (“Additional Rent”). Base Rent and Additional Rent hereinafter collectively shall be referred to as “Rent”.

C. Payment of Seventh Month's Rent. Upon execution hereof by Sublessee, Sublessee shall pay to Sublessor the sum of Two Hundred Forty-One Thousand Four Hundred Sixty-Six and 75/100 Dollars (\$241,466.75), which shall constitute Base Rent for the seventh month of the Term.

5. Security Deposit: On the Effective Date, Sublessee shall deposit with Sublessor the sum of Eight Hundred Sixty Thousand Three Hundred Sixty and 25/100 Dollars (\$860,360.25) (the "Security Deposit"), in cash, as security for the performance by Sublessee of the terms and conditions of this Sublease. If Sublessee fails to pay Rent or other charges due hereunder or otherwise defaults with respect to any provision of this Sublease after expiration of the applicable cure period, then Sublessor may draw upon, use, apply or retain all or any portion of the Security Deposit for the payment of any Rent or other charge in default, for the payment of any other sum which Sublessor has become obligated to pay by reason of Sublessee's default, or to compensate Sublessor for any loss or damage which Sublessor has suffered thereby, including future rent damages under California Civil Code Section 1951.2, without prejudice to any other remedy provided herein or by law. Sublessee hereby waives the provisions of any law, now or hereafter in force, including, without limitation, California Civil Code Section 1950.7, that provides that Sublessor may claim from a security deposit only those sums reasonably necessary to remedy defaults in the payment of Rent, to repair damage caused by Sublessee, or to clean the Subleased Premises, it being agreed that Sublessor, in addition, may claim those sums reasonably necessary to compensate Sublessor for any other loss or damage, foreseeable or unforeseeable, caused by the act or omission of Sublessee, including future rent damages following the termination of this Sublease. If Sublessor so uses or applies all or any portion of the Security Deposit, then Sublessee, within ten (10) days after demand therefor, shall deposit cash with Sublessor in the amount required to restore the Security Deposit to the full amount stated above. Within thirty (30) days of the expiration of this Sublease, if Sublessee is not in default after the expiration of any applicable cure period, Sublessor shall return to Sublessee so much of the Security Deposit as has not been applied by Sublessor pursuant to this paragraph, or which is not otherwise required to cure Sublessee's defaults. Sublessee shall have the right to instead provide the Security Deposit upon execution hereof in the form of a letter of credit in a form and from a bank that are reasonably acceptable to Sublessor, which shall be held in accordance with the terms of Article 21 of the Master Lease, as incorporated herein. Sublessor expressly acknowledges and agrees that the Security Deposit shall be and shall remain the property of Sublessee and shall not constitute property of Sublessor's estate subject to the claims of Sublessor's creditors in any Sublessor bankruptcy. Notwithstanding anything to the contrary herein, provided that Sublessee meets the Required Conditions (as defined below), then on the later of (a) thirtieth (30th) month of the Term and (b) one (1) month following Sublessor's receipt of evidence for item (iv) below and confirmation that Sublessee meets the Required Conditions, Sublessee shall have the right to reduce the amount of the Security Deposit to Two Hundred Eighty-Six Thousand Seven Hundred Eight-Six and 75/100 Dollars (\$286,786.75) by requesting such reduction in writing and providing evidence required by Sublessor that Sublessee has met the net worth and credit requirements of item (iv) below. In the event that Sublessee elected to provide the Security Deposit in the form of a letter of credit, upon any reduction of the Security Deposit Sublessee shall either deliver an amendment to the existing letter of credit or a replacement letter of credit in the new amount that otherwise complies with all other applicable requirements specified in this Section 5 and is in a form reasonably acceptable to Sublessor. The term "Required Conditions" as set forth above shall mean satisfaction of all of the following: (i) Sublessee has not committed a monetary or material default within the six (6) month period prior to Sublessee's request, (ii) Sublessee has not been in default of this Sublease after expiration of the applicable cure period, (iii) Sublessee is not then currently in default, and an event or circumstance does not then exist that would constitute a default by Sublessee under this Sublease without regard to any notice and cure period, and (iv) Sublessee's tangible net worth (i.e., net worth without taking into account intangible assets such as goodwill, copyrights and other intellectual property) and credit worthiness is not less than that of Sublessee as of the Effective Date of this Sublease.

6. Holdover: In the event that Sublessee does not surrender the Subleased Premises by the Expiration Date in accordance with the terms of this Sublease, Sublessee shall indemnify, defend, protect and hold harmless Sublessor from and against all loss and liability resulting from Sublessee's delay in surrendering the Subleased Premises and pay Sublessor holdover rent as provided in Section 16 of the Master Lease, as incorporated herein, and, if the holdover extends beyond the termination of the Master Lease, the terms of Section 16 of the Master Lease.

7. Repairs: Sublessor represents and warrants to Sublessee that, to Sublessor's actual knowledge, (a) any mechanical, electrical, plumbing, HVAC systems and life safety systems (collectively, "Systems"), emergency generator and boiler serving the Subleased Premises are in good operating condition and (b) the Subleased Premises are in compliance with all laws (in each case given the level of improvements in the Subleased Premises). Sublessee shall have ninety (90) days after the Possession Date to notify Sublessor if any of the Systems, the emergency generator and boiler serving the Subleased Premises were not in good operating condition on the Possession Date. The parties acknowledge and agree that Sublessor has made no representations or warranties with respect to the condition of the Subleased Premises except as otherwise provided herein. Sublessor shall have no obligation whatsoever to make or pay the cost of any alterations, improvements or repairs to the Subleased Premises, including, without limitation, any improvement or repair required to comply with any law. Master Lessor shall be solely responsible for performance of any repairs required to be performed by Master Lessor under the terms of the Master Lease. For the avoidance of doubt, Sublessee shall be responsible for maintaining the air handlers serving the labs in the Subleased Premises

8. Assignment and Subletting: Sublessee may not assign this Sublease, sublet the Subleased Premises, transfer any interest of Sublessee therein or permit any use of the Subleased Premises by another party (collectively, "Transfer"), without the prior written consent of Sublessor and Master Lessor; provided, however, Sublessor's consent shall not be required for a transfer as described in the first sentence of Section 14.8 of the Master Lease. Sublessee acknowledges that the Master Lease contains a "recapture" right in Section 14.4, and that Sublessor may withhold consent to a proposed Transfer in its sole discretion unless Master Lessor confirms in writing that the recapture right does not apply to the Subleased Premises or otherwise waives such right pursuant to the Master Lessor Consent. Any Transfer shall be subject to the terms of Section 14 of the Master Lease, as incorporated herein.

9. Use: Sublessee may use the Subleased Premises only for the following uses: general office, laboratory, research and development, lab scale manufacturing, vivarium and all other lawful uses reasonably related to or incidental to such specified uses, all consistent with first class life science projects in the City of Brisbane, and in compliance with, and subject to, applicable laws and the terms of the Master Lease and this Sublease; provided, however, if the Subleased Premises are expanded to include premises on the second (2nd) floor of the Premises, the second floor may only be used for office use and other lawful uses reasonably related to or incidental to such specified uses, all (i) consistent with first class life sciences projects in Brisbane, California, and (ii) in compliance with, and subject to, applicable laws and the terms of this Sublease. Sublessee shall not use, store, transport or dispose of any Hazardous Materials in or about the Subleased Premises except as expressly permitted under the Master Lease, as incorporated herein, including Section 5.3 thereof. Sublessee shall be responsible for its own wastewater permits and for properly disposing of any hazardous or medical waste it generates.

10. Delivery and Acceptance: By taking possession of the Subleased Premises, Sublessee conclusively shall be deemed to have accepted the Subleased Premises in their as-is, then-existing condition, without any warranty whatsoever of Sublessor with respect thereto except as may be otherwise provided herein.

11. Improvements:

A. No alteration or improvements shall be made to the Subleased Premises, except in accordance with the Master Lease, and with the prior written consent of both Master Lessor and Sublessor (which consent by Sublessor shall not be unreasonably withheld, conditioned or delayed). Notwithstanding the foregoing, Sublessee shall be permitted to make alterations in the Subleased Premises without Sublessor's prior written consent, but subject to the prior written consent of Master Lessor, to the extent required under the Master Lease, and with ten (10) business days' notice to Sublessor, to the extent such alterations (i) are non-structural, (ii) cost less than \$50,000 for the particular job or work, (iii) are not visible from the exterior

of the Building, and (iv) do not affect the Systems or equipment (other than minor changes such as adding or relocating electrical outlets and thermostats). Notwithstanding anything to the contrary herein, if the Subleased Premises are expanded to include premises on the second floor of the Premises, only general office improvements may be made on the second floor.

B. Sublessor shall provide Sublessee with an allowance to perform certain alterations and improvements in the initial Subleased Premises only (the "Initial Alterations"), in accordance with the terms attached as Exhibit C hereto.

12. Insurance; Waiver of Subrogation: Sublessee shall obtain and keep in full force and effect, at Sublessee's sole cost and expense, during the Term, the insurance required under Section 10 of the Master Lease. Sublessee shall name Master Lessor and Sublessor as additional insureds under its liability insurance policy. The release and waiver of subrogation set forth in Section 10.5 of the Master Lease, as incorporated herein, shall be binding on the parties.

13. Default: Sublessee shall be in default under this Sublease if Sublessee commits any act or omission which constitutes a default under the Master Lease, which has not been cured after delivery of written notice and passage of the applicable grace period provided in the Master Lease as modified, if at all, by the provisions of this Sublease. In the event of any default by Sublessee, Sublessor shall have all remedies provided pursuant to Section 19.2 of the Master Lease and by applicable law, including damages that include the worth at the time of award of the amount by which the unpaid rent for the balance of the term after the time of award exceeds the amount of such rental loss that the lessee proves could be reasonably avoided and the remedy described in California Civil Code Section 1951.4 (lessor may continue lease in effect after lessee's breach and abandonment and recover rent as it becomes due, if lessee has right to sublet or assign, subject only to reasonable limitations).

14. Surrender: Prior to expiration of this Sublease, Sublessee shall have the right to remove from the Subleased Premises all of its movable trade fixtures installed by Sublessee so long as Sublessee repairs any damage resulting from such removal, if permitted by the Master Lease, and shall surrender the Subleased Premises in the condition described in the Master Lease. If the Subleased Premises are not so surrendered, then Sublessee shall be liable to Sublessor for all liabilities Sublessor incurs as a result thereof, including costs incurred by Sublessor in returning the Subleased Premises to the required condition.

15. Broker: Sublessor and Sublessee each represents to the other that it has dealt with no real estate brokers, finders, agents or salesmen other than Cornish & Carey Commercial dba Newmark Knight Frank representing Sublessor and Sublessee, in connection with this transaction. Each party agrees to hold the other party harmless from and against all claims for brokerage commissions, finder's fees or other compensation made by any other agent, broker, salesman or finder as a consequence of such party's actions or dealings with such agent, broker, salesman, or finder.

16. Notices: Unless at least five (5) days' prior written notice is given in the manner set forth in this paragraph, the address of each party for all purposes connected with this Sublease shall be the applicable address set forth below its signature at the end of this Sublease. All notices, demands or communications in connection with this Sublease shall be (a) personally delivered; or (b) properly addressed and (i) submitted to an overnight courier service, charges prepaid, or (ii) deposited in the mail (certified, return receipt requested, and postage prepaid). Notices shall be deemed delivered upon receipt, if personally delivered, one (1) business day after being submitted to an overnight courier service and three (3) business days after mailing, if mailed as set forth above. All notices given to Master Lessor under the Master Lease shall be considered received only when delivered in accordance with the Master Lease.

17. Miscellaneous: Sublessor has not had an inspection of the Premises performed by a Certified Access Specialist as described in California Civil Code § 1938. A Certified Access Specialist (CASp) can inspect the Subleased Premises and determine whether the Subleased Premises complies with all of the

applicable construction-related accessibility standards under state law. Although state law does not require a CASp inspection of the Subleased Premises, the commercial property owner or lessor may not prohibit the lessee or tenant from obtaining a CASp inspection of the Subleased Premises for the occupancy or potential occupancy of the lessee or tenant, if requested by the lessee or tenant. The parties shall mutually agree on the arrangements for the time and manner of the CASp inspection, the payment of the fee for the CASp inspection, and the cost of making any repairs necessary to correct violations of construction-related accessibility standards within the Subleased Premises.

18. Other Sublease Terms:

A. Incorporation by Reference. Except as set forth below, the terms and conditions of this Sublease shall include all of the terms of the Master Lease and such terms are incorporated into this Sublease as if fully set forth herein, except that: (i) each reference in such incorporated sections to “Lease” shall be deemed a reference to “Sublease”; (ii) each reference to the “Premises”, “Lease Term” and “Base Rent” shall be deemed a reference to the “Subleased Premises”, “Term” and “Base Rent” under this Sublease, respectively; (iii) each reference to “Landlord” and “Tenant” shall be deemed a reference to “Sublessor” and “Sublessee”, respectively, except as otherwise expressly set forth herein; (iv) with respect to work, services, repairs, restoration, insurance, indemnities, representations, warranties or the performance of any other obligation of Master Lessor under the Master Lease, the sole obligation of Sublessor shall be to request the same in writing from Master Lessor as and when requested to do so by Sublessee, and to use Sublessor’s reasonable efforts (without requiring Sublessor to spend more than a nominal sum unless Sublessee pays the full amount of any additional costs and provided in no event shall Sublessor be required to engage in litigation) to obtain Master Lessor’s performance; (v) with respect to any obligation of Sublessee to be performed under this Sublease, wherever the Master Lease grants to Sublessor a specified number of days to perform its obligations under the Master Lease, except as otherwise provided herein, Sublessee shall have three (3) fewer days to perform the obligation, including, without limitation, curing any defaults (provided, that Sublessee shall have two (2) fewer days if the time period permitted for such obligation is less than three (3) days); (vi) with respect to any approval required to be obtained from the “Landlord” under the Master Lease, such consent must be obtained from both Master Lessor (unless such approval has been obtained in the Master Lessor Consent in which case Master Lessor’s consent is not required) and Sublessor, and the approval of Sublessor may not be (unless another standard is expressly set forth in the Master Lease or this Sublease) unreasonably withheld, conditioned or delayed, but may be withheld if Master Lessor’s consent is not obtained; (vii) in any case where the “Landlord” reserves or is granted the right to manage, supervise, control, repair, alter, regulate the use of, enter or use the Premises or any areas beneath, above or adjacent thereto, perform any actions or cure any failures, such reservation or right shall be deemed to be for the benefit of both Master Lessor and Sublessor provided such benefit is conducted in accordance with the terms and provisions of the Master Lease; (viii) in any case where “Tenant” is to indemnify, release or waive claims against “Landlord”, such indemnity, release or waiver shall be deemed to cover, and run from Sublessee to, both Master Lessor and Sublessor; (ix) in any case where “Tenant” is to execute and/or deliver certain documents or notices to “Landlord”, such obligation shall be deemed to run from Sublessee to both Master Lessor and Sublessor; (x) all payments shall be made to Sublessor; (xi) Sublessee shall pay all consent and review fees set forth in the Master Lease to either Master Lessor or Sublessor, as designated by Sublessor, and any caps shall apply to such designee; and (xii) Sublessor’s obligations under Section 4 are limited to forwarding statements and refunds provided by Master Lessor, and Sublessee shall have no right to dispute or audit such statements. Except as expressly provided in Paragraph 4(A) above, under no circumstances shall rent abate under this Sublease except to the extent that rent correspondingly abates under the Master Lease as to the Subleased Premises.

Notwithstanding the foregoing, the following provisions of the Master Lease shall not be incorporated herein: Summary of Basic Lease Information, Sections 1.1.1, 1.1.2 (the first sentence only), 2.1 (except the first, third and fourth sentences), 2.2, 3, 4.6, 5.3.1.4.3 (with respect to the indemnification only), 6.1 (the first clause in the last sentence only), 6.5 (the clause beginning with “which” and ending with “Landlord’s Work” only), 7.3, 8.1 (except the first sentence), 8.5 (the fifth – seventh sentences only), 9 (the first clause of the

second sentence but it is replaced with “Except as to Alterations not requiring consent”), 14.3 (the penultimate sentence and the parentheticals in the second sentence only), 14.4 (the last three sentences), 14.8, 18 (the first and third sentences only), 23.1 (the first sentence and the last two sentences only), 29.13 (the first sentence only), 29.18, 29.24; Exhibits A, B, F, G and H. In addition, notwithstanding subpart (iii) of the foregoing paragraph, (a) references in the following provisions to “Landlord” shall mean Master Lessor only: Sections 1.1.2(iv), 1.1.3, 4.2.4, 4.3, 6.1 (the first sentence only), 6.5 (the second sentence only), 7.2, 8.4 (the last reference in the first sentence), 10.2, 11.1 (the second and third sentences only), 11.2 (except the last instance), 13 (the first sentence), 15.2 (the last reference of the first sentence only), 29.26 (the first sentence) and 29.29.1; and (b) references in the following provisions to “Landlord” shall mean Master Lessor and Sublessor: Sections 4.5, 5.3.1.2, 5.3.2, 5.3.4.1, 6.4, 10.3.4, 10.4, 17, 24 (the third sentence only) and 26.2; (d) references to the “Permitted Use” shall mean the use permitted under Section 9 above; (e) the number of parking spaces in Section 9 of the Summary of Basic Lease Information (as referenced in Section 28 of the Master Lease) shall be eighty-eight (88); (f) Tenant’s Share shall mean the Pro Rata Share; (g) in Section 14.3, Sublessee shall pay Sublessor the entire premium payable to Master Lessor under the Master Lease; (h) Sublessee’s right to use the Storage Room under Section 6.6 shall commence on the Possession Date and be limited to the room with the double door (Sublessor shall retain the exclusive use of the small room); and (i) if Sublessee requires more than its Pro Rata Share of the Generator capacity, Sublessee shall be solely responsible for any increased or additional generator capacity, subject to the terms of this Sublease and the Master Lease, including obtaining Master Lessor’s and Sublessor’s prior written consent thereto.

Notwithstanding the foregoing, the second sentence of Section 5.3.4.3 of the Master Lease shall be incorporated herein with the following addition to the end of such sentence: “and Sublessor and Sublessee shall reasonably cooperate to obtain and deliver to Master Landlord such a letter or other written determination.”

Sublessor shall not do or fail to do anything that would constitute a default under the Master Lease so as to result in a termination of the Master Lease unless Master Lessor or a successor tenant agrees to permit Sublessee to continue to occupy the Subleased Premises on the terms of this Sublease for the remainder of the Term. Sublessor hereby represents and warrants to Sublessee that as of the Effective Date: (i) the Master Lease is in full force and effect; (ii) no lender of Sublessor must consent to this Sublease; and (iii) Sublessor has not received from Master Lessor a notice of any default by Sublessor that remains uncured. Sublessor shall deliver to Sublessee any notice of default from Master Lessor and any other notice from Master Lessor that would adversely affect Sublessee’s occupancy of the Subleased Premises within five (5) days of receipt.

B. Assumption of Obligations. This Sublease is and at all times shall be subject and subordinate to the Master Lease and the rights of Master Lessor thereunder. Sublessee hereby expressly assumes and agrees: (i) to comply with all provisions of the Master Lease which are incorporated hereunder; and (ii) to perform all the obligations on the part of the “Tenant” to be performed under the terms of the Master Lease during the Term of this Sublease that are incorporated hereunder. In the event the Master Lease is terminated for any reason whatsoever, this Sublease shall terminate simultaneously with such termination (unless Master Lessor or a successor tenant agrees to permit Sublessee to continue to occupy the Subleased Premises on the terms of this Sublease for the remainder of the Term), without any liability of Sublessor to Sublessee except in the event of a termination due to a violation of this Sublease by Sublessor. Sublessor shall indemnify Sublessee for, and shall hold it harmless from and against, any and all losses, damages, penalties, liabilities, costs and expenses, including, without limitation, reasonable attorneys’ fees and disbursements, which may be sustained or incurred by Sublessee by reason of Sublessor’s failure to keep, observe or perform any of the terms, provisions, covenants, conditions and obligations on Sublessor’s part to be kept, observed or performed under this Sublease. Sublessor shall not voluntarily terminate the Master Lease except if Master Lessor or a successor tenant agrees to permit Sublessee to continue to occupy the Subleased Premises on the terms of this Sublease for the remainder of the Term or pursuant to a right expressly set forth in the Master Lease, and Sublessor shall not amend the Master Lease in a manner that is materially adverse to Sublessee without Sublessee’s prior written consent which may be granted or withheld in Sublessee’s sole discretion. In the event of a conflict between the provisions of this Sublease and the Master Lease, as between Sublessor and Sublessee, the provisions of this Sublease shall control. In the event of a conflict between the express

provisions of this Sublease and the provisions of the Master Lease, as incorporated herein, the express provisions of this Sublease shall prevail.

19. Master Lessor Consent: This Sublease and Sublessor's and Sublessee's obligations hereunder are conditioned upon obtaining the Master Lessor's Consent. Sublessor and Sublessee shall use commercially reasonable efforts to obtain the Master Lessor's Consent. If Sublessor fails to obtain the Master Lessor Consent within thirty (30) days after the Effective Date, then Sublessor or Sublessee may terminate this Sublease by giving the other party written notice thereof prior to the date such consent is received, and Sublessor shall return to Sublessee its payment of the seventh month's Rent paid by Sublessee pursuant to Paragraph 4 hereof and the Security Deposit.

20. Termination; Recapture: Notwithstanding anything to the contrary herein, Sublessee acknowledges that, under the Master Lease, both Master Lessor and Sublessor have certain termination and recapture rights, including, without limitation, in Sections 11, 13 and 14.4. Nothing herein shall prohibit Master Lessor or Sublessor from exercising any such rights and neither Master Lessor nor Sublessor shall have any liability to Sublessee as a result thereof provided such rights by Sublessor are exercised in accordance with the terms and provisions of the Master Lease or this Sublease, as applicable. In the event Master Lessor or Sublessor exercise any such termination or recapture rights as to all of the Subleased Premises, provided such rights by Sublessor are exercised in accordance with the terms and provisions of the Master Lease or this Sublease, as applicable, this Sublease shall terminate without any liability to Master Lessor or Sublessor.

21. Inducement Recapture: Any agreement for free or abated Base Rent set forth in Paragraph 4(A) is hereinafter referred to as "Inducement Provisions". Inducement Provisions shall be deemed conditioned upon Sublessee's full and faithful performance of all of the terms, covenants and conditions of this Sublease. Upon a termination of this Sublease, any such Inducement Provision shall automatically be deemed deleted from this Sublease and no further force or effect, and any Base Rent theretofore abated, given or paid by Sublessor under such an Inducement Provision shall be immediately due and payable by Sublessee to Sublessor.

22. Parking and Signage: Sublessee shall have the right to park in eighty-eight (88) parking spaces in the on-site parking lot and garage that serves the Building, on an unreserved basis, as provided in Section 28 of the Master Lease, as incorporated herein. Subject to Master Lessor's and Sublessor's consent and Section 23 of the Master Lease, Sublessee shall have the right to install its name and/or logo or any of its affiliates' names and/or logos on (i) signage within the Subleased Premises, (ii) signage in one (1) location on the exterior rooftop of the Building to be reasonably and mutually agreed upon by Sublessor and Sublessee, and (iii) monument signage as permitted in the Master Lease provided that Sublessor shall be entitled to maintain its name in the monument signage.

23. Extension Option: Provided that no default after expiration of the applicable cure period has occurred more than twice in the two (2) years prior to the date of Sublessee's exercise notice and no default exists on such exercise date as to which Sublessor has delivered notice to Sublessee, Sublessee shall have one (1) option to extend the Term of this Sublease (the "Extension Option") to expire on January 3, 2032 (the "Option Term") by providing written notice to Sublessor of its desire to exercise such option at least nine (9) months prior to the expiration of the Term. The monthly Base Rent for the first year of the Option Term shall initially be 3.5% more than the amount of the Base Rent in the last month of the initial Term, and shall increase at a rate of 3.5% per year on each anniversary of the Commencement Date. There shall be no additional Allowance or Inducement Provisions during the Option Term.

24. Right of First Offer: Subject to Master Lessor's consent, provided that no default after expiration of the applicable cure period has occurred more than twice in the two (2) years prior to the date of Sublessor's notice in this sentence and no default exists on such notice date as to which Sublessor has delivered notice to Sublessee, if Sublessor determines to sublease all or any part of the second floor of the

Premises (the "ROFO Space") other than to a Permitted Transferee, then Sublessor shall notify Sublessee of the terms on which Sublessor is willing to lease such ROFO Space to Sublessee (the "Offer Sheet"). If Sublessee, within ten (10) business days after receipt of Sublessor's written notice indicates in writing (the "ROFO Exercise Notice") its agreement to sublease the applicable ROFO Space on the terms stated in the Offer Sheet, then Sublessor shall sublease to Sublessee and Sublessee shall sublease from Sublessor the applicable ROFO Space on the economic terms stated in the Offer Sheet and otherwise on the terms of this Sublease, except as otherwise stated herein; provided, however, Sublessee's right to sublease ROFO Space that, taken with the initial Subleased Premises and any other portions of the Premises that are subleased, would cause fifty percent (50%) or more of the Premises to be subleased for more than fifty percent (50%) of the remaining Lease Term shall be conditioned upon Master Lessor's waiver of its rights under Section 14.4 of the Master Lease. If the ROFO Exercise Notice is delivered within the final 18 months of the Term, the term of the sublease for the ROFO Space shall be the term stated in the Offer Sheet. If the ROFO Exercise Notice is delivered prior to the final 18 months of the Term, the term of the sublease for the ROFO Space shall be equal to the lesser of (x) the term stated in the Offer Sheet, and (y) the remainder of the Term of this Sublease, in which case any rent or other concessions (such as allowances and improvements) offered in the Offer Sheet shall be prorated to account for such lesser term. If Sublessee does not indicate in writing its agreement to sublease the ROFO Space within such ten (10) business day period, then Sublessor thereafter shall have the right to sublease the ROFO Space to a third party on any terms; provided however, if the economic terms (on a net effective basis) are more than five percent (5%) more favorable to the subtenant than the terms offered by Sublessor to Sublessee, then the terms of this paragraph shall again be applicable, but the reference to ten (10) business days shall be revised to five (5) business days. If Sublessee properly exercises the right of first offer, the parties shall enter into an amendment to this Sublease incorporating the ROFO Space on the terms set forth in this paragraph. Sublessee's right of first offer shall be a continuing right during the Term.

25. Expansion Option: Subject to Master Lessor's consent, provided that no default after expiration of the applicable cure period has occurred and no default exists on such notice date as to which Sublessor has delivered notice to Sublessee, Sublessee shall have the option (the "Expansion Option") to expand the Subleased Premises under this Sublease to include one of the portions of the second floor of the Premises shown on Exhibit D hereto (the "Expansion Premises") on the Commencement Date by providing written notice to Sublessor exercising such option prior to April 30, 2023, which notice to be valid must designate the applicable portion of the Expansion Premises shown on Exhibit D that Sublessee desires to sublease (the "Applicable Space"). If Sublessee properly exercises the Expansion Option, as of the Commencement Date, (i) references in this Sublease to the Subleased Premises shall be deemed to include the Applicable Space, (ii) Base Rent under this Sublease shall be increased on a pro rata basis (at the same per square foot rental rate) based on the additional rentable square footage of the Applicable Space, as reasonably determined by Sublessor, (iii) Sublessee's Pro Rata Share as set forth in Paragraph 4(B) above shall be increased based on the additional rentable square footage of the Applicable Space, (iv) the amount of the Security Deposit required hereunder shall be increased by an amount equal to the last three (3) months of Base Rent for the Expansion Premises and (v) there shall be no additional Allowance. Notwithstanding the foregoing, Sublessee's right to sublease any Expansion Premises that, taken with the initial Subleased Premises and any other portions of the Premises that are subleased, would cause fifty percent (50%) or more of the Premises to be subleased for more than fifty percent (50%) of the remaining Lease Term shall be conditioned upon Master Lessor's waiver of its rights under Section 14.4 of the Master Lease.

26. Termination of Master Lease. If the Master Lease is terminated due to Sublessor's default of the Master Lease and such termination of the Master Lease results in an early termination of this Sublease through no fault or action of Sublessee, then, as an obligation that survives the termination of this Sublease, in addition to other damages to which Sublessee may be entitled hereunder, Sublessor agrees that, subject to the penultimate sentence of this Paragraph 26, Sublessor shall pay to Sublessee an amount equal to the unamortized amount, as of the date of the termination of this Sublease, of the actual out-of-pocket costs incurred by Sublessee in excess of the Allowance for the Initial Alterations performed by Sublessee pursuant to Exhibit C of this Sublease (the "Excess Sublessee Improvement Costs"). For purposes of this Paragraph 26, the Excess Sublessee Improvement Costs shall be amortized on a straight-line basis over the Term commencing from and after the Commencement Date (or a pro rata per diem portion thereof for any partial month). If despite such Master Lease termination the then-current Master Lessor under the Master Lease, or its successor as owner of the Premises, agrees to a continuation of this Sublease or enters into a replacement lease with Sublessee or its affiliate for Sublessee's (or its affiliate's) continued occupancy of the Premises then, notwithstanding any contrary provision of this Paragraph 26, Sublessor shall have no obligation under

this Paragraph 26. Notwithstanding anything to the contrary in this Paragraph 26, in no event shall Sublessee's right to recovery under this Sublease as a result of such termination exceed the amount of damages recoverable by Sublessee under California Civil Code Section 3300 taking into account Sublessee's duty to mitigate damages. This Paragraph 26 shall survive termination of this Sublease.

[SIGNATURES ON FOLLOWING PAGE]

IN WITNESS WHEREOF, the parties have executed this Sublease as of the day and year first above written.

SUBLESSOR: SUBLESSEE:

ARCUS BIOSCIENCES, INC., PROTHENA BIOSCIENCES INC,
a Delaware corporation a Delaware corporation

By: /s/ Bob Geoltz By: /s/ Tran Nguyen

Name: Bob Geoltz Name: Tran Nguyen

Its: Chief Financial Officer Its: Chief Financial Officer

Address: Arcus Biosciences, Inc. Address for Notices:
3928 Point Eden Way
Hayward, CA 94545 Before the Commencement Date:
Attn: Legal

Prothema Biosciences Inc
331 Oyster Point Boulevard
South San Francisco, CA 94080
Attn: Legal Department

After the Commencement Date:

Prothema Biosciences Inc
1800 Sierra Point Pkwy
Brisbane, CA 94005
Attn: Legal Department

EXHIBIT A

MASTER LEASE

EXHIBIT B

SUBLEASED PREMISES AND SHARED AREAS

Subleased Premises: Area shown in green and labeled 102

Storage Space: Area shown in green and labeled 101

Shared Areas: Areas shown in blue and labeled Main Lobby, RR/Shower, Stairs, Elevator and Trash Area

EXHIBIT C

WORK LETTER

A. Sublessee and its contractors shall not have the right to perform Initial Alterations in the Premises except in compliance with the terms of Article 8 of the Master Lease, as incorporated herein, including approval by Sublessor (which approval shall not be unreasonably withheld, conditioned or delayed), and Master Lessor to the extent required under the Master Lease, of the final plans for the Initial Alterations and the architect and contractor to be retained by Sublessee to perform the Initial Alterations. Subject to its review of more detailed plans and specifications, and Master Lessor's consent, Sublessor conceptually approves of the preliminary plans for the Initial Alterations attached hereto as Schedule 1 (the "Preapproved Alterations"). Sublessee shall not be required to restore the Preapproved Alterations at the end of the Term except to the extent required by Master Lessor. Prior to the Commencement Date, as part of the Initial Alterations, Sublessee shall install separate meters or submeters for electricity, water and all other utilities and systems serving the Subleased Premises, including the air handlers serving the labs in the Subleased Premises. Sublessee shall substantially complete the Initial Alterations (or other improvements reasonably approved by Master Lessor and Sublessor that constitute a commercially reasonable level of improvement as described in Section 2(a) of Exhibit B of the Master Lease) by June 30, 2024.

B. Prior to Sublessee's execution of the construction contract and general conditions with its contractor to perform the Initial Alterations (the "Contract"), Sublessee shall submit the Contract to Sublessor for its review. Prior to the commencement of construction of the Initial Alterations, Sublessee shall provide Sublessor with a detailed written estimated cost breakdown, by trade, of the final costs to be incurred, or which have been incurred, in connection with the design, permitting and construction of the Initial Alterations (which costs form a basis for the amount of the Contract) (the "Final Costs"). Sublessor shall contribute the sum of \$9,347,100 (the "Allowance") toward the cost of performing the Initial Alterations within the Subleased Premises. The Allowance may only be used for the cost of preparing design and construction documents for the Initial Alterations, the cost of construction management and/or supervision costs, permit fees and hard construction costs (including any permanently fixed laboratory equipment, e.g., permanently affixed laboratory benches, sinks, mechanical systems, fume hoods, which, for the avoidance of doubt, shall be owned by Sublessor and may not be removed by Sublessee) in connection with the Initial Alterations. The Allowance shall be paid to Sublessee, during the design and construction of the Initial Alterations, within thirty (30) days following receipt by Sublessor of: (1) invoices from all of contractors, subcontractors, laborers, materialmen and suppliers for labor rendered and materials expended and used in the Initial Alterations; (2) a sworn contractor's affidavit from the general contractor and a request to disburse from Sublessee containing an approval by Sublessee of the work done, in a form reasonably acceptable to Sublessor; (3) for work in connection with amounts subject to disbursement, executed conditional, and for all previous work, executed unconditional, mechanics' lien releases, as applicable, from all contractors, subcontractors, laborers, materialmen and suppliers, which shall comply with the appropriate provisions, as reasonably determined by Sublessor, of the California Civil Code; (4) for the final disbursement request, as-built plans of the Initial Alterations; (5) the certification of Sublessee and its architect that the applicable portion of the Initial Alterations have been installed in a good and workmanlike manner in accordance with the approved plans, and in accordance with applicable laws; and (6) all other information required by Master Lessor to disburse the Additional TI Allowance under the Master Lease. Within thirty (30) days thereafter, but not more frequently than monthly, Sublessor shall deliver a check to Sublessee made payable to Sublessee in payment of the lesser of (a) a fraction of the amounts requested by Sublessee in which the numerator is the amount of the Allowance and the denominator is the Final Costs, and (b) the balance of any remaining available portion of the Allowance, provided that Sublessor does not dispute any request for payment based on non-compliance of any work with the approved plans or due to any substandard work. Notwithstanding anything herein to the contrary, (i) Sublessee shall be responsible for all costs as they become due except to the extent set forth in this section, and (ii) Sublessor shall not be obligated to disburse any portion of the Allowance during the continuance of a default under the Sublease as to which Sublessor has provided Sublessee notice, and Sublessor's obligation to disburse shall only resume when and if such default is cured. Any construction management fees payable to Master Lessor by Sublessor for the Initial Alterations shall be paid for by Sublessee. The Allowance may also be used by Sublessor to pay any costs or fees charged by Master Lessor under the Master Lease.

C. Except as expressly set forth above, in no event shall the Allowance be used for the purchase of equipment, furniture or other items of personal property of Sublessee. In the event Sublessee does not properly request the entire Allowance before June 30, 2024, any unused amount shall accrue to the sole benefit of Sublessor, it being understood that Sublessee shall not be entitled to any credit, abatement or other concession in connection therewith. Sublessee shall be responsible for all applicable state sales or use taxes, if any, payable in connection with the Initial Alterations and/or Allowance.

D. No additional or increased Allowance shall be provided in the event of a renewal or extension of the initial Term of the Sublease or an expansion of the Subleased Premises, whether by any options under the Sublease or otherwise.

E. Sublessee shall have no obligation to perform ADA upgrades outside of the Subleased Premises except to the extent required by law as a result of the Initial Alterations or future Alterations performed by Sublessee or Sublessee's particular use of the Subleased Premises (whether such requirement is pursuant to the Master Lease, insurance requirements, or any law, statute, ordinance, order or other governmental decision including permit requirements issued in connection with the the Initial Alterations or future Alterations performed by or on behalf of Sublessee).

SCHEDULE 1
PREAPPROVED ALTERATIONS

EXHIBIT D

POTENTIAL EXPANSION OPTION BLOCKS

Applicable Space:

Area shown in yellow or
Area shown in blue or
Entire rentable area on second floor

EXHIBIT E
MASTER LESSOR CONSENT

CONSENT TO SUBLEASE AGREEMENT

THIS CONSENT TO SUBLEASE AGREEMENT (this "**Agreement**") is made as of October 28, 2022, by and among HCP LS BRISBANE, LLC, a Delaware limited liability company ("**Landlord**"), ARCUS BIOSCIENCES, INC., a Delaware corporation ("**Tenant**"), and PROTHENA BIOSCIENCES INC, a Delaware corporation ("**Subtenant**").

R E C I T A L S

A. Reference is hereby made to that certain Lease dated December 30, 2020, between Landlord and Tenant (the "**Lease**"), for approximately 109,237 rentable square feet of space (the "**Premises**") located on the first (1st), second (2nd) and third (3rd) floors of the building located at 1800 Sierra Point Parkway, Brisbane, California 94005 (the "**Building**"), which Building is part of an office/laboratory project ("**Project**") as defined in the Lease.

B. Pursuant to the terms of Article 14 of the Lease, Tenant has requested Landlord's consent to that certain Sublease dated October 28, 2022, between Tenant and Subtenant (the "**Sublease**"), with respect to a subletting by Subtenant of a portion of the Premises consisting of approximately 31,157 rentable square feet of space, as more particularly described in the Sublease (the "**Sublet Premises**"). A copy of the Sublease is attached hereto as Exhibit A. Landlord is willing to consent to the Sublease on the terms and conditions contained herein.

C. All defined terms not otherwise expressly defined herein shall have the respective meanings given in the Lease.

A G R E E M E N T

1. Landlord's Consent. Landlord hereby consents to the Sublease (including any right of Subtenant thereunder to enter the Sublet Premises upon the execution of the Sublease); provided, however, notwithstanding anything contained in the Sublease to the contrary, such consent is granted by Landlord only upon the terms and conditions set forth in this Agreement. The Sublease is subject and subordinate to the Lease. Neither the Lease, the Sublease nor this Agreement shall be deemed to grant Subtenant any rights whatsoever against Landlord. Subtenant hereby acknowledges and agrees that Subtenant shall have no direct recourse against Landlord for any alleged or actual breach of its rights in connection with the Sublease or the Sublet Premises. In the event of any conflict or inconsistency between the terms and conditions of the Lease and the terms and conditions of the Sublease, the terms and conditions of the Lease shall govern and control. Landlord shall not be bound by any of the terms, covenants, conditions, provisions or agreements of the Sublease. Subtenant acknowledges for the benefit of Landlord that (i) as among Landlord, Tenant and Subtenant, Subtenant accepts the Sublet Premises in their presently existing, "as-is" condition (but as between Tenant and Subtenant, the terms and conditions of the Sublease shall control), and (ii) that Landlord has made no representation or warranty to Subtenant as to the compliance of the Sublet Premises with any law, statute, ordinance, rule or regulation. Tenant and Subtenant hereby represent and warrant to Landlord that the copy of the Sublease attached hereto is a full, complete and accurate copy of the Sublease, and that there are no other documents or instruments relating to the use of the Sublet Premises by Subtenant other than the Sublease.

2. Reimbursement of Landlord. Within thirty (30) days after invoice, Tenant shall reimburse Landlord all of Landlord's reasonable review and processing fees, as well as any reasonable professional fees (including, without limitation, attorneys', accountants', architects', engineers' and consultants' fees) incurred by Landlord in connection with its review and consent of the Sublease and preparation and negotiation of this Agreement, not to exceed Three Thousand Five Hundred and 00/100 Dollars (\$3,500.00).

3. Non-Release of Tenant; Further Transfers. Neither the Sublease nor this consent thereto shall release or discharge Tenant from any obligation or liability, whether past, present or future, under the Lease or alter the primary liability of Tenant to pay the rent and perform and comply with all of the obligations of Tenant to be performed under the Lease (including the payment of all bills rendered by Landlord for charges incurred by Subtenant for services and materials supplied to the Sublet Premises). Neither the Sublease nor this consent thereto shall change, modify or amend the Lease in any manner or be construed as a waiver of Landlord's right to consent to any further subletting either by Tenant or by Subtenant (including, without limitation, pursuant to the exercise of the right of first offer set forth in the Sublease, which shall require Landlord's prior written consent), or to any assignment by Tenant of the Lease or assignment by Subtenant of the Sublease, or as a consent to any portion of the Sublet Premises being used or occupied by any other party. Notwithstanding the foregoing, Landlord hereby consents to (and Landlord's further consent shall not be required for) the extension of the Sublease term or expansion of the Sublet Premises pursuant to Paragraphs 23 and 25 of the Sublease, as applicable; provided that (i) any such extension or expansion shall comply with the terms and conditions of Paragraphs 23 and 25 of the Sublease, as those provisions are currently drafted in the Sublease attached to this Agreement, without modification, and (ii) Tenant shall give Landlord written notice of Subtenant's exercise of such rights within five (5) business days following such exercise. Landlord may consent to subsequent sublettings and assignments of the Lease or the Sublease or any amendments or modifications thereto without notifying Tenant nor anyone else liable under the Lease and without obtaining their consent. No such action by Landlord shall relieve such persons from any duty, obligation or liability to Landlord or otherwise with regard to the Sublet Premises. Notwithstanding the foregoing, Landlord hereby agrees that Landlord's prior consent shall not be required for assignments and subleases made by Subtenant to a "Permitted Transferee" as defined in and on the terms contained in Section 14.8 of the Lease.

4. Relationship With Landlord. Tenant hereby assigns and transfers to Landlord Tenant's interest in the Sublease and all rentals and income arising therefrom, subject to the terms of this Section 4. Landlord, by consenting to the Sublease agrees that until a default beyond applicable notice and cure periods shall occur in the performance of Tenant's obligations under the Lease, Tenant may receive, collect and enjoy the rents accruing under the Sublease. In the event Tenant shall default beyond applicable notice and cure periods in the performance of its obligations to Landlord under the Lease (whether or not Landlord terminates the Lease), Landlord may at its option by notice to Tenant, either (i) terminate the Sublease (only if Landlord terminates the Lease), (ii) elect to receive and collect, directly from Subtenant, all rent and any other sums owing and to be owed under the Sublease, as further set forth in Section 4.1 below, or (iii) elect to succeed to Tenant's interest in the Sublease and cause Subtenant to attorn to Landlord, as further set forth in Section 4.2 below (only if Landlord terminates the Lease).

4.1 Landlord's Election to Receive Rents. Landlord shall not, by reason of the Sublease, nor by reason of the collection of rents or any other sums from Subtenant pursuant to Section 4, item (ii) above, be deemed liable to Subtenant for any failure of Tenant to perform and comply with any obligation of Tenant, and Tenant hereby irrevocably authorizes and directs Subtenant, upon receipt of any written notice from Landlord stating that a default beyond applicable notice and cure periods exists in the performance of Tenant's obligations under the Lease, to pay to Landlord the rents and any other sums due and to become due under the Sublease. Tenant agrees that Subtenant shall have the right to rely upon any such statement and request from Landlord, and that Subtenant shall pay any such rents and any other sums to Landlord without any obligation or right to inquire as to whether such default exists and notwithstanding any notice from or claim from Tenant to the contrary. Tenant shall not have any right or claim against Subtenant for any such rents or any other sums so paid by Subtenant to Landlord. Landlord shall credit Tenant with any rent received by Landlord under such assignment but the acceptance of any payment on account of rent from Subtenant as the result of

any such default shall in no manner whatsoever be deemed an attornment by Landlord to Subtenant or by Subtenant to Landlord, be deemed a waiver by Landlord of any provision of the Lease, or serve to release Tenant from any liability under the terms, covenants, conditions, provisions or agreements under the Lease. Notwithstanding the foregoing, any other payment of rent from Subtenant directly to Landlord, regardless of the circumstances or reasons therefor, shall in no manner whatsoever be deemed an attornment by Subtenant to Landlord in the absence of a specific written agreement signed by Landlord to such an effect.

4.2 Landlord's Election of Subtenant's Attornment. In the event Landlord elects, at its option, to cause Subtenant to attorn to Landlord pursuant to Section 4, item (iii) above, Landlord shall undertake the obligations of Tenant under the Sublease from the time of the exercise of the option, but Landlord shall not (i) be liable for any prepayment of more than one month's rent or any security deposit paid by Subtenant, (ii) be liable for any previous act, omission, breach or default of Tenant under the Lease or for any act, omission, breach or default of Tenant under the Sublease other than defaults that continue after the attornment (provided that Landlord shall be responsible only for the portion of the default continuing after the attornment), (iii) be subject to any defenses or offsets previously accrued which Subtenant may have against Tenant, or (iv) be bound by any changes or modifications made to the Sublease without the written consent of Landlord.

4.3 Operational Matters. Notwithstanding Landlord's consent to the Sublease as set forth herein, Landlord shall not be obligated to accept from Subtenant any payments of Base Rent or Additional Rent due under the Lease, all of which shall be paid by Tenant as set forth in the Lease. Requests for Building services as provided under the Lease, including without limitation, parking privileges, repair and maintenance services, or any other services or obligations to be performed by Landlord under the terms of the Lease, shall be made by Tenant, and Landlord shall have no obligation to respond to any direct request of Subtenant regarding the same.

4.4 Parking. Notwithstanding any provisions to the contrary contained in the Sublease, or any other sublease, assignment, amendment or other agreement between Tenant and Subtenant, any and all unreserved parking spaces allocated to Subtenant for the Sublet Premises are limited to such unreserved parking spaces that make up a portion of Tenant's allotment of unreserved parking spaces provided under the Lease. The total number of unreserved parking spaces provided under the Lease will not increase or decrease irrespective of how Tenant allocates such parking spaces under the Sublease or otherwise.

4.5 No Waiver. The acceptance of any amounts by Landlord from Subtenant or any other party shall not be deemed a waiver by Landlord of the obligation of Tenant to pay any or all amounts due and owing under the Lease. The performance of any obligation required by Tenant under the Lease by Subtenant or any other party shall not be deemed a waiver by Landlord of the duty of Tenant to perform such obligation or any other obligation as to which performance is or becomes due under the Lease.

4.6 Acts of Subtenant. As between Landlord and Tenant, any act or omission by Subtenant, or by any other person or entity for whose acts or omissions Tenant is liable or responsible under the terms of the Lease, that violates any of the provisions of the Lease, shall be deemed a violation of the Lease by Tenant, subject to any applicable notice and cure provisions contained in the Lease.

4.7 Indemnification. Subtenant hereby assumes all risk of damage to property or injury to persons in, upon or about the Sublet Premises from any cause whatsoever (including, but not limited to, any personal injuries resulting from a slip and fall in, upon or about the Sublet Premises) and agrees that, to the maximum extent permitted by law, Landlord, its partners,

subpartners and their respective officers, agents, servants, employees, and independent contractors shall not be liable for, and are hereby released from any responsibility for, any damage either to person or property or resulting from the loss of use thereof, which damage is sustained by Subtenant or by other persons claiming through Subtenant. Subtenant shall indemnify, defend, protect, and hold Landlord harmless from any and all loss, cost, damage, expense and liability (including without limitation court costs and reasonable attorneys' fees) incurred in connection with or arising from any cause in, on or about the Sublet Premises (including, but not limited to, a slip and fall), any acts, omissions or negligence of Subtenant or of any person claiming by, through or under Subtenant, or of the contractors, agents, servants, employees, invitees, guests or licensees of Subtenant or any such person, in, on or about the Building, provided that the terms of the foregoing indemnity shall not apply to the gross negligence or willful misconduct of Landlord. The provisions of this Section 4.7 shall survive the expiration or sooner termination of the Sublease with respect to any claims or liability arising in connection with any event occurring prior to such expiration or termination. The indemnity and all rights granted to Landlord pursuant to this Section 4.7 shall be in addition to, and shall not limit, the indemnifications and rights granted to Landlord under the Lease or otherwise available at law or in equity.

4.8 Insurance. Prior to Subtenant's occupancy of the Sublet Premises, Subtenant shall provide Landlord with certificates of all of the insurance required to be carried by Subtenant by the terms of the Sublease, which shall show Landlord and Landlord's property manager as being additional insureds thereunder. The waiver of subrogation contained in Section 10.5 of the Lease shall apply as between Landlord and Subtenant.

4.9 No Consent to Alterations or Particular Use. Notwithstanding anything contained in the Sublease to the contrary, Landlord's consent to the Sublease as contained in this Agreement shall not be deemed to be a consent to (i) any alteration or work of improvement that Tenant or Subtenant may desire or intend in the Sublet Premises, except that Landlord hereby consents to the Preapproved Alterations (as such Preapproved Alterations are depicted on Schedule 1 to Exhibit C attached to the Sublease) which shall be subject to and performed in accordance with the terms of Section 8 of the Lease, and which Preapproved Alterations Landlord shall not elect, pursuant to Section 8.5 of the Lease, to require Subtenant to remove at the expiration or sooner termination of the Sublease, provided that such Preapproved Alterations conform to Schedule 1 of Exhibit C attached to the Sublease in all material respects, (ii) any use of hazardous, radioactive or toxic materials in or about the Sublet Premises, except as expressly provided in Section 4.9.1 below, or (iii) any signage proposed to be installed for the benefit of Subtenant, except that Subtenant shall be permitted to have, at Subtenant's sole cost and expense, the following signage: (a) identification signage on the monument sign outside the front entrance to the Building (in addition to such existing signage for Tenant, which existing signage shall remain), (b) signage within the Sublet Premises, and (c) signage in one (1) location on the exterior rooftop of the Building to be reasonably and mutually agreed upon by Landlord, Tenant and Subtenant, in accordance with Article 23 of the Lease, provided that all such signage shall be considered "Tenant Signage" as defined in the Lease, such rights are within and not in addition to the existing rights provided to Tenant by Section 23.1 of the Lease, except as expressly stated above with respect to Tenant's identification signage on the monument sign, and such signage shall remain subject to Landlord's approval rights (including with respect to the "Sign Specifications," as defined in the Lease) in connection with Tenant Signage under Article 23 of the Lease.

4.9.1 Hazardous Materials. Landlord hereby approves of Subtenant's use and/or storage in the Sublet Premises of the chemicals or materials, in the referenced quantities, set forth in that certain Environmental Questionnaire for Commercial and Industrial Properties dated as of September 28, 2022, executed by Subtenant and delivered to Landlord (the "**Approved Environmental Questionnaire**"). Any proposed changes to such use and/or

storage, and/or to the Approved Environmental Questionnaire, shall be subject to Landlord's prior consent in accordance with the procedures set forth in Section 5.3 of the Lease, and, as between Landlord and Subtenant, Subtenant shall comply with the terms of the Lease in connection therewith. As between Tenant and Subtenant, the terms and conditions of the Sublease shall control with respect to Subtenant's use and/or storage in the Sublet Premises of the chemicals and materials set forth in the Approved Environmental Questionnaire.

4.10 Surrender. Notwithstanding anything contained in the Sublease to the contrary, all Alterations made by Subtenant to the Sublet Premises, subject to Landlord's right to require removal or to elect ownership, shall become the property of Landlord at the end of the term of the Sublease in accordance with Section 8.5 of the Lease.

4.11 Transfer Premium. Tenant shall comply with Section 14.3 of the Lease and pay to Landlord fifty percent (50%) of any "Transfer Premium" (as that term is defined therein) in accordance with the provisions of the Lease. Tenant acknowledges and agrees that if during the term of the Sublease there is a Transfer Premium as provided in Section 14.3 of the Lease, then Tenant shall pay to Landlord its monthly share of the Transfer Premium as Additional Rent under the Lease.

4.12 No Existing Mortgage. Landlord hereby represents and warrants that the Project is not currently subject to any ground lease, or to the lien of any mortgage or deed of trust.

5. General Provisions.

5.1 Consideration for Sublease. Tenant and Subtenant represent and warrant that there are no additional payments of rent or any other consideration of any type payable by Subtenant to Tenant with regard to the Sublet Premises other than as disclosed in the Sublease.

5.2 Brokerage Commission. Tenant and Subtenant covenant and agree that under no circumstances shall Landlord be liable for any brokerage commission or other charge or expense in connection with the Sublease and Tenant and Subtenant agree to protect, defend indemnify and hold Landlord harmless from and against the same and from any cost or expense (including, but not limited to, attorneys' fees) incurred by Landlord in resisting any claim for any such brokerage commission.

5.3 Recapture. This Agreement shall in no manner be construed as limiting Landlord's ability to exercise any rights to recapture any portion of the Premises, as set forth in the Lease, in the event of a proposed future sublease or assignment of such portion of the Premises; provided, however, that Landlord hereby agrees to waive its right to recapture the Sublet Premises (as it may be expanded) in the event Tenant proposes a future expansion of the Sublet Premises subleased by Subtenant (including any expansion of the Sublet Premises pursuant to Paragraphs 24 and 25 of the Sublease) which results in the Sublet Premises constituting in the aggregate more than fifty percent (50%) of the Building.

5.4 Controlling Law. The terms and provisions of this Agreement shall be construed in accordance with and governed by the laws of the State of California.

5.5 Binding Effect. This Agreement shall be binding upon and inure to the benefit of the parties hereto, their heirs, successors and permitted assigns. As used herein, the singular number includes the plural and the masculine gender includes the feminine and neuter.

5.6 Entire Agreement; No Further Modification. The agreements contained herein constitute the entire understanding between the parties with respect to the subject matter

hereof and supersede all prior agreements, written or oral, inconsistent herewith. No amendment, modification or change to this Agreement will be effective unless in writing and signed by all parties hereto.

5.7 Captions. The paragraph captions utilized herein are in no way intended to interpret or limit the terms and conditions hereof; rather, they are intended for purposes of convenience only.

5.8 Partial Invalidity. If any term, provision or condition contained in this Agreement shall, to any extent, be invalid or unenforceable, the remainder of this Agreement, or the application of such term, provision or condition to persons or circumstances other than those with respect to which it is invalid or unenforceable, shall not be affected thereby, and each and every other term, provision and condition of this Agreement shall be valid and enforceable to the fullest extent permitted by law.

5.9 Attorneys' Fees. If any party hereto commences litigation against another party hereto for the specific performance of this Agreement, for damages for the breach hereof or otherwise for enforcement of any remedy hereunder, the parties hereto agree to and hereby do waive any right to a trial by jury and, in the event of any such commencement of litigation, the prevailing party shall be entitled to recover from the other non-prevailing party such costs and reasonable attorneys' fees as may have been incurred.

5.10 Counterparts; Manner of Execution. This Agreement may be executed in one or more counterparts and/or via facsimile, pdf or electronic signature (e.g., via DocuSign), and the parties hereto hereby acknowledge and agree that the same shall be fully effective in the same manner as if all parties hereto had executed the same document in original counterparts by hand. If applicable, all counterparts shall be construed together and shall constitute a single, original document.

[Signatures follow on the next page.]

IN WITNESS WHEREOF, the parties have executed this Consent to Sublease Agreement as of the day and year first above written.

"Landlord"

HCP LS BRISBANE, LLC,
a Delaware limited liability company

By: /s/Scott R. Bohn
Name: Scott R. Bohn
Its: Executive Vice President

"Tenant"

ARCUS BIOSCIENCES, INC.,
a Delaware corporation

By: /s/ Bob Goeltz
Name: Bob Goeltz
Its: Chief Financial Officer

"Subtenant"

PROTHENA BIOSCIENCES INC,
a Delaware corporation

By: /s/ Tran Nguyen
Name: Tran Nguyen
Its: Chief Financial Officer

EXHIBIT A
SUBLEASE

4890-2246-3025.6
372423.00001/1-1-00/mjh/mjh

EXHIBIT A
-1-

THE SHORE AT SIERRA POINT
Consent to Sublease Agreement
Prothena Biosciences Inc

**FIRST AMENDMENT TO THE
PROTHENA CORPORATION PLC
2020 EMPLOYMENT INDUCEMENT INCENTIVE PLAN**

This First Amendment (this “First Amendment”) to the Prothena Corporation plc 2020 Employment Inducement Incentive Plan (“2020 EIIP”), was made and adopted by the Board of Directors (“Board”) of Prothena Corporation plc, a public limited company organized under the laws of Ireland (the “Company”), on April 1, 2020 (the “Amendment Date”).

RECITALS

WHEREAS, the Company maintains the 2020 EIIP; and

WHEREAS, the Board believes it is in the best interests of the Company and its shareholders to amend the 2020 EIIP to increase the number of ordinary shares authorized for issuance under the 2020 EIIP.

NOW, THEREFORE, BE IT RESOLVED, that the 2020 EIIP is hereby amended as follows, effective as of the Amendment Date:

AMENDMENT

1. Section 2.28 of the 2020 EIIP is hereby amended and restated in its entirety as follows:
“2.28 “***Overall Share Limit***” means 360,000 Shares.”
2. This First Amendment shall be and hereby is incorporated into and forms a part of the 2020 EIIP, and except as expressly provided herein, all terms and conditions of the 2020 EIIP shall remain in full force and effect.

**SECOND AMENDMENT TO THE
PROTHENA CORPORATION PLC
2020 EMPLOYMENT INDUCEMENT INCENTIVE PLAN**

This Second Amendment (this “Second Amendment”) to the Prothena Corporation plc 2020 Employment Inducement Incentive Plan (“2020 EIIP”), was made and adopted by the Board of Directors (“Board”) of Prothena Corporation plc, a public limited company organized under the laws of Ireland (the “Company”), on July 15, 2020 (the “Amendment Date”).

RECITALS

WHEREAS, the Company maintains the 2020 EIIP; and

WHEREAS, the Board believes it is in the best interests of the Company and its shareholders to amend the 2020 EIIP to increase the number of ordinary shares authorized for issuance under the 2020 EIIP.

NOW, THEREFORE, BE IT RESOLVED, that the 2020 EIIP is hereby amended as follows, effective as of the Amendment Date:

AMENDMENT

1. Section 2.28 of the 2020 EIIP is hereby amended and restated in its entirety as follows:
“2.28 “***Overall Share Limit***” means 420,000 Shares.”
2. This Second Amendment shall be and hereby is incorporated into and forms a part of the 2020 EIIP, and except as expressly provided herein, all terms and conditions of the 2020 EIIP shall remain in full force and effect.

**THIRD AMENDMENT TO THE
PROTHENA CORPORATION PLC
2020 EMPLOYMENT INDUCEMENT INCENTIVE PLAN**

This Third Amendment (this “Third Amendment”) to the Prothena Corporation plc 2020 Employment Inducement Incentive Plan (“2020 EIIP”), was made and adopted by the Board of Directors (“Board”) of Prothena Corporation plc, a public limited company organized under the laws of Ireland (the “Company”), on September 1, 2020 (the “Amendment Date”).

RECITALS

WHEREAS, the Company maintains the 2020 EIIP; and

WHEREAS, the Board believes it is in the best interests of the Company and its shareholders to amend the 2020 EIIP to increase the number of ordinary shares authorized for issuance under the 2020 EIIP.

NOW, THEREFORE, BE IT RESOLVED, that the 2020 EIIP is hereby amended as follows, effective as of the Amendment Date:

AMENDMENT

1. Section 2.28 of the 2020 EIIP is hereby amended and restated in its entirety as follows:
“2.28 “***Overall Share Limit***” means 480,000 Shares.”
2. This Third Amendment shall be and hereby is incorporated into and forms a part of the 2020 EIIP, and except as expressly provided herein, all terms and conditions of the 2020 EIIP shall remain in full force and effect.

**FOURTH AMENDMENT TO THE
PROTHENA CORPORATION PLC
2020 EMPLOYMENT INDUCEMENT INCENTIVE PLAN**

This Fourth Amendment (this “Fourth Amendment”) to the Prothena Corporation plc 2020 Employment Inducement Incentive Plan (“2020 EIIP”), was made and adopted by the Board of Directors (“Board”) of Prothena Corporation plc, a public limited company organized under the laws of Ireland (the “Company”), on October 1, 2020 (the “Amendment Date”).

RECITALS

WHEREAS, the Company maintains the 2020 EIIP; and

WHEREAS, the Board believes it is in the best interests of the Company and its shareholders to amend the 2020 EIIP to increase the number of ordinary shares authorized for issuance under the 2020 EIIP.

NOW, THEREFORE, BE IT RESOLVED, that the 2020 EIIP is hereby amended as follows, effective as of the Amendment Date:

AMENDMENT

1. Section 2.28 of the 2020 EIIP is hereby amended and restated in its entirety as follows:
“2.28 “***Overall Share Limit***” means 530,000 Shares.”
2. This Fourth Amendment shall be and hereby is incorporated into and forms a part of the 2020 EIIP, and except as expressly provided herein, all terms and conditions of the 2020 EIIP shall remain in full force and effect.

**FIFTH AMENDMENT TO THE
PROTHENA CORPORATION PLC
2020 EMPLOYMENT INDUCEMENT INCENTIVE PLAN**

This Fifth Amendment (this “Fifth Amendment”) to the Prothena Corporation plc 2020 Employment Inducement Incentive Plan (“2020 EIIP”), was made and adopted by the Board of Directors (“Board”) of Prothena Corporation plc, a public limited company organized under the laws of Ireland (the “Company”), on November 2, 2020 (the “Amendment Date”).

RECITALS

WHEREAS, the Company maintains the 2020 EIIP; and

WHEREAS, the Board believes it is in the best interests of the Company and its shareholders to amend the 2020 EIIP to increase the number of ordinary shares authorized for issuance under the 2020 EIIP.

NOW, THEREFORE, BE IT RESOLVED, that the 2020 EIIP is hereby amended as follows, effective as of the Amendment Date:

AMENDMENT

1. Section 2.28 of the 2020 EIIP is hereby amended and restated in its entirety as follows:
“2.28 “*Overall Share Limit*” means 620,000 Shares.”
2. This Fifth Amendment shall be and hereby is incorporated into and forms a part of the 2020 EIIP, and except as expressly provided herein, all terms and conditions of the 2020 EIIP shall remain in full force and effect.

**SIXTH AMENDMENT TO THE
PROTHENA CORPORATION PLC
2020 EMPLOYMENT INDUCEMENT INCENTIVE PLAN**

This Sixth Amendment (this “Sixth Amendment”) to the Prothena Corporation plc 2020 Employment Inducement Incentive Plan (“2020 EIIP”), was made and adopted by the Board of Directors (“Board”) of Prothena Corporation plc, a public limited company organized under the laws of Ireland (the “Company”), on December 1, 2020 (the “Amendment Date”).

RECITALS

WHEREAS, the Company maintains the 2020 EIIP; and

WHEREAS, the Board believes it is in the best interests of the Company and its shareholders to amend the 2020 EIIP to increase the number of ordinary shares authorized for issuance under the 2020 EIIP.

NOW, THEREFORE, BE IT RESOLVED, that the 2020 EIIP is hereby amended as follows, effective as of the Amendment Date:

AMENDMENT

1. Section 2.28 of the 2020 EIIP is hereby amended and restated in its entirety as follows:
“2.28 “***Overall Share Limit***” means 710,000 Shares.”
2. This Sixth Amendment shall be and hereby is incorporated into and forms a part of the 2020 EIIP, and except as expressly provided herein, all terms and conditions of the 2020 EIIP shall remain in full force and effect.

**SEVENTH AMENDMENT TO THE
PROTHENA CORPORATION PLC
2020 EMPLOYMENT INDUCEMENT INCENTIVE PLAN**

This Seventh Amendment (this “Seventh Amendment”) to the Prothena Corporation plc 2020 Employment Inducement Incentive Plan (“2020 EIIP”), was made and adopted by the Board of Directors (“Board”) of Prothena Corporation plc, a public limited company organized under the laws of Ireland (the “Company”), on February 1, 2021 (the “Amendment Date”).

RECITALS

WHEREAS, the Company maintains the 2020 EIIP; and

WHEREAS, the Board believes it is in the best interests of the Company and its shareholders to amend the 2020 EIIP to increase the number of ordinary shares authorized for issuance under the 2020 EIIP.

NOW, THEREFORE, BE IT RESOLVED, that the 2020 EIIP is hereby amended as follows, effective as of the Amendment Date:

AMENDMENT

1. Section 2.28 of the 2020 EIIP is hereby amended and restated in its entirety as follows:
“2.28 “***Overall Share Limit***” means 785,000 Shares.”
2. This Seventh Amendment shall be and hereby is incorporated into and forms a part of the 2020 EIIP, and except as expressly provided herein, all terms and conditions of the 2020 EIIP shall remain in full force and effect.

**EIGHTH AMENDMENT TO THE
PROTHENA CORPORATION PLC
2020 EMPLOYMENT INDUCEMENT INCENTIVE PLAN**

This Eighth Amendment (this “Eighth Amendment”) to the Prothena Corporation plc 2020 Employment Inducement Incentive Plan (“2020 EIIP”), was made and adopted by the Board of Directors (“Board”) of Prothena Corporation plc, a public limited company organized under the laws of Ireland (the “Company”), on April 1, 2021 (the “Amendment Date”).

RECITALS

WHEREAS, the Company maintains the 2020 EIIP; and

WHEREAS, the Board believes it is in the best interests of the Company and its shareholders to amend the 2020 EIIP to increase the number of ordinary shares authorized for issuance under the 2020 EIIP.

NOW, THEREFORE, BE IT RESOLVED, that the 2020 EIIP is hereby amended as follows, effective as of the Amendment Date:

AMENDMENT

1. Section 2.28 of the 2020 EIIP is hereby amended and restated in its entirety as follows:
“2.28 “**Overall Share Limit**” means 1,065,000 Shares.”
2. This Eighth Amendment shall be and hereby is incorporated into and forms a part of the 2020 EIIP, and except as expressly provided herein, all terms and conditions of the 2020 EIIP shall remain in full force and effect.

**NINTH AMENDMENT TO THE
PROTHENA CORPORATION PLC
2020 EMPLOYMENT INDUCEMENT INCENTIVE PLAN**

This Ninth Amendment (this “Ninth Amendment”) to the Prothena Corporation plc 2020 Employment Inducement Incentive Plan (“2020 EIIP”), was made and adopted by the Board of Directors (“Board”) of Prothena Corporation plc, a public limited company organized under the laws of Ireland (the “Company”), on May 3, 2021 (the “Amendment Date”).

RECITALS

WHEREAS, the Company maintains the 2020 EIIP; and

WHEREAS, the Board believes it is in the best interests of the Company and its shareholders to amend the 2020 EIIP to increase the number of ordinary shares authorized for issuance under the 2020 EIIP.

NOW, THEREFORE, BE IT RESOLVED, that the 2020 EIIP is hereby amended as follows, effective as of the Amendment Date:

AMENDMENT

1. Section 2.28 of the 2020 EIIP is hereby amended and restated in its entirety as follows:
“2.28 “***Overall Share Limit***” means 1,220,000 Shares.”
2. This Ninth Amendment shall be and hereby is incorporated into and forms a part of the 2020 EIIP, and except as expressly provided herein, all terms and conditions of the 2020 EIIP shall remain in full force and effect.

**TENTH AMENDMENT TO THE
PROTHENA CORPORATION PLC
2020 EMPLOYMENT INDUCEMENT INCENTIVE PLAN**

This Tenth Amendment (this “Tenth Amendment”) to the Prothena Corporation plc 2020 Employment Inducement Incentive Plan (“2020 EIIP”), was made and adopted by the Board of Directors (“Board”) of Prothena Corporation plc, a public limited company organized under the laws of Ireland (the “Company”), on September 1, 2021 (the “Amendment Date”).

RECITALS

WHEREAS, the Company maintains the 2020 EIIP; and

WHEREAS, the Board believes it is in the best interests of the Company and its shareholders to amend the 2020 EIIP to increase the number of ordinary shares authorized for issuance under the 2020 EIIP.

NOW, THEREFORE, BE IT RESOLVED, that the 2020 EIIP is hereby amended as follows, effective as of the Amendment Date:

AMENDMENT

1. Section 2.28 of the 2020 EIIP is hereby amended and restated in its entirety as follows:
“2.28 “*Overall Share Limit*” means 1,245,000 Shares.”
2. This Tenth Amendment shall be and hereby is incorporated into and forms a part of the 2020 EIIP, and except as expressly provided herein, all terms and conditions of the 2020 EIIP shall remain in full force and effect.

**ELEVENTH AMENDMENT TO THE
PROTHENA CORPORATION PLC
2020 EMPLOYMENT INDUCEMENT INCENTIVE PLAN**

This Eleventh Amendment (this “Eleventh Amendment”) to the Prothena Corporation plc 2020 Employment Inducement Incentive Plan (“2020 EIIP”), was made and adopted by the Board of Directors (“Board”) of Prothena Corporation plc, a public limited company organized under the laws of Ireland (the “Company”), on October 1, 2021 (the “Amendment Date”).

RECITALS

WHEREAS, the Company maintains the 2020 EIIP; and

WHEREAS, the Board believes it is in the best interests of the Company and its shareholders to amend the 2020 EIIP to increase the number of ordinary shares authorized for issuance under the 2020 EIIP.

NOW, THEREFORE, BE IT RESOLVED, that the 2020 EIIP is hereby amended as follows, effective as of the Amendment Date:

AMENDMENT

1. Section 2.28 of the 2020 EIIP is hereby amended and restated in its entirety as follows:
“2.28 “***Overall Share Limit***” means 1,385,000 Shares.”
2. This Eleventh Amendment shall be and hereby is incorporated into and forms a part of the 2020 EIIP, and except as expressly provided herein, all terms and conditions of the 2020 EIIP shall remain in full force and effect.

**TWELFTH AMENDMENT TO THE
PROTHENA CORPORATION PLC
2020 EMPLOYMENT INDUCEMENT INCENTIVE PLAN**

This Twelfth Amendment (this “Twelfth Amendment”) to the Prothena Corporation plc 2020 Employment Inducement Incentive Plan (“2020 EIIP”), was made and adopted by the Board of Directors (“Board”) of Prothena Corporation plc, a public limited company organized under the laws of Ireland (the “Company”), on July 1, 2022 (the “Amendment Date”).

RECITALS

WHEREAS, the Company maintains the 2020 EIIP; and

WHEREAS, the Board believes it is in the best interests of the Company and its shareholders to amend the 2020 EIIP to increase the number of ordinary shares authorized for issuance under the 2020 EIIP.

NOW, THEREFORE, BE IT RESOLVED, that the 2020 EIIP is hereby amended as follows, effective as of the Amendment Date:

AMENDMENT

3. Section 2.28 of the 2020 EIIP is hereby amended and restated in its entirety as follows:

“2.28 “***Overall Share Limit***” means 1,435,000 Shares.”

4. This Twelfth Amendment shall be and hereby is incorporated into and forms a part of the 2020 EIIP, and except as expressly provided herein, all terms and conditions of the 2020 EIIP shall remain in full force and effect.

**THIRTEENTH AMENDMENT TO THE
PROTHENA CORPORATION PLC
2020 EMPLOYMENT INDUCEMENT INCENTIVE PLAN**

This Thirteenth Amendment (this “Thirteenth Amendment”) to the Prothena Corporation plc 2020 Employment Inducement Incentive Plan (“2020 EIIP”), was made and adopted by the Board of Directors (“Board”) of Prothena Corporation plc, a public limited company organized under the laws of Ireland (the “Company”), on August 1, 2022 (the “Amendment Date”).

RECITALS

WHEREAS, the Company maintains the 2020 EIIP; and

WHEREAS, the Board believes it is in the best interests of the Company and its shareholders to amend the 2020 EIIP to increase the number of ordinary shares authorized for issuance under the 2020 EIIP.

NOW, THEREFORE, BE IT RESOLVED, that the 2020 EIIP is hereby amended as follows, effective as of the Amendment Date:

AMENDMENT

5. Section 2.28 of the 2020 EIIP is hereby amended and restated in its entirety as follows:
“2.28 “***Overall Share Limit***” means 1,470,000 Shares.”
6. This Thirteenth Amendment shall be and hereby is incorporated into and forms a part of the 2020 EIIP, and except as expressly provided herein, all terms and conditions of the 2020 EIIP shall remain in full force and effect.

List of Subsidiaries

Subsidiary Name	Jurisdiction of Incorporation or Organization
Prothena Biosciences Limited	Ireland
Prothena Biosciences Inc	Delaware
Prothena Finance Inc	Delaware
Othair Prothena Limited	Ireland
Prothena Pharma Limited	Ireland
Prothena Platform Technologies Limited	Ireland

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the registration statements (Nos. 333-266744, 333-258586, 333-244366, 333-226724, 333-218184, 333-211653, 333-196572 and 333-187726) on Form S-8 and the registration statements (Nos. 333-254622, 333-231675, 333-223207, 333-203528, 333-197006, 333-196965 and 333-193416) on Form S-3 of our report dated February 28, 2023, with respect to the consolidated financial statements of Prothena Corporation plc and the effectiveness of internal control over financial reporting.

/s/ KPMG LLP

San Francisco, California
February 28, 2023

**CERTIFICATION OF CHIEF EXECUTIVE OFFICER
PURSUANT TO RULE 13a-14(a)/15d-14(a), AS ADOPTED PURSUANT TO SECTION 302 OF
THE SARBANES-OXLEY ACT OF 2002**

I, Gene G. Kinney, certify that:

1. I have reviewed this Annual Report on Form 10-K of Prothena Corporation plc;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;
 - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 28, 2023

/s/ Gene G. Kinney

Gene G. Kinney
President and Chief Executive Officer
(Principal Executive Officer)

**CERTIFICATION OF CHIEF FINANCIAL OFFICER
PURSUANT TO RULE 13a-14(a)/15d-14(a), AS ADOPTED PURSUANT TO SECTION 302 OF
THE SARBANES-OXLEY ACT OF 2002**

I, Tran B. Nguyen, certify that:

1. I have reviewed this Annual Report on Form 10-K of Prothena Corporation plc;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;
 - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 28, 2023

/s/ Tran B. Nguyen

Tran B. Nguyen
Chief Financial Officer
(Principal Financial Officer)

**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**

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Gene G. Kinney, President and Chief Executive Officer of Prothena Corporation plc (the “Company”) and Tran B. Nguyen, Chief Financial Officer of the Company, each hereby certify that, to the best of his knowledge:

1. The Company’s Annual Report on Form 10-K for the fiscal year ended December 31, 2022, to which this Certification is attached as Exhibit 32.1 (the “Report”) fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 28, 2023

/s/ Gene G. Kinney

Gene G. Kinney
President and Chief Executive Officer
(Principal Executive Officer)

/s/ Tran B. Nguyen

Tran B. Nguyen
Chief Financial Officer
(Principal Financial Officer)

A signed original of this written statement required by Rule 13a-14(b) of the Securities Exchange Act of 1934 and 18 U.S.C. Section 1350 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.