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Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes No

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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 if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§232.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or 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 is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes No

As of June 29, 2018, 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 \$406.7 million, based on the last reported sale of the registrant's ordinary shares on the Nasdaq Global Market on such date. 39,863,711 of the Registrant's ordinary shares, par value \$0.01 per share, were outstanding as of March 11, 2019.

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 21, 2019 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, 2018.

PROTHENA CORPORATION PLC
 Annual Report on Form 10-K
 For the Year Ended December 31, 2018
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PART I

ITEM 1. BUSINESS

Overview

Prothena Corporation plc (“Prothena” or the “Company”) is a clinical-stage neuroscience company focused on the discovery and development of novel therapies with the potential to fundamentally change the course of progressive, life-threatening diseases. Fueled by its deep scientific understanding built over decades of neuroscience research, Prothena is advancing a pipeline of therapeutic candidates for a number of indications and novel targets including Parkinson’s disease and other related synucleinopathies (prasinezumab - PRX002/RG7935) and ATTR amyloidosis (PRX004), as well as tau, A β (Amyloid beta), and TDP-43, where its scientific understanding of disease pathology can be leveraged.

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 neuroscience company focused on the discovery and development of novel therapies for the treatment of neurological diseases. Key elements of our strategy to achieve this 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 proprietary technology to develop innovative therapeutics for the potential treatment of neurological diseases with major unmet medical needs. To date, our scientists are primarily focused on the biology of diseases caused by protein misfolding and our approach leverages the unique insights derived from our decades of research and development in this area. Our approach to advancing new compounds from discovery through clinical development is based on a deep understanding of how to optimally target proteins, assess target engagement and disease progression and develop potential therapeutics that relevantly influence biology. Once we formulate a novel hypothesis or approach, we determine how to optimally intervene against a known target. For example, if we select an antibody approach, we generate antibodies against a target, characterize specific and selective antibodies in vitro and then use them to test the initial hypothesis in vivo using animal models of disease. We sometimes rely on the use of animal models that have been extensively developed by external laboratories. To establish early clinical 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 potential partners.

- Focus on diseases that lack effective therapies.

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

In Parkinson’s disease, currently approved therapies focus on the alleviation of symptoms without addressing the underlying cause of the disease. Prothena is focusing its 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. Prothena's scientists have developed prasinezumab (PRX002/RG7935) - 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.

Moving forward, we intend to advance new discovery-stage therapeutics for other neurological diseases with unmet medical needs, and our discovery efforts targeting tau, A β and TDP-43 for the potential treatment of Alzheimer's disease (AD), frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS) are examples of this.

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

We rely on strategic business development and R&D collaborations and a combination of internal and external resources to advance our objectives.

Our robust discovery engine generates monoclonal antibodies that have the potential to treat unmet medical needs. For investigational therapeutic antibody 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 Celgene that is focused on three proteins implicated in the pathogenesis of several neurodegenerative diseases are good examples of this.

We also consider highly focused opportunities to acquire or license rights to differentiated neuroscience product candidates or technologies to complement our existing R&D pipeline. Our license and option agreement with Bioasis Technologies Inc. to explore the application of Bioasis's xB platform technology to increase the delivery of therapeutics across the blood-brain barrier (BBB) is an example of this.

We also collaborate with scientific and clinical experts in disease areas of interest to test and characterize our potential therapeutic antibody candidates and to gain feedback and guidance on our programs.

Although 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 consultants who have certain functional and/or disease area expertise to help us execute specific activities related to our programs.

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, whereby we jointly sell and market the product; regional licensing for markets where we do not have expertise or infrastructure; and out-licensing our product, whereby another pharmaceutical or biotechnology company sells and markets our 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 Research and Development Pipeline

Our research and development pipeline includes two therapeutic antibody programs in clinical development: Prasinezumab, in collaboration with Roche, for the potential treatment of Parkinson's disease and other related synucleinopathies; and PRX004, for the potential treatment of ATTR amyloidosis.

In addition to our clinical development pipeline, we have a number of discovery-stage programs targeting proteins implicated in neurological diseases including tau and A β for the potential treatment of Alzheimer's disease and other neurodegenerative disorders and TDP-43 for the potential treatment of amyotrophic lateral sclerosis and frontotemporal dementia. Tau, TDP-43 and a third undisclosed neurodegenerative target are the focus of our collaboration with Celgene.

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In April 2018, we announced the discontinuation of development of NEOD001, an investigational antibody that was being evaluated for the treatment of AL amyloidosis. The decision was based on results from the Phase 2b PRONTO study which did not meet its primary or secondary endpoints, and a futility analysis of the Phase 3 VITAL study.

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

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Prasinezumab (PRX002/RG7935) for the Potential Treatment of Parkinson's Disease and Other Synucleinopathies

Prasinezumab is an investigational monoclonal antibody targeting α -synuclein, and is designed to slow the progressive neurodegeneration associated with synuclein misfolding and/or the cell-to-cell transmission of the pathogenic forms of synuclein in Parkinson's disease and other synucleinopathies. Prasinezumab is the focus of our worldwide collaboration with Roche.

In December 2013, we entered into a License, Development, and Commercialization Agreement (the "License Agreement") with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. (collectively, "Roche") to develop and commercialize certain antibodies that target α -synuclein, including prasinezumab. Together with Roche, we aim to develop prasinezumab as a potential treatment to alter the progression of underlying disease pathology for Parkinson's disease and possibly other synucleinopathies. For more information on the License Agreement, see the information below.

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 degenerative disorder of the central nervous system (CNS) that affects approximately seven to ten million people worldwide, with incidence increasing based on an aging population. It is the second most common neurodegenerative disease after Alzheimer's. 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 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 primarily directed at managing the early motor symptoms of the disease, mainly through the use of levodopa and dopamine agonists 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. The goal of our approach is to slow the progressive neurodegenerative consequences of disease, a current unmet need. Prasinezumab preferentially targets aggregated α -synuclein and may slow or reduce the neurodegeneration associated with synuclein misfolding and/or transmission.

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.

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, were presented in June 2015 as part of the late breaking session at the 19th International Congress of Parkinson's Disease and Movement Disorders and published in December 2016 in the journal *Movement Disorders*. The data demonstrated that prasinezumab was safe and well-tolerated in healthy volunteers, meeting the primary objective of the study. Further, results from this study showed that administration of prasinezumab led to a mean reduction of free serum α -synuclein levels of up to 96.5%. These overall results were statistically significant ($p < 0.0001$). Reduction of free serum α -synuclein, a protein potentially involved in the onset and progression of Parkinson's disease and the target of prasinezumab, was shown to be rapid, and dose- and time-dependent after a single dose. No serious adverse events or hypersensitivity reactions were reported. Prasinezumab demonstrated favorable pharmacokinetic properties. The most common treatment emergent adverse events were headache, nausea, vessel puncture site pain, viral infection, and viral upper respiratory tract infection. In this study, all prasinezumab-related adverse events were mild, no dose limiting toxicities were observed and no anti-drug antibodies were detected.

Results of the second study, a Phase 1b double-blind, placebo-controlled, multiple ascending dose study of prasinezumab in 80 patients with Parkinson's disease that was designed to assess the safety, tolerability, pharmacokinetics and immunogenicity of prasinezumab, were presented by Dr. Joseph Jankovic of Baylor College of Medicine in April 2017 in a late-breaking therapeutic strategies session at the 13th International Conference on Alzheimer's and Parkinson's Disease (AD/PD).

The 80 patients with Parkinson's disease in this study were randomized into six escalating dose cohorts to receive prasinezumab or placebo (2:1 randomization for 0.3, 1, 3 or 10 mg/kg, and 3:1 randomization for 30 or 60 mg/kg). In this six-month study, patients received three monthly doses (intravenous infusion once every 28 days) of prasinezumab or placebo and were followed for an observational period of three months. All dose levels of prasinezumab were found to have an acceptable safety and tolerability profile 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. No serious or severe treatment emergent adverse events (TEAEs) were reported in prasinezumab treated patients. No TEAEs were observed in ten percent or more of prasinezumab treated patients. TEAEs greater than placebo in five percent or more of prasinezumab treated patients, regardless of relationship to prasinezumab, included constipation, infusion related reactions (IRRs), diarrhoea, headache, peripheral oedema, post lumbar puncture syndrome and upper respiratory tract infection. Mild-to-moderate IRRs, that all resolved, were limited to the 60 mg/kg dose cohort and were observed in four of 12 treated patients. No dose-limiting toxicities were observed. Prasinezumab demonstrated acceptable pharmacokinetic properties.

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.”

The results from this study further supported advancing prasinezumab into the Phase 2 study, PASADENA, which was initiated by Roche in the second quarter of 2017 and is fully enrolled. PASADENA is a two-part Phase 2 clinical study in early Parkinson's disease patients that is being conducted by Roche. Part 1 is a randomized, double-blind, placebo-controlled, three-arm study and has enrolled 316 patients to evaluate the efficacy and safety of prasinezumab in patients over 52 weeks. In part 1, patients have been randomized on a 1:1:1 basis to receive one of two active doses (1500 mg or 4500 mg) of prasinezumab or placebo via intravenous infusion once every 4 weeks. Patients enrolled in the study must not be on dopaminergic therapy and are not be expected to require dopaminergic therapy for at least 52 weeks. Part 2 of the study is a 52-week blinded extension phase in which patients from the placebo arm of the study will be re-randomized onto one of two active doses on a 1:1 basis, so that all participants will be 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 will be allowed to use concomitant dopaminergic therapy. Any patient who medically requires initiation of dopaminergic therapy during part 1 will have their subsequent data censored for the primary endpoint analysis.

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The primary endpoint of the Phase 2 PASADENA study is the comparison of change from baseline in the Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) total score (sections 1, 2 and 3) at the completion of part 1 (week 52) in each treatment group vs. the placebo group. The study is 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. A prespecified exploratory analysis will compare the results of the two pooled treatment arms vs. placebo. Key secondary endpoints include safety, tolerability and DaT-SPECT imaging.

For more information on the Phase 2 PASADENA study, please visit clinicaltrials.gov and search NCT #03100149.

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 has 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 million milestone payment from Roche to Prothena, which was earned in the second quarter of 2017. Prothena has so far received a total of \$75 million in upfront and development milestone payments.

Pursuant to the License Agreement, we are collaborating with Roche to research and develop antibody products targeting α -synuclein. Roche is providing funding for this research collaboration, which is focused on optimizing early stage antibodies targeting α -synuclein, potentially including incorporation of Roche’s proprietary Brain Shuttle™ technology to increase delivery of therapeutic antibodies to the brain. 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.

In addition to the \$30.0 million upfront payment and clinical milestone payment of \$15.0 million (both in 2014) and the clinical milestone payment of \$30.0 million in 2017, Roche is also obligated to pay:

- up to \$350.0 million upon the achievement of additional development, regulatory and various first commercial sales milestones;

- up to an additional \$175.0 million in ex-U.S. commercial sales milestones; and

- tiered, high single-digit to high double-digit royalties in the teens on ex-U.S. annual net sales, subject to certain adjustments.

In the U.S., Prothena and Roche share all development and commercialization costs, as well as profits, all of which will be allocated 70% to Roche and 30% to us, for prasinezumab in the Parkinson’s disease indication, as well as any other licensed products and/or indications for which we opt in to co-develop and co-fund. We may opt out of the co-development and cost and profit sharing on any co-developed licensed products and instead receive U.S. commercial sales milestones totaling up to \$155.0 million and tiered, single-digit to high double-digit royalties in the teens based on U.S. annual net sales, subject to certain adjustments, with respect to the applicable licensed product. 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.

PRX004 for the Potential Treatment of ATTR Amyloidosis

PRX004 is an investigational antibody designed to target and clear the pathogenic, non-native or misfolded forms of the TTR protein (misTTR) found in Transthyretin amyloidosis (ATTR amyloidosis) without affecting the native, or normal tetrameric form of the protein.

ATTR amyloidosis is a rare, progressive and often fatal disease characterized by deposition of aggregates of misfolded protein, or amyloid in various tissues and organs. The TTR protein is produced primarily in the liver and in its normal tetrameric form serves as a carrier for thyroxin and vitamin A and is also implicated in neuroprotective functions. ATTR amyloidosis can be either hereditary or sporadic.

In hereditary ATTR amyloidosis, mutations in the TTR gene cause misfolded amyloid proteins to accumulate and damage body organs and tissue, such as the peripheral nerves and heart. This results in predominant symptoms of neuropathy (hereditary ATTR amyloidosis with polyneuropathy or hATTR-PN) and/or cardiomyopathy (hereditary ATTR with cardiomyopathy or hATTR-CM), as well as other disease manifestations. In hereditary ATTR (hATTR), the body makes a mutant form of the TTR protein. There are more than 100 reported types of TTR mutations that promote amyloid fibril formation, which most commonly affect the heart (hATTR-CM) and nervous system (hATTR-PN). 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.

Wild-type ATTR (wtATTR) occurs sporadically and also primarily involves cardiomyopathy. Wild-type ATTR is similar to hereditary ATTR except that the protein that is deposited is the misfolded, non-mutated transthyretin protein. The wild-type transthyretin protein is less prone to forming amyloid deposits than the mutated form and patients usually develop the disease at 65 years of age or older. The prevalence of wild-type ATTR is uncertain, but many clinical experts believe there are many multiples more wild-type than hereditary patients world-wide.

Recently, new therapeutics 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 block or inhibit production of native forms of the TTR protein or bind to TTR and prevent tetramer dissociation but do not target the misfolded, pathogenic form of the TTR protein directly.

Clinical Development Program for PRX004

We have generated monoclonal antibodies that selectively bind to amyloidogenic (diseased) forms of the transthyretin (ATTR) protein and do not recognize the native, tetrameric form of TTR protein. Preclinical data published in March 2016 in the journal *Amyloid* suggest that our antibodies have unique biological activity that may lead to the prevention of deposition, and enhancement of clearance, of ATTR in patients with both wild type and hereditary TTR-mediated amyloidosis.

Additionally, we have developed a proprietary, high-sensitivity assay that specifically detects circulating non-native hATTR in plasma across multiple TTR mutations and can be used in clinical studies to monitor pharmacodynamic response to PRX004 in plasma.

In March 2018, we presented new research related to PRX004 for the potential treatment of ATTR amyloidosis at the 16th International Symposium on Amyloidosis (ISA) including data on our proprietary assay that specifically detects circulating non-native hATTR in plasma across multiple TTR mutations using a TTR antibody that binds to an epitope uniquely exposed on misfolded TTR but hidden in the native tetramer. Additional preclinical research was presented at ISA showing that conformation-specific antibodies target non-native TTR and immune mediated clearance through phagocytosis.

In May 2018, we announced the initiation of first-in-human dosing in a Phase 1 clinical study of PRX004 in patients with ATTR amyloidosis. The Phase 1 study is designed to enroll up to 36 patients with hATTR amyloidosis and is an open-label, dose escalation study to evaluate determine the safety, tolerability, pharmacokinetic, pharmacodynamic and maximum tolerated dose of PRX004 in patients with ATTR amyloidosis to inform possible future studies. The Phase 1 study includes the use of our propriety misTTR assay as a pharmacodynamic measure of the levels of non-native TTR species in plasma across multiple hereditary TTR mutations.

NEOD001 for the Potential Treatment of AL Amyloidosis

NEOD001 is an investigational monoclonal antibody that is designed to target and clear the amyloid that accumulates in AL amyloidosis.

Background on NEOD001

AL amyloidosis, is a rare, progressive and typically fatal disease caused by extracellular deposition of misfolded immunoglobulin light chains. Plasma cells normally produce light chains that pair with heavy chains to make functional antibodies. But in AL amyloidosis, something goes awry - the cause remains unknown - whereby a subset of clonal plasma cells overproduce a single light chain, or fragment thereof, in great abundance. These amyloid light chains (AL) misfold to form toxic soluble and insoluble aggregates that deposit in vital organs such as heart, kidneys, and/or the autonomic or peripheral nerves, causing extensive damage, and potentially organ failure and death. In many cases, patients have multiple organ involvement.

There are no approved treatments for AL amyloidosis and there is a large unmet need for therapies that specifically target soluble toxic aggregates and deposited amyloid fibrils, thereby preserving and improving vital organ function. The Amyloidosis Foundation estimates that approximately 30,000 to 45,000 patients are living with AL amyloidosis in the U.S. and European Union (the "EU") today. It is estimated that there are approximately 10,000 to 15,000 new cases of AL amyloidosis diagnosed annually in the U.S. and EU. The cause of AL amyloidosis remains poorly understood, and we believe this disease is significantly underdiagnosed.

Current treatment for patients with AL amyloidosis may include autologous stem cell transplant or the administration of off-label chemotherapeutic and/or oncologic therapies. The goal of these treatments is to control the hematologic burden by targeting clonal plasma cells in order to decrease the production of new light chain. These chemotherapeutic and/or oncologic agents are associated with known adverse event profiles and patients often become refractory to their hematologic effect and/or relapse. In addition, the target of these therapies is the plasma cells responsible for production of light chain, rather than the toxic light chain in circulation or built up in the organs. Delaying time to organ progression is the goal in the treatment of AL amyloidosis and as such, there remains a significant unmet need to directly target and remove the amyloid deposited on organs.

NEOD001 specifically targets the disease-causing, misfolded light chain aggregates in AL amyloidosis. Preclinical testing has demonstrated that NEOD001 reacts only with a "cryptic" epitope that is exposed only in the misfolded form of the light chain. The proposed mechanism of action of NEOD001 is to neutralize circulating soluble aggregates and clear deposited insoluble aggregates from organs. NEOD001 received Fast Track designation from the FDA in December 2014. In addition, NEOD001 was granted orphan drug designation for the treatment of AL and AA amyloidosis by the FDA in 2012 and for the treatment of AL amyloidosis by the European Medicines Agency (the "EMA") in 2013.

Clinical Development Program for NEOD001

Prior to discontinuation of the program, Prothena had two ongoing global, multi-center, randomized, double-blind, placebo-controlled clinical studies for NEOD001: the PRONTO study (NCT# 02632786, EudraCT# 2015-004318-14) evaluated NEOD001 in previously-treated patients with AL amyloidosis and persistent cardiac dysfunction, and The VITAL Amyloidosis Study (NCT# 02312206, EudraCT# 2014-003865-11) evaluated NEOD001 in newly-diagnosed, treatment-naïve patients with AL amyloidosis and cardiac dysfunction.

The VITAL Amyloidosis Study was initiated in December 2014 and was a Phase 3 global, multi-center, randomized, double-blind, placebo-controlled clinical trial for NEOD001 in patients with AL amyloidosis. The study enrolled 260 newly diagnosed, treatment-naïve patients with AL amyloidosis and cardiac dysfunction. Patients were randomized on a 1:1 basis to receive 24 mg/kg of NEOD001 or placebo via intravenous infusion every 28 days, with both groups receiving concurrent standard of care therapy. The composite primary endpoint was event-based, with all-cause mortality or cardiac hospitalizations as qualifying events. Secondary endpoints of the study included evaluation of the quality of life evaluation Short Form-36 ("SF-36") and Six-Minute Walk Test.

The PRONTO study was initiated in October 2015 and was a Phase 2b global, multi-center, randomized, double-blind, placebo-controlled clinical trial for NEOD001 in previously-treated patients with AL amyloidosis and persistent cardiac dysfunction. The study enrolled 129 previously-treated patients with AL amyloidosis and persistent cardiac dysfunction. Patients were randomized on a 1:1 basis to receive 24 mg/kg of NEOD001 or placebo via intravenous infusion every 28 days. The primary endpoint was best response over 12 months of the cardiac biomarker NT-proBNP, defined by the consensus criteria of NT-proBNP change. Secondary endpoints include evaluations of SF-36 and Six-Minute Walk Test.

Results of the PRONTO study were announced in April 2018. No statistically significant differences were observed between the treatment groups on either the primary or the secondary endpoints. NEOD001 was generally safe and well tolerated.

Based on the results of the PRONTO study, we asked the independent DMC of the Phase 3 VITAL study to review a futility analysis of interim data from the ongoing VITAL study. The DMC recommended discontinuation of the VITAL study for futility.

The futility analysis was based on 103 adjudicated events of the 156 events specified to complete the study and was not statistically significant. The hazard ratio was 0.84 favoring NEOD001 vs. control arm. We therefore decided to discontinue all development of NEOD001, including the VITAL study as well as the open label extension studies. Since then, we have been undertaking an analysis of the VITAL study data.

Our Discovery Programs

We are also advancing several discovery-stage programs for neurodegenerative diseases that lack effective therapies such as Alzheimer's disease (AD), frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS). Our discovery pipeline includes our proprietary A β program as well as three programs that are the focus of our collaboration with Celgene (discussed below).

If promising, we expect to advance our discovery programs into preclinical development. New target discovery will focus on the potential treatment of neurodegenerative indications where we can bring these therapies to patients expeditiously through our internal expertise and resources. Existing late discovery-stage programs may be partnered or out-licensed. Targets in our discovery pipeline include the following:

A β , or Amyloid Beta, a protein implicated in Alzheimer's disease (AD). Our scientists have advanced the understanding of the biology of AD and made particularly impactful and fundamental discoveries that elucidated the role amyloid plays in the disease. Today, we are advancing a new approach to design a more potent anti-A β antibody.

Tau, a protein implicated in diseases including AD, FTD, progressive supranuclear palsy (PSP), chronic traumatic encephalopathy (CTE) and other tauopathies. We have identified antibodies targeting novel epitopes on the tau protein with the potential to block misfolded tau from binding to cells and to inhibit cell-to-cell transmission, preventing downstream toxic functional effects.

Master Collaboration Agreement with Celgene

In March 2018, we entered into the Master Collaboration Agreement (the "Collaboration Agreement") with Celgene, under which Celgene 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.

On a program-by-program basis, following Prothena's filing of an investigational new drug (IND) application for any of our three collaboration programs to Celgene, Celgene 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 Celgene exercises the US Rights for a collaboration program, it is obligated to pay Prothena an exercise fee of approximately \$80 million per program. Thereafter, Celgene 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 Celgene has previously exercised its US Rights, Celgene 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 Celgene exercises its Global Rights, Celgene 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 Celgene 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.

Celgene 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 Celgene 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 Celgene 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 Celgene challenges a patent licensed by Prothena to Celgene under the Collaboration Agreement.

Under the SSA, Celgene 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 the 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, Celgene 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 (the “Securities Act”).

In November 2018, we announced that we had entered into a multi-target license and option agreement with Bioasis Technologies, Inc. Under the agreement, Prothena made an upfront payment of \$1 million to Bioasis and is exploring the application of Bioasis’s xB³ platform technology to increase the delivery of therapeutics across the blood-brain barrier (BBB) for neuroscience disorders. Prothena has the option to exercise exclusive worldwide rights to additional therapeutic products incorporating Bioasis’s BBB technology for neuroscience targets.

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, and promotion of pharmaceutical products, including biologics. 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 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 restrictions.

The pricing of pharmaceutical 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 drug candidates are regulated as biologic pharmaceuticals, or biologics. The FDA regulates biologics under the U.S. Food, Drug, and Cosmetics Act, U.S. Public Health Service Act and its 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 the following:

• submission to the FDA of an Investigational New Drug Application (“IND”), which must become effective before human clinical trials may begin and must be updated annually;

• completion of extensive nonclinical laboratory tests and animal studies, performed in accordance with the FDA’s Good Laboratory Practice (“GLP”) regulations;

• 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”) process and procedures to establish the safety and quality of the pharmaceutical product in accordance with FDA’s current good manufacturing practices (“cGMP”) regulations;

• submission to the FDA of a 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; 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 efficacy 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 general investigational plan and the proposed protocol(s) 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 concerns or questions related to initiation of the proposed clinical trial(s). In such a case, the IND may be placed on 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.

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 for 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 trial 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:

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Phase 1. Phase 1 includes the initial introduction of an investigational product into humans. Phase 1 clinical trials are typically 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 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 limited patient population, usually involving no more than several hundred participants; and

Phase 3. Phase 3 clinical trials are generally 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. 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 unacceptable health risk. 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 marketing authorization.

The results of the nonclinical and clinical testing, along with information regarding the chemistry, manufacturing and controls of the product and proposed product labeling, are evaluated and, if determined appropriate, submitted to the FDA 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 standard goal is to review applications within ten months of the filing date for Standard Review or, in the case of Priority Review, six months from the accepted-for-filing date. The review process is often significantly extended by FDA 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.

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 the 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. The Accelerated Approval designation allows the FDA to approve a product based on an effect on a surrogate or intermediate endpoint that is reasonably likely to predict a product's clinical benefit and generally requires the sponsor to conduct required post-approval confirmatory trials to verify the clinical benefit. The Priority Review designation signifies that the FDA review clock for the BLA is six months, compared to ten months following the accepted-for-filing date under standard review.

After the FDA evaluates the BLA and conducts pre-approval inspections of manufacturing facilities where the candidate product and/or its active pharmaceutical ingredient will be produced, of clinical sites and of the sponsor, if deemed necessary, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes

commercial marketing of the biologic with specific prescribing information 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 could approve the BLA with a Risk Evaluation and Mitigation Strategy (“REMS”) plan 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. The FDA also may impose conditions for approval including but not limited to, changes to proposed labeling, changes to manufacturing controls and specifications, or a commitment to conduct one or more post-marketing studies or additional clinical trials. Such post-marketing commitments 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 EC 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 biological 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. The packaging and labeling of all products developed by us are also subject to FDA approval and ongoing regulation.

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 certain quality processes, manufacturing controls and documentation requirements upon us and our third-party manufacturers in order to ensure that the product is safe, has the identity and strength, and meets the 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 letters, civil and criminal penalties, seizures, and injunctive action.

FDA regulations also require 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 FDA approval, 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 adverse publicity, warning 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

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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. 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. 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 seek licenses from others as appropriate to enhance or maintain our competitive position.

Our intellectual property is primarily directed to immunological approaches to the treatment of diseases that involve amyloid or cell adhesion, and other proprietary technologies and processes related to our lead product development candidates.

We own or hold exclusive licenses to a number of issued U.S. patents and pending U.S. patent applications, as well as issued non-U.S. patents and pending Patent Cooperation Treaty applications and non-U.S. counterparts. As of December 31, 2018, our patent portfolio included the following patents or patent applications that we own or have exclusively licensed from other parties:

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Approximately 17 patent families related to Parkinson's disease and other synucleinopathies, including our prasinezumab program, including a composition of matter patent expiring in 2032 (subject to potential increases or decreases in patent term as described below);

Approximately 7 patent families related to ATTR amyloidosis, including our PRX004 program, including a composition of matter patent expiring in 2036 (subject to potential increases or decreases in patent term as described below); and

Approximately 24 patent families related to other potential targets of intervention and diseases, including A β , tau, TDP-43, AL or AA (e.g., NEOD001), and MCAM (e.g., PRX003).

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 the FDA regulatory review process. 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 regulatory review. 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 applicable to an approved drug may be extended. 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, we expect to apply for patent term extensions for patents covering our product candidates and their methods of use.

The patents referenced above have expiration dates ranging from 2020 through 2039 (excluding any available patent term extensions).

University of Tennessee License Agreement: Under a License Agreement with the University of Tennessee Research Foundation, we have exclusively licensed from the University of Tennessee its joint ownership interest in certain patents jointly owned with us. Those patents relate to our program targeting amyloidosis (NEOD001). Under that sublicensable, worldwide license, we are required to pay to the University of Tennessee an amount equal to 1% of net sales of any product covered by any licensed patent, plus certain additional payments in the event that all or a portion of the license is sublicensed. To date, we have not paid or incurred any royalties to the University of Tennessee under our agreement. The agreement is effective on a country-by-country basis for the longer of (i) a period of twenty years from the effective date of the agreement, or (ii) in each country in which a valid claim for any licensed patent or patent application exists, expiration of such valid claim. The agreement will terminate prior to the end of its term if we become insolvent unless the University of Tennessee elects to allow the agreement to remain in effect. The University of Tennessee may terminate the agreement prior to the end of its term upon our failure to make payment under the agreement within 120 days of notice of such failure or upon our material breach of the agreement, which breach has not been cured within 60 days of written notice of such breach. We may terminate the agreement prior to the end of its term if we have paid all amounts due to the University of Tennessee through the effective date of the termination and provide three months' written notice to the University of Tennessee or upon material breach of the agreement by the University of Tennessee, which breach has not been cured within 60 days of written notice of such breach.

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

notice of such default. We may terminate the agreement prior to the end of its term upon a 90 day written notice to the University of California.

University Health Network License Agreement: Under a License Agreement with the University Health Network (“UHN”), we have exclusively licensed its joint interest in certain patents jointly owned with us, as well as its entire interest in certain patents solely owned by UHN (“UHN Background IP”). Those patents relate to our program targeting ATTR amyloidosis (PRX004). Under that sublicensable, worldwide license, we are required to pay to UHN royalties on net sales of any diagnostic or therapeutic product covered by a licensed patent in the U.S. and outside of the U.S., plus certain additional payments for milestones achieved and sublicense revenue. In addition, we are required to pay to UHN a royalty on net sales of any product that is not a diagnostic or therapeutic product. To date, we have not paid or incurred any royalties to UHN 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 (i) upon the filing of a petition for relief under the U.S. Bankruptcy Code by or against us as a debtor or alleged debtor, (ii) upon the filing of a claim by us challenging the validity of a patent within UHN Background IP, or (iii) by mutual written agreement of the parties. UHN may terminate the agreement prior to the end of its term upon our default, if we fail to cure the default within 90 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 UHN.

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

We do not own or operate facilities for the manufacture, packaging, labeling, storage, testing or distribution of preclinical 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 all pre-clinical development 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.

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.

PRX004 - Rentschler Biopharma SE (formerly known as Rentschler Biotechnologie GmbH) (“Rentschler”) is our third-party manufacturer of clinical supplies of our drug candidate PRX004. We are dependent on Rentschler to manufacture these clinical supplies for our ongoing Phase 1 and any subsequent clinical trials for PRX004.

NEOD001 - BI manufactured clinical supplies of our drug candidate NEOD001 for all of its clinical trials.

Research and Development

Our research and development expenses totaled \$101.2 million, \$134.5 million and \$119.5 million in 2018, 2017 and 2016, respectively. For more information, see “Management’s Discussion and Analysis of Financial Condition and Results of Operations.”

Employees

As of December 31, 2018, we had 59 employees, of whom 36 were engaged in research and development activities and the remainder were working in general and administrative areas. The vast majority of these employees are in the U.S.

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 T804, Ireland, and our telephone number at that address is 011-353-1-236-2500. 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 T804, Ireland, 011-353-1-236-2500, 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 report 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, which could result in a complete loss on your investment.

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

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

We may not generate the cash that is necessary to finance our operations in the foreseeable future. We incurred net losses of \$155.6 million, \$153.2 million and \$160.1 million for the years ended December 31, 2018, 2017 and 2016,

respectively. We expect to continue to incur substantial losses for the foreseeable future as we: support the Phase 2 PASADENA clinical trial for prasinezumab (PRX002/RG7935) being conducted by Roche, conduct our Phase 1 clinical trial for PRX004 and possibly initiate additional clinical trials for these and other programs;

- develop and commercialize our product candidates, including prasinezumab and PRX004;

undertake nonclinical development of other product candidates and initiate clinical trials, if supported by nonclinical data; and

pursue our early stage research and seek to identify additional drug candidates and potentially acquire rights from third parties to drug candidates 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, 2018, we had cash and cash equivalents of \$427.7 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 the future 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 initiation, progress, results and costs of our clinical trials, including the Phase 2 clinical trial for prasinezumab and our Phase 1 clinical trial for PRX004;

- the timing, initiation, progress, results and costs of these and our other research, development and commercialization activities;

- the results of our research, nonclinical and clinical studies;

- the costs of manufacturing our drug candidates for clinical development as well as for future commercialization needs;

- 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 research collaborations, strategic collaborations, licensing or other arrangements;

- the timing, receipt and amount of any 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 product 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 product 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 product 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 ongoing 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 product 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. We cannot assure that additional funds will be available when we need them on terms that are acceptable to us, or at all. General market conditions may make it very difficult for us to seek or obtain financing from the capital markets. If we raise additional funds by issuing equity securities, 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 announced withdrawal from the European Union could have a negative effect on global economic conditions and financial markets, European Union regulatory procedures and our business.

In June 2016, a majority of voters in the United Kingdom (the "UK") elected in a national referendum to withdraw from the European Union (the "EU"). In March 2017, the UK government formally initiated the withdrawal process, which is still underway. That withdrawal has created significant uncertainty about the future relationship between the UK and the EU, including with respect to the laws and regulations that will apply as the UK determines which EU laws to replace or replicate upon withdrawal. The pending withdrawal has also given rise to calls for the governments of other EU member states to consider withdrawal. These developments, or the perception that any of them could occur, have 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 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.

Recruiting 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. Failure to recruit and retain qualified personnel could have a material adverse effect on our business, financial condition, results of operations and 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 or other natural disasters.

Our key facility and almost all 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, in certain cases, 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.

Accordingly, such a natural disaster or similar event 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. The size and complexity of those systems make them vulnerable to breakdown, malicious intrusion and computer viruses. We have developed systems and processes that are designed to protect our information technology systems and prevent data loss and other security breaches, including systems and processes designed to reduce the impact of a security breach. However, such measures cannot provide absolute security. Any breakdown, malicious intrusion or computer virus could result in the impairment of key business processes or breach of data security, which could cause us to lose 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. Such an event could have an adverse effect on our business, financial condition or results of operations.

We are subject to increasingly complex data protection laws and regulations.

We are subject to various data protection laws and regulations, which are expanding and becoming more complex. In May 2018, the EU General Data Protection Regulation (the “GDPR”) was adopted in the EU and superseded the previous EU data protection legislation. Under the GDPR, enhanced data protection requirements as well as substantial fines for breaches of personal data apply and increase our obligations and potential liabilities for the personal data that we process or control. We may be required to implement additional controls to facilitate compliance with the GDPR and other new or evolving data protection laws and regulations. Ensuring our compliance with these 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 operations are found to be in violation of any of such laws and regulations, we may be subject to significant civil, criminal and administrative damages, penalties and fines, as well as reputational harm, which could have a material adverse effect on our business, financial condition or results of operations.

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

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

The success of our business depends substantially upon our ability to discover, develop, obtain regulatory approval for and commercialize our drug candidates successfully. Our research and development programs are prone to the significant and likely risks of failure inherent in drug development. We intend to continue to invest most of our time and financial resources in our research and development programs.

Although we have an ongoing Phase 2 clinical trial for prasinezumab and an ongoing Phase 1 clinical trial for PRX004, there is no assurance that the results of these trials 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 U.S. Food and Drug Administration

(the “FDA”); in the EU this must be done to the satisfaction of 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 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 our drug candidates, which 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 and may enter into additional collaborations in the future, and we might not realize the anticipated benefits of such collaborations.

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

- collaborators have significant 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 development and commercialization of product candidates in the territories in which our collaboration partners lead development and commercialization;
- collaborators might not pursue research, development and commercialization of collaboration product candidates or might elect not to continue or renew research, development or commercialization programs based on 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 clinical trials for collaboration product candidates or require a new formulation of a product candidate for clinical testing;
- collaborators could develop or acquire products outside of the collaboration that compete directly or indirectly with our product candidates or require a new formulation of a product candidate for clinical testing;

collaborators with sales, marketing and distribution rights to one or more product candidates might not commit sufficient resources to sales, marketing and distribution or might otherwise fail to successfully commercialize those product 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 product candidates, which could limit our rights or ability to research, develop or commercialize our product candidates;

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 development or commercialization of our product candidates.

In addition, funding provided by a collaborator might not be sufficient to advance product candidates under the collaboration. For example, although Celgene made a \$100 million upfront payment to us and made a \$50 million equity investment in us upon entering into the Collaboration Agreement, we might need additional funding to advance product candidates prior to when Celgene decides whether to exercise its license rights to those product candidates.

We also note that, on January 3, 2019, Bristol-Myers Squibb (BMS) and Celgene announced that they had entered into an agreement for BMS to acquire Celgene. If and when that acquisition is completed, BMS might take a different approach to our collaboration with Celgene or determine not to continue that collaboration.

If a collaborator terminates a collaboration or a development 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 product candidate or abandon that program, the development of the relevant product candidate could be significantly delayed, and our cash expenditures could increase significantly if we are to continue research, development and commercialization of the relevant product candidates.

Any one or more of these risks, if realized, could reduce or eliminate future revenue from product 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, which would require us to incur additional costs and delay our receipt of any revenue from potential product sales.

We cannot predict whether we will encounter problems with the Phase 2 clinical trial for prasinezumab, our Phase 1 clinical trial for PRX004 or any other future clinical trials that will cause us or any regulatory authority to delay or suspend 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 agency agreement 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 study drug, 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.

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

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

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

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

Both before and after regulatory approval to market a particular drug candidate, adverse event reporting, manufacturing, labeling, packaging, storage, distribution, advertising, promotion, record keeping and reporting related to the product are subject to extensive, ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, as well as continued compliance with current good manufacturing practice ("cGMP") requirements and current good clinical practice ("cGCP") requirements for any clinical trials that we conduct post-approval. 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 with our third-party manufacturers or manufacturing processes, or failure to comply with the regulatory requirements of the FDA, the EMA and 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;

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- 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 FDA's, the EMA's or other comparable regulatory authorities' policies 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 after they are approved and 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 warnings or contraindications, or impose additional safety monitoring or reporting requirements;
- we may be required to change the way the product is administered, 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 is 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, if we opt out of profit and loss sharing with Roche, our revenues from prasinezumab 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, Roche may determine that the outcomes of clinical trials have 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, 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.

Furthermore, pursuant to the License Agreement, we are responsible for 30% of all development and commercialization costs for prasinezumab for the treatment of Parkinson's disease in the U.S., and for any future Licensed Products and/or indications 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 prasinezumab will be reduced.

Our right to co-develop prasinezumab and other Licensed Products under the License Agreement 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 our participation in profit and loss sharing, and may result in lower levels of income than if we marketed or developed our product 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 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 product.

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 product 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 "Healthcare Reform Law"), was enacted. The Healthcare Reform Law substantially changed the way healthcare is financed by both governmental and private insurers and significantly affects the pharmaceutical industry. Among the provisions of the Healthcare Reform Law 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;

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a new Medicare Part D coverage gap discount program, under which manufacturers must agree to offer 50 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 Healthcare Reform Law was enacted. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in 2013 and will stay in effect through 2024 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.

We expect that the Healthcare Reform Law, as well as 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;

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- 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 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 approved by the FDA until 12 years after the original branded product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our biologic products.

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 are subject to healthcare and other laws and regulations, including anti-bribery, anti-kickback, fraud and abuse, false claims, physician payment transparency and health information privacy and security 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;

- U.S. federal and state 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;

the U.S. Health Insurance Portability and Accountability Act of 1996 (“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, and under the Health Information Technology for Economic and Clinical Health Act of 2009 (“HITECH”) imposes obligations, including mandatory contractual terms, on certain types of individuals and entities with respect to safeguarding the privacy, security and transmission of individually identifiable health information and places restrictions on the use of such information for marketing communications;

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 and teaching hospitals and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by the physicians and their immediate family members;

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.

Further, the Healthcare Reform Law, among other things, amended the intent requirements of the U.S. Anti-Kickback Statute and the criminal statutes governing healthcare fraud. A person or entity can now be found guilty of violating the statute without actual knowledge of the statute or specific intent to violate it. In addition, the Healthcare Reform Law provided that the government may assert that a claim including items or services resulting from a violation of the U.S. Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the U.S. False Claims Act.

Ensuring our compliance with applicable healthcare and other 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 operations are found to be in violation of any of such laws and regulations, we may be subject to significant civil, criminal and administrative damages, penalties and fines, as well 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; and
- 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 cGMP regulations. 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 and development plans. Our drug research and development programs 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 development and 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 products 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 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 product 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 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 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 products, cause a delay or suspension of nonclinical or clinical development, product approval and commercialization of our drug candidates or drug products, 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 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 growth prospects.

Roche, with whom we are collaborating on development of prasinezumab, is manufacturing clinical supplies for the Phase 2 clinical trial 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.

Rentschler Biopharma SE (“Rentschler”) is our third-party manufacturer of clinical supplies of our drug candidate PRX004. We are dependent on Rentschler to manufacture these clinical supplies in order to continue our Phase 1 and initiate any other clinical trials for PRX004.

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 and factual 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.

In addition, 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 product 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.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. In 2011, the U.S. Leahy-Smith America Invents Act (the “Leahy-Smith Act”) was signed into law. 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, may affect patent litigation, and switch the U.S. patent system from a “first-to-invent” system to a “first-to-file” system. Under a “first-to-file” system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to the patent on an invention regardless of whether another inventor had made the invention earlier. The USPTO subsequently developed new regulations and procedures to govern administration of the Leahy-Smith Act, but many of the substantive changes to patent law associated with the Leahy-Smith Act continue to be the subject of litigation and USPTO rule changes. Accordingly, it is not clear

what, if any, impact the Leahy-Smith Act will have on the operation of our business. 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 and financial condition.

We may be subject to a third-party preissuance submission of prior art to the USPTO, 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 reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. We may not be able to protect our intellectual property rights throughout the world.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as in the U.S. and many companies have encountered significant difficulties in protecting and defending such rights in other jurisdictions. If we encounter such difficulties in protecting or are otherwise precluded from effectively protecting our intellectual property rights in other jurisdictions, our business prospects could be substantially harmed.

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 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 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.

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.

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. 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.

In addition, third parties may challenge or infringe upon our existing or future patents. 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.

Even if we are successful in these proceedings, we may incur substantial costs and divert management time and attention in pursuing these proceedings, which could have a material adverse effect on us.

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;

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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.

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 registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition by potential partners or customers in our markets of interest. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected.

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. In addition, others may independently discover our trade secrets and proprietary information. 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.

We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

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. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

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 non clinical research and clinical trials;
- our collaborations with third parties, including with Roche and Celgene;
- 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 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;
- 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.

We are a defendant in a purported securities class action lawsuit, which could result in substantial costs, divert our management's time and attention from our business and have an adverse outcome.

As described in Note 7, "Commitments and Contingencies - Legal Proceedings" of the Notes to Consolidated Financial Statements and Item 3 - Legal Proceedings of this Form 10-K, a purported class action lawsuit has been filed against us and certain of our current and former officers. This lawsuit seeks, among other things, compensatory damages and attorneys' fees and costs. We believe that the lawsuit lacks merit and we intend to vigorously defend against it.

However, this lawsuit, like any litigation, is subject to inherent uncertainties, the outcome is necessarily uncertain and we might not prevail. Moreover, defending against the lawsuit could result in substantial costs and be time-consuming and distracting to our management and internal resources, which could have an adverse effect on our business, results of operations or financial condition.

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 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, 2018, the number of ordinary shares available for issuance pursuant to outstanding and future equity awards under our equity plan was 8,262,086.

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. 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 condensed consolidated financial statements may be materially misstated. We or our independent registered public accounting firm, when 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, when 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 (the "income test"), or (ii) 50% or more of our assets produce passive income (the "asset test"). Changes in the composition of our active or passive income, passive assets or 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 years ended December 31, 2018, or any prior year. 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 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 in any of these jurisdictions could adversely affect our ability to do so in the future. Taxing authorities, such as the IRS, 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 and other taxing authorities from time to time, and the IRS 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 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. In addition, the 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,” 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 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 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 (the “Companies Act”), which differ 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.

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 Panel Act, 1997, Takeover Rules, 2013. Under those Irish Takeover Rules, 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, 2022 (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, 2017, 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, 2022, 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, 2022, 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 product 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 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 ever turn a profit, we intend to retain future earnings, if any, for the development, operation and expansion of our business. Thus, 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 20%) 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). 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 133 square feet of office under a lease which expires on November 30, 2019.

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.

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

ITEM 3. LEGAL PROCEEDINGS

On July 16, 2018, a purported class action lawsuit entitled Granite Point Capital v. Prothena Corporation plc, et al., Civil Action No. 18-cv-06425, was filed in the U.S. District Court for the Southern District of New York against the Company and certain of its current and former officers. The plaintiff seeks compensatory damages, costs and expenses in an unspecified amount on behalf of a putative class of persons who purchased the Company's ordinary shares between October 15, 2015 and April 20, 2018, inclusive. The complaint alleges that the defendants violated federal securities laws by allegedly making false and misleading statements and omitting certain material facts in certain public statements and in the Company's filings with the U.S. Securities and Exchange Commission during the putative class period, regarding the clinical trial results and prospects for approval of the Company's NEOD001 drug development program. On October 31, 2018, the Court issued an order naming Granite Point Capital and Simon James, an individual, as the lead plaintiffs in the purported class action, which is now entitled In re Prothena Corporation plc Securities Litigation.

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. The following table sets forth the high and low intraday per share sale prices of our ordinary shares as reported by Nasdaq during each of the previous eight quarters.

	Price Range Per Share	
	High	Low
Fiscal 2018		
Fourth quarter	\$ 13.83	\$ 8.63
Third quarter	\$ 15.91	\$ 12.23
Second quarter	\$ 44.75	\$ 10.43
First quarter	\$ 46.14	\$ 27.19
Fiscal 2017		
Fourth quarter	\$ 64.96	\$ 34.85
Third quarter	\$ 70.00	\$ 52.92
Second quarter	\$ 59.10	\$ 48.23
First quarter	\$ 63.14	\$ 45.13

On March 11, 2019, the closing price of our ordinary shares was \$13.11.

Holders

There were approximately 1,166 shareholders of record of our ordinary shares as of March 11, 2019. 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 the 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, 2013 through December 31, 2018 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	12/31/2013	12/31/2014	12/31/2015	12/31/2016	12/31/2017	12/31/2018
Prothena Corporation plc	\$100	\$ 78	\$ 257	\$ 185	\$ 141	\$ 39
Nasdaq Composite Index	\$100	\$ 113	\$ 120	\$ 129	\$ 165	\$ 159
Nasdaq Biotechnology Index	\$100	\$ 134	\$ 149	\$ 117	\$ 142	\$ 128

⁽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, Burma (Myanmar), Belarus, certain persons indicted by the International Criminal Tribunal for the former Yugoslavia, the late Osama bin Laden, Al-Qaida, the Taliban of Afghanistan, 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, 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 the standard rate of income tax (currently 20%), unless an exemption applies. Dividends on our ordinary shares that are owned by residents of the U.S. and held beneficially through the Depositary 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 tax on capital 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

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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. SELECTED FINANCIAL DATA

The following selected consolidated financial information has been derived from our audited consolidated financial statements. The information set forth below is not necessarily indicative of results of future operations and should not be relied upon as an indicator of our future performance. The selected consolidated financial data should be read in conjunction with Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the Consolidated Financial Statements and notes thereto included in Item 8 of this Form 10-K in order to fully understand factors that may affect the comparability of the information presented below.

The following tables set forth our selected consolidated financial data for the periods indicated below (amounts in thousands except for per share amounts).

	Year Ended December 31,				
	2018	2017	2016	2015	2014
Consolidated Statement of Operations Data:					
Collaboration revenue	\$955	\$27,519	\$1,055	\$1,607	\$50,320
Revenue—related party	—	—	—	—	534
Total revenue	955	27,519	1,055	1,607	50,854
Operating expenses:					
Research and development	101,183	134,547	119,534	58,439	38,452
General and administrative	42,482	48,226	41,056	23,105	19,051
Restructuring and related impairment charges	16,145	—	—	—	—
Total operating expenses	159,810	182,773	160,590	81,544	57,503
Loss from operations	(158,855)	(155,254)	(159,535)	(79,937)	(6,649)
Other income (expense):					
Interest income (expense), net	2,692	(142)	556	196	79
Other income (expense), net	48	(2,207)	15	(170)	231
Total other income (expense), net	2,740	(2,349)	571	26	310
Loss before income taxes	(156,115)	(157,603)	(158,964)	(79,911)	(6,339)
Provision for (benefit from) income taxes	(470)	(4,366)	1,144	701	811
Net loss	\$(155,645)	\$(153,237)	\$(160,108)	\$(80,612)	\$(7,150)
Basic and diluted net loss per share	\$(3.93)	\$(4.07)	\$(4.66)	\$(2.66)	\$(0.29)
Shares used to compute basic and diluted net loss per share	39,559	37,654	34,351	30,326	24,672

	Year Ended December 31,				
	2018	2017	2016	2015	2014
Consolidated Balance Sheet Data:					
Cash and cash equivalents and restricted cash	\$431,715	\$421,676	\$390,979	\$370,586	\$293,579
Total assets	498,796	496,329	459,976	385,236	304,116
Other non-current liabilities	160,872	51,769	53,498	2,351	2,188
Total liabilities	175,798	89,140	94,573	24,567	14,227
Shareholders' equity	322,998	407,189	365,403	360,669	289,889

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

This Annual Report on Form 10-K, including under Item 1- Business and in this Management's Discussion and Analysis of Financial Condition and Results of Operations, contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended. These statements relate to, among other things: our goal to advance a pipeline of therapeutic candidates; key elements of our strategy; our intent to advance new discovery-stage therapeutics for neurological diseases; the treatment potential and proposed mechanisms of action of prasinezumab and PRX004; the potential to receive future milestones and royalties under the Roche collaboration; the potential to receive future exercise payments, milestones and royalties under the Celgene collaboration; expected terms of our patents; our expected research and development ("R&D") and general and administrative ("G&A") expenses in 2019; the sufficiency of our cash and cash equivalents to meet our obligations; our anticipated need for additional capital; our current intention not to repatriate funds to Ireland; and our estimates of certain future contractual obligations. 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," "position," "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. Forward-looking statements are subject to risks and uncertainties, and actual events or results may differ materially. Factors that could cause our

actual results to differ materially include, but are not limited to, the risks and uncertainties listed below as well as those discussed under Item 1A - Risk Factors of this Form 10-K.

- 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 with third parties, including Roche and Celgene;
- our ability to protect our patents and other intellectual property;
- our ability to hire and retain key employees;
- tax treatment of our separation from Elan and subsequent distribution of our ordinary shares;
- 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;
- potential disruptions in the U.S. and global capital and credit markets;
- government regulation of our industry;
- the volatility of our ordinary share price;
- business disruptions; and
- the other risks and uncertainties described in Item 1A - Risk Factors of this Form 10-K.

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 report.

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

Overview

Prothena Corporation plc (“Prothena” or the “Company”) is a clinical-stage neuroscience company focused on the discovery and development of novel therapies with the potential to fundamentally change the course of progressive, life-threatening diseases. Fueled by its deep scientific understanding built over decades of neuroscience research, Prothena is advancing a pipeline of therapeutic candidates for a number of indications and novel targets including Parkinson’s disease and other related synucleinopathies (prasinezumab - PRX002/RG7935) and ATTR amyloidosis (PRX004), as well as tau, A β (Amyloid beta), and TDP-43, where its scientific understanding of disease pathology can be leveraged.

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

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 contains 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 Roche and Roche's 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.

We do not disclose the value of unsatisfied performance obligations for (i) contracts with an original expected length of one year or less and (ii) contracts for which we recognize revenue at the amount to which we have the right to invoice for services performed.

Collaboration Revenue

Upon adoption of Financial Accounting Standards Board (the "FASB") Accounting Standards Codification ("ASC") 606 on January 1, 2018, we recognize research and development ("R&D") reimbursements as collaboration revenue earned over time as services are performed. Prior to adoption of ASC 606, we recorded research reimbursement as collaboration revenue and development reimbursement as an offset to R&D expense once the license revenue cap was met.

Milestone Revenue

We generally classify 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 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 the U.S. Food and Drug Administration (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.

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.

Profit Share Revenue

For agreements, with profit sharing arrangements, we will record our 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

We will recognize revenue from royalties based on licensees' sales of our products or products using our 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.

Taxes, Shipping and Handling

We exclude 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 us from a customer (e.g., sales, use, value added, some excise taxes). In addition, we account for shipping and handling as activities that are performed after our 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, we 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.

Build-to-Suit Lease Accounting

In certain lease arrangements, we are involved in the construction of the building. To the extent we are involved with structural improvements of the construction project or take construction risk prior to the commencement of a lease, ASC 840-40, Leases – Sale-Leaseback Transactions (Subsection 05-5), requires us to be considered the owner for accounting purposes of these types of projects during the construction period. Therefore, we record an asset in property and equipment, net on the Consolidated Balance Sheets, including capitalized interest costs, for the replacement cost of the pre-existing building plus the amount of estimated construction costs and tenant improvements incurred by the landlord and us as of the balance sheet date. We record a corresponding build-to-suit lease obligation on our Consolidated Balance Sheets representing the amounts paid by the lessor.

Once construction is complete, we consider the requirements for sale-leaseback accounting treatment, including evaluating whether all risks of ownership have been transferred back to the landlord, as evidenced by a lack of continuing involvement in the leased property. If the arrangement does not qualify for sale-leaseback accounting treatment, the building asset remains on our consolidated balance sheets at its historical cost, and such asset is depreciated over its estimated useful life of 30 years. We bifurcate our lease payments into a portion allocated to the building, and a portion allocated to the parcel of land on which the building has been built. The portion of the lease payments allocated to the land are treated for accounting purposes as operating lease payments, and therefore recorded as rent expense in the consolidated statements of operations. The portion of the lease payments allocated to the building is further bifurcated into a portion allocated to interest expense and a portion allocated to reduce the build-to-suit lease obligation.

The interest rate used for the build-to-suit lease obligation represents our estimated incremental borrowing rate, adjusted to reduce any built in loss.

The initial recording of these assets and liabilities is classified as non-cash investing and financing items, respectively, for purposes of the consolidated statements of cash flows.

The most significant estimates used by management in accounting for build-to-suit leases and the impact of these estimates are as follows:

Expected lease term- Our expected lease term includes the contractual lease period. The expected lease term is used in determining the depreciable life of the asset or the straight-line rent recognition period for the portion of the lease payment allocable to the land component.

Incremental borrowing rate- We estimate our incremental borrowing rate. For build-to-suit leases recorded on our Consolidated Balance Sheets with a related build-to-suit lease obligation, the incremental borrowing rate is used in allocating our rental payments between interest expense and a reduction of the outstanding build-to-suit lease obligation.

Fair market value of leased asset- The fair market value of a build-to-suit lease property is based on replacement cost of the pre-construction shell and comparable market data. Fair market value is used in determining the amount of the property asset and related build-to-suit lease obligation to be recognized on our Consolidated Balance Sheet for build-to-suit leases.

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 and investigative sites. 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. 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 we have expended. As such, expense accruals related to clinical trials are recognized based on our estimate of the degree of completion of the events specified in the specific clinical study or trial contract. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in 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.

Restructuring Charges

We recognize restructuring charges related to our reorganization plan. In connection with these activities, we record restructuring charges for contractual employee termination benefits, one-time employee termination benefits and contract termination costs. We account for our restructuring charges as a liability when the obligations are incurred and record such charges at fair value.

The recognition of restructuring charges requires us to make certain judgments and estimates regarding the nature, timing and amount of costs associated with the planned reorganization plan. To the extent the actual results differ from its estimates and assumptions, we may be required to revise the estimates of future liabilities, requiring the recognition of additional restructuring

charges or the reduction of liabilities already recognized. Such changes to previously estimated amounts may be material to the Consolidated Financial Statements. Changes in the estimates of the restructuring charges are recorded in the period the change is determined.

At the end of each reporting period, we evaluate the remaining accrued balances to ensure that no excess accruals are retained and the utilization of the provisions are for their intended purpose in accordance with developed restructuring plans.

Share-based Compensation

We account for our share-based compensation in accordance with the fair value recognition provisions of current authoritative guidance. Share-based awards, including stock options, are measured at fair value as of the grant date and recognized to expense over the requisite service period (generally the vesting period), which we have elected to amortize on a straight-line basis. Since share-based compensation expense is based on awards ultimately expected to vest, it has been reduced by an estimate for future forfeitures. Forfeitures are estimated based on historical experience. We estimate forfeitures at the time of grant and revise our estimate, if necessary, in subsequent periods. We estimate the fair value of options granted using the Black-Scholes option valuation model. Significant 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. We use the historical volatility of our shares to estimate expected volatility. Through December 31, 2017, the expected volatility was based on a combination of historical volatility for our shares and the historical volatilities of several of our publicly traded comparable companies. These peer companies are publicly traded, have similar industry, life cycle, revenue and market capitalization. In addition, since we do not have sufficient historical employee share option exercise data, the simplified method has been used to estimate the expected life of all options.

These assumptions consist of estimates of future market conditions, which are inherently uncertain, and therefore subject to our judgment and therefore any changes in assumptions could significantly impact the future grant date fair value of share-based awards.

Total share-based compensation expense for the years ended December 31, 2018, 2017 and 2016 was \$27.0 million, \$26.8 million and \$24.9 million, respectively.

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, 2018, 2017 and 2016

Revenue

	Year Ended December		Percentage	
	2018	2017	2018/2017	Change
	2018	2017	2018	2017/2016
	(Dollars in thousands)			
Collaboration revenue	\$955	\$27,519	\$1,055	(97)% 2,508 %
Total revenue	\$955	\$27,519	\$1,055	(97)% 2,508 %

Total revenue was \$1.0 million, \$27.5 million and \$1.1 million for the years ended December 31, 2018, 2017 and 2016, respectively.

Collaboration revenue includes reimbursements under our License Agreement with Roche. For the year ended December 31, 2017, collaboration revenue recognized also includes \$26.6 million of a \$30.0 million clinical milestone from Roche. See Note 8, “Significant Agreements” to the Consolidated Financial Statements regarding the Roche License Agreement for more information.

Operating Expenses

	Year Ended December 31,			Percentage Change	
	2018	2017	2016	2018/2017	2017/2016
	(Dollars in thousands)				
Research and development	\$ 101,183	\$ 134,547	\$ 119,534	(25)%	13 %
General and administrative	42,482	48,226	41,056	(12)%	17 %
Restructuring and related impairment charges	16,145	—	—	nm	— %
Total operating expenses	\$ 159,810	\$ 182,773	\$ 160,590	(13)%	14 %

nm = not meaningful

Total operating expenses consist of R&D expenses, general and administrative (“G&A”) expenses and restructuring and related impairment charges. Our operating expenses were \$159.8 million, \$182.8 million and \$160.6 million for the years ended December 31, 2018, 2017 and 2016, respectively.

Our R&D expenses primarily consist of personnel costs and related expenses, including share-based compensation and external costs associated with nonclinical activities and drug development related to our drug programs, including NEOD001, prasinezumab, PRX004 and our discovery programs. Pursuant to our License Agreement with Roche, we make payments to Roche for our share of the development expenses incurred by Roche related to prasinezumab program, which is included in our R&D expense. Prior to January 1, 2018, we recorded reimbursements from Roche for development as an offset to R&D expense.

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

Research and Development Expenses

Our R&D expense decreased by \$33.4 million, or 25%, for the year ended December 31, 2018, compared to the prior year. The decrease for year ended December 31, 2018 was primarily due to lower manufacturing and clinical costs associated primarily with NEOD001 and PRX003 programs, lower personnel costs (including share-based compensation expense) and lower consulting expenses, offset in part by higher expense associated with prasinezumab. For the year ended December 31, 2017, our R&D expenses increased by \$15.0 million, or 13%, compared to the prior year. The increase for the year ended December 31, 2017 was primarily due to higher personnel costs (including share-based compensation expenses), and to a lesser extent higher clinical trial costs associated primarily with the NEOD001 program, higher consulting expenses and higher expense associated with prasinezumab, which was partially offset by a decrease in external expenses related to product manufacturing.

Our research activities are aimed at developing new drug products. Our development activities involve the translation of our research into potential new drugs. R&D expenses include personnel costs and related expenses, external expenses associated with nonclinical and drug development and materials, equipment and facilities costs that are allocated to clearly related R&D activities.

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 NEOD001, prasinezumab, PRX003 and PRX004) and other R&D expenses for the years ended December 31, 2018, 2017 and 2016, and the cumulative amounts to date (in thousands):

	Year Ended December 31,			Cumulative to Date
	2018	2017	2016	
NEOD001 ⁽¹⁾	\$ 56,436	\$ 101,492	\$ 81,405	\$ 308,644
PRX002/RG7935 ⁽²⁾	14,782	6,412	6,554	65,530
PRX003 ⁽³⁾	336	9,234	15,135	59,010
PRX004 ⁽⁴⁾	16,515	13,218	12,397	46,680
Other R&D ⁽⁵⁾	13,114	4,191	4,043	
	\$ 101,183	\$ 134,547	\$ 119,534	

(1) Cumulative R&D costs to date for NEOD001 include the costs incurred from the date when the program has been 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. In April 2018, we announced that we were discontinuing development of NEOD001. Since that date we have incurred costs associated with the close out of our Phase 2b PRONTO, Phase 3 VITAL as well as the open label extension studies of NEOD001.

(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. Prasinezumab costs include payments to Roche for our share of the development expenses incurred by Roche related to prasinezumab programs and, through December 31, 2017, is net of reimbursements from Roche for development and supply services recorded as an offset to R&D expense. For the year ended December 31, 2018, \$1.0 million of reimbursements from Roche for development services were recorded as part of collaboration revenue as a result of the adoption of new revenue standard. For the years ended December 31, 2017 and 2016, \$5.1 million and \$3.6 million, respectively, were recorded as an offset to R&D expenses including \$3.4 million (for a portion of the \$30.0 million milestone payment received from Roche in the year ended December 31, 2017).

(3) Cumulative R&D costs to date for PRX003 include the costs incurred from the date when the program has been 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 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.

(5) 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.

As a result of the restructuring and the discontinuation of NEOD001, we expect our R&D expenses to decrease in 2019 over the prior year.

General and Administrative Expenses

Our G&A expenses decreased by \$5.7 million, or 12%, for the year ended December 31, 2018, compared to the prior year. The decrease for the year ended December 31, 2018, compared to the prior year, was primarily due to lower consulting expenses, lower personnel costs and lower marketing research services as a result of the discontinuation of NEOD001 program, offset in part by a gain recognized from the assignment of an operating lease in 2017 with no corresponding amount in 2018 and higher legal and accounting fees.

For the year ended December 31, 2017, our G&A expenses increased by \$7.2 million, or 17%, compared to the prior year. The increase for the year ended December 31, 2017 was primarily due to higher personnel costs, and to a lesser extent higher consulting and other expenses, which were partially offset by lower share-based compensation expense of \$7.7 million and \$1.0 million related to the accelerated vesting of stock options upon the passing of our former CEO and accelerated vesting of stock options due to our former Chief Commercial Officer under a separation agreement for the year ended December 31, 2016, and the \$2.4 million gain recognized from the assignment of our former South San Francisco facility lease in January 2017.

As a result of the restructuring, we expect our G&A expenses to decrease in 2019 over the prior year.

Restructuring and Impairment Related Charges

In May 2018, we commenced a reorganization plan to reduce our operating costs and better align our workforce with the needs of our business following our decision in April 2018 to discontinue further development of NEOD001. We have incurred aggregate restructuring and impairment related charges of approximately \$16.1 million for the year ended December 31, 2018. Restructuring charges incurred under this plan primarily consist of employee termination benefit and contract termination costs (including costs associated with the termination of our Commercial Supply

Contract with Rentschler Biopharma SE). Employee termination benefits include severance costs, employee-related benefits, supplemental one-time termination payments and non-cash share-based compensation expense related to the acceleration of stock options. Substantially all of the cash payments are expected to be paid out by the end of the first quarter of 2019.

Impairment charges relate to the write off of approximately \$500,000 of long-lived assets surrendered to the landlord as part of the full and final settlement of our office lease in Dún Laoghaire, Ireland. On October 30, 2018, we entered into a surrender agreement for our office space in Dún Laoghaire, Ireland.

We may also incur additional costs not currently contemplated due to events that may occur as a result of, or that are associated with, the workforce reduction. See Note 12, “Restructuring” to the Consolidated Financial Statements for more information.

Other Income (Expense)

	Year Ended December 31,			Percentage Change		
	2018	2017	2016	2018/2017	2017/2016	
	(Dollars in thousands)					
Interest income	\$6,389	\$3,546	\$1,419	80	%	150 %
Interest expense	(3,697)	(3,688)	(863)	—	%	327 %
Interest income (expense), net	2,692	(142)	556	(1,996)	%	(126) %
Other income (expense), net	48	(2,207)	15	(102)	%	nm
Total Other Income (Expense), net	\$2,740	\$(2,349)	\$571	(217)	%	(511) %

nm = not meaningful

Interest income (expense), net increased by \$2.8 million, or 1,996%, for the year ended December 31, 2018, compared to the prior year, primarily due to \$2.8 million higher interest income associated with higher interest rates and higher balances in our cash and money market accounts. Other income, net for the year ended December 31, 2018 was primarily foreign exchange gains from transactions with vendors denominated in Euros.

Interest income (expense), net decreased by \$698,000, or 126%, for the year ended December 31, 2017, compared to the same period in the prior year. The decrease for the year ended December 31, 2017 was primarily due to higher interest expense associated with our built-to-suit lease, which was partially offset by higher interest income associated with higher balances in our cash and money market accounts. Other expense, net for the year ended December 31, 2017 was primarily foreign exchange losses from transactions with vendors denominated in Euros.

Provision for (benefit from) Income Taxes

	Year Ended December 31,			Percentage Change	
	2018	2017	2016	2018/2017	2017/2016
	(Dollars in thousands)				
Provision for (benefit from) income taxes	\$(470)	\$(4,366)	\$1,144	(89)%	(482) %

The provision for (benefit from) income taxes were \$(0.5) million, \$(4.4) million and \$1.1 million for the years ended December 31, 2018, 2017 and 2016, respectively. The benefit from income taxes decreased by \$3.9 million for the year ended December 31, 2018, compared to the prior year, primarily due to lower excess tax benefits in the year ended December 31, 2018.

The benefit from income taxes increased by \$5.5 million for the year ended December 31, 2017, compared to the prior year, primarily due to the excess tax benefits of \$5.3 million recorded to the tax provision associated with the adoption of ASU 2016-09, Improvements to Employee Share-Based Payment Accounting, on January 1, 2017.

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, and to a lesser extent 2018 and 2017 also include Swiss taxes associated with intercompany services that our Swiss subsidiary performed 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.

On December 22, 2017, the U.S. Tax Cuts and Jobs Act (the “TCJA”) was signed into law. The TCJA was effective in the first quarter of 2018 and, among other things, lowered our U.S. federal income tax rate from 34% to 21%. We recorded a provisional tax benefit of \$0.4 million during the year ended December 31, 2017 related to the

remeasurement of our U.S. deferred tax assets to reflect the lower statutory tax rate. As of December 31, 2018, we have completed our accounting for the tax effects of TCJA and no adjustments were made to the provisional net tax benefit we reported as of the year ended December 31, 2017.

Liquidity and Capital Resources

Overview

	December 31,	
	2018	2017
Working capital	\$416,464	\$388,956
Cash and cash equivalents	427,659	417,620
Total assets	498,796	496,329
Total liabilities	175,798	89,140
Total shareholders' equity	322,998	407,189

Working capital was \$416.5 million as of December 31, 2018, an increase of \$27.5 million from working capital of \$389.0 million as of December 31, 2017. This increase in working capital during the year ended December 31, 2018 was primarily attributable to a higher net cash and cash equivalents balance resulting from a \$100.0 million upfront payment from the Celgene Collaboration Agreement and to a lesser extent from the proceeds of \$50.0 million from our share subscription agreement with Celgene, which was partially offset by use of \$159.8 million for operating expenses (adjusted to exclude non-cash charges).

As of December 31, 2018, we had \$427.7 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. As of December 31, 2018, \$104.7 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.

We have based this estimate 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 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. Pursuant to the License Agreement with Roche, in the U.S., we and Roche share all development and commercialization costs, as well as profits, all of which will be allocated 70% to Roche and 30% to us, for prasinezumab, as well as any other Licensed Products and/or indications for which we opt in to co-develop and co-fund. Pursuant to the Collaboration Agreement with Celgene the Company is eligible to receive payments for commercial and regulatory milestones and royalties on net sales of Collaboration Products. 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. 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.

Cash Flows for the Year Ended December 31, 2018, 2017 and 2016

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

	Year Ended December 31,		
	2018	2017	2016
Net cash used in operating activities	\$(28,276)	\$(131,183)	\$(116,250)
Net cash used in investing activities	(1,729)	(3,521)	(16,644)

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Net cash provided by financing activities	40,044	165,401	153,287
Net increase in cash and cash equivalents and restricted cash	\$ 10,039	\$ 30,697	\$ 20,393

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Cash Used in Operating Activities

Net cash used in operating activities was \$28.3 million for the year ended December 31, 2018, primarily due to use of \$159.8 million for operating expense (adjusted to exclude non-cash charges) and a decrease in account payables and accrued liabilities, which were partially offset by \$110.2 million in deferred revenue related largely to the upfront payment from the Celgene Collaboration Agreement and reduction in prepaid and other assets.

Net cash used in operating activities was \$131.2 million for the year ended December 31, 2017, primarily due to use of \$182.8 million for operating expenses (adjusted to exclude non-cash charges) and an increase in prepaid expenses and other assets.

Net cash used in operating activities was \$116.3 million for the year ended December 31, 2016, primarily due to use of \$160.6 million for operating expenses (adjusted to exclude non-cash charges), which was partially offset by an increase in accounts payable and accrued liabilities.

Cash Used in Investing Activities

Net cash used in investing activities was \$1.7 million, \$3.5 million and \$16.6 million for the years ended December 31, 2018, 2017 and 2016, respectively. Net cash used in investing activities for the years ended December 31, 2018, 2017 and 2016 primarily related to purchases of property and equipment.

Cash Provided by Financing Activities

Net cash provided by financing activities was \$40.0 million for the year ended December 31, 2018, primarily from the \$39.8 million proceeds from Celgene's subscription of ordinary shares at market value and, to a lesser extent, from the \$4.7 million proceeds from issuances of ordinary shares upon exercises of stock options, which were partially offset by cash payments of \$4.4 million related to a build-to-suit lease obligation.

Net cash provided by financing activities was \$165.4 million for the year ended December 31, 2017, primarily from the \$150.3 million net proceeds from our March 2017 public offering and \$17.8 million from issuances of ordinary shares upon exercises of stock options, which were partially offset by cash payments of \$2.8 million related to a build-to-suit lease obligation.

Net cash provided by financing activities was \$153.3 million for the year ended December 31, 2016, primarily from the net proceeds of \$128.8 million from our January 2016 public offering, \$14.2 million from our landlord for tenant improvement allowance related to our build-to-suit lease and \$10.5 million from issuances of ordinary shares upon exercises of stock options.

Off-Balance Sheet Arrangements

At December 31, 2018, 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, 2018 consisted primarily of minimum cash payments under a build-to-suit lease obligation of \$30.8 million, purchase obligations of \$1.2 million (of which \$1.0 million is included in accrued current liabilities), contractual obligations under license agreements of \$1.3 million (of which \$0.2 million is included in accrued current liabilities) and operating leases of \$23,000 for our future minimum rental commitments under our non-cancelable operating leases.

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 \$30.8 million remains outstanding as of December 31, 2018.

In September 2018, we entered into an agreement to lease an office space in Dublin, Ireland. The lease term expires on November 30, 2019. As of December 31, 2018, we are obligated to make lease payments over the term of the lease of approximately €22,000, or \$25,000 as converted using an exchange rate as of December 31, 2018.

The following is a summary of our contractual obligations as of December 31, 2018 (in thousands):

	Total	2019	2020	2021	2022	2023	Thereafter
Operating leases ⁽¹⁾	\$23	\$23	\$—	\$—	\$—	\$—	\$ —
Minimum cash payments under build-to-suit lease obligation ⁽¹⁾	30,832	5,803	5,979	6,165	6,350	6,535	—
Purchase obligations ⁽²⁾	1,218	1,218	—	—	—	—	—
Obligations under restructuring plan	461	461	—	—	—	—	—
Contractual obligations under license agreements ⁽³⁾	1,300	415	95	95	80	80	535
Total	\$33,834	\$7,920	\$6,074	\$6,260	\$6,430	\$6,615	\$ 535

⁽¹⁾ See Note 7, “Commitments and Contingencies” to our consolidated financial statements.

⁽²⁾ Purchase obligations consist of non-cancelable purchase commitments to suppliers.

⁽³⁾ Excludes future obligations pursuant to the cost-sharing arrangement under our License Agreement with Roche. Amounts of such obligations, if any, cannot be determined at this time.

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 gain on foreign currency exchange rate differences of approximately \$49,000 during the year ended December 31, 2018, a loss on foreign currency exchange rate differences of approximately \$2.2 million during the year ended December 31, 2017, and a gain of approximately \$21,000 during the year ended December 31, 2016. If we continue or increase our business activities that require the use of foreign currencies, we may incur further 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 intend to 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

Our receivable from Roche are amounts due from Roche entities located in the U.S. and Switzerland under the License Agreement with Roche.

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.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA
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Report of Independent Registered Public Accounting Firm

To the stockholders and board of directors

Prothena Corporation plc:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Prothena Corporation plc and subsidiaries (the Company) as of December 31, 2018 and 2017, the related consolidated statements of operations, stockholders' equity, and cash flows for each of the years in the three year period ended December 31, 2018, and the related notes (collectively, the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the years in the three year period ended December 31, 2018, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the Company's internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission, and our report dated March 15, 2019 expressed an unqualified opinion on the effectiveness of the Company's internal control over financial reporting.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits. We are a public accounting firm registered with the 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 audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. Our audits 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. We believe that our audits provide a reasonable basis for our opinion.

/s/ KPMG LLP

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

San Francisco, California

March 15, 2019

Report of Independent Registered Public Accounting Firm

To the stockholders and board of directors

Prothena Corporation plc:

Opinion on Internal Control Over Financial Reporting

We have audited Prothena Corporation plc and subsidiaries (the Company) internal control over financial reporting as of December 31, 2018, 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 Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (“PCAOB”), the consolidated balance sheets of the Company as of December 31, 2018 and 2017, the related consolidated statements of operations, stockholders’ equity, and cash flows for each of the years in the three-year period ended December 31, 2018, and the related notes (collectively, the “consolidated financial statements”), and our report dated March 15, 2019 expressed an unqualified opinion on those consolidated financial statements.

Basis for Opinion

The Company’s management is responsible 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 “Item 9A, Controls and Procedures”. Our responsibility is to express an opinion on the Company’s internal control over financial reporting based on our audit. We are a public accounting firm registered with the 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 audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. 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 audit also included performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

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.

/s/ KPMG LLP

San Francisco, California

March 15, 2019

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

	December 31,	
	2018	2017
Assets		
Current assets:		
Cash and cash equivalents	\$427,659	\$417,620
Receivable from Roche	2	240
Prepaid expenses and other current assets	3,729	8,467
Total current assets	431,390	426,327
Non-current assets:		
Property and equipment, net	52,835	54,990
Deferred tax assets	9,702	8,113
Restricted cash	4,056	4,056
Other non-current assets	813	2,843
Total non-current assets	67,406	70,002
Total assets	\$498,796	\$496,329
Liabilities and Shareholders' Equity		
Current liabilities:		
Accounts payable	\$1,470	\$13,633
Accrued research and development	5,370	13,509
Income taxes payable, current	54	311
Build-to-suit lease obligation, current	1,645	733
Restructuring liability	461	—
Other current liabilities	5,926	9,185
Total current liabilities	14,926	37,371
Non-current liabilities:		
Deferred revenue	110,242	—
Deferred rent	176	254
Build-to-suit lease obligation, non-current	49,901	51,515
Other liabilities	553	—
Total non-current liabilities	160,872	51,769
Total liabilities	175,798	89,140
Commitments and contingencies (Note 7)		
Shareholders' equity:		
Euro deferred shares, €22 nominal value:	—	—
Authorized shares — 10,000 at December 31, 2018 and 2017		
Issued and outstanding shares — none at December 31, 2018 and 2017		
Ordinary shares, \$0.01 par value:	399	385
Authorized shares — 100,000,000 at December 31, 2018 and 2017		
Issued and outstanding shares — 39,863,711 and 38,482,764 at December 31, 2018 and 2017, respectively		
Additional paid-in capital	920,594	849,154
Accumulated deficit	(597,995)	(442,350)
Total shareholders' equity	322,998	407,189
Total liabilities and shareholders' equity	\$498,796	\$496,329
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,		
	2018	2017	2016
Collaboration revenue	\$955	\$27,519	\$1,055
Total revenue	955	27,519	1,055
Operating expenses:			
Research and development	101,183	134,547	119,534
General and administrative	42,482	48,226	41,056
Restructuring and related impairment charges	16,145	—	—
Total operating expenses	159,810	182,773	160,590
Loss from operations	(158,855)	(155,254)	(159,535)
Other income (expense):			
Interest income (expense), net	2,692	(142)	556
Other income (expense), net	48	(2,207)	15
Total other income (expense), net	2,740	(2,349)	571
Loss before income taxes	(156,115)	(157,603)	(158,964)
Provision for (benefit from) income taxes	(470)	(4,366)	1,144
Net loss	\$(155,645)	\$(153,237)	\$(160,108)
Basic and diluted net loss per share	\$(3.93)	\$(4.07)	\$(4.66)
Shares used to compute basic and diluted net loss per share	39,559	37,654	34,351

See accompanying Notes to Consolidated Financial Statements.

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

	Year Ended December 31,		
	2018	2017	2016
Operating activities			
Net loss	\$(155,645)	\$(153,237)	\$(160,108)
Adjustments to reconcile net loss to cash used in operating activities:			
Depreciation and amortization	3,216	3,067	2,427
Share-based compensation	26,062	26,764	24,929
Restructuring share-based compensation	948	—	—
Deferred income taxes	(1,589)	(2,200)	(3,248)
Interest expense under build-to-suit lease obligation	3,696	3,688	863
Gain from early lease retirement	—	(2,096)	—
Loss (gain) from disposal of fixed assets	584	(5)	—
Changes in operating assets and liabilities:			
Accounts receivable	238	(62)	331
Prepaid and other assets	9,139	(7,249)	3,363
Deferred revenue	110,242	—	—
Accounts payable, accruals and other liabilities	(25,628)	147	15,193
Restructuring liability	461	—	—
Net cash used in operating activities	(28,276)	(131,183)	(116,250)
Investing activities			
Purchases of property and equipment	(1,768)	(3,626)	(16,644)
Proceeds from disposal of fixed assets	39	105	—
Net cash used in investing activities	(1,729)	(3,521)	(16,644)
Financing activities			
Proceeds from issuance of ordinary shares in public offering, net	—	150,323	128,777
Proceeds from subscription of ordinary shares	39,758	—	—
Proceeds from issuance of ordinary shares upon exercise of stock options	4,686	17,838	10,516
Reduction of build-to-suit lease obligation	(4,400)	(2,760)	(169)
Proceeds from tenant improvement allowance under build-to-suit transaction	—	—	14,163
Net cash provided by financing activities	40,044	165,401	153,287
Net increase in cash, cash equivalents and restricted cash	10,039	30,697	20,393
Cash, cash equivalents and restricted cash, beginning of the year	421,676	390,979	370,586
Cash, cash equivalents and restricted cash, end of the period	\$431,715	\$421,676	\$390,979
Supplemental disclosures of cash flow information			
Cash paid (refunds received) for income taxes, net	\$(995)	\$294	\$575
Supplemental disclosures of non-cash investing and financing activities			
Acquisition of property and equipment included in accounts payable and accrued liabilities	\$90	\$175	\$575
Stock option shortfall	\$—	\$—	\$(258)
Amounts capitalized under build-to-suit lease transaction	\$2	\$—	\$36,805
Interest capitalized during construction period for build-to-suit lease transaction	\$—	\$—	\$1,179
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,		
	2018	2017	2016
Cash and cash equivalents	\$427,659	\$417,620	\$386,923
Restricted cash	4,056	4,056	4,056
Total cash, cash equivalents and restricted cash, end of the period	\$431,715	\$421,676	\$390,979

Prothena Corporation plc and Subsidiaries
 Consolidated Statements of Shareholders' Equity
 (in thousands, except share data)

	Ordinary Shares		Additional	Accumulated	Total
	Shares	Amount	Paid-in Capital	Deficit	Shareholders' Equity
Balances at December 31, 2015	31,744,102	\$ 317	\$ 489,455	\$(129,103)	\$ 360,669
Issuance of ordinary shares in public offering, net of issuance costs of \$8.5 million	2,587,500	26	128,610	—	128,636
Share-based compensation	—	—	24,929	—	24,929
Excess tax benefit from share-based award exercises	—	—	761	—	761
Issuance of ordinary shares upon exercise of stock options	420,514	5	10,511	—	10,516
Net loss	—	—	—	(160,108)	(160,108)
Balances at December 31, 2016	34,752,116	348	654,266	(289,211)	365,403
Issuance of ordinary shares in public offering, net of issuance costs of \$4.9 million	2,700,000	27	150,296	—	150,323
Share-based compensation	—	—	26,764	—	26,764
Issuance of ordinary shares upon exercise of stock options	1,030,648	10	17,828	—	17,838
Cumulative adjustment to accumulated deficit upon adoption of ASU 2016-09	—	—	—	98	98
Net loss	—	—	—	(153,237)	(153,237)
Balances at December 31, 2017	38,482,764	385	849,154	(442,350)	407,189
Issuance of ordinary shares under share subscription agreement with Celgene	1,174,536	12	39,746	—	39,758
Share-based compensation	—	—	26,062	—	26,062
Restructuring share-based compensation	—	—	948	—	948
Issuance of ordinary shares upon exercise of stock options	206,411	2	4,684	—	4,686
Net loss	—	—	—	(155,645)	(155,645)
Balances at December 31, 2018	39,863,711	\$ 399	\$ 920,594	\$(597,995)	\$ 322,998

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 clinical-stage neuroscience company focused on the discovery and development of novel therapies with the potential to fundamentally change the course of progressive, life-threatening diseases. Fueled by its deep scientific understanding built over decades of neuroscience research, Prothena is advancing a pipeline of therapeutic candidates for a number of indications and novel targets including Parkinson’s disease and other related synucleinopathies (prasinezumab - PRX002/RG7935) and ATTR amyloidosis (PRX004), as well as tau, A β (Amyloid beta), and TDP-43, where its scientific understanding of disease pathology can be leveraged.

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, 2018, the Company had an accumulated deficit of \$598.0 million and cash and cash equivalents of \$427.7 million.

Based on the Company's business plans, management believes that the Company’s cash and cash equivalents at December 31, 2018 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 Celgene, 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.

The Company is subject to a number of risks, including but not limited to: the uncertainty of the Company’s research and development (“R&D”) efforts resulting in future successful commercial products; obtaining regulatory approval for its product candidates; its ability to successfully commercialize its product candidates, if approved; significant competition from larger organizations; reliance on the proprietary technology of others; dependence on key personnel; uncertain patent protection; dependence on corporate partners and collaborators; and possible restrictions on reimbursement from governmental agencies and healthcare organizations, as well as other changes in the healthcare industry.

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. 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.

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 and research and development expenses. The Company bases its estimates on historical experience and on various other market specific and other relevant assumptions that management believes to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from

other sources. Because of the uncertainties inherent in such estimates, actual results may differ materially from these estimates.

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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, 2018, the Company had \$4.1 million of restricted cash held by a bank in a certificate of deposit as collateral to a standby letter of credit under a build-to-suit lease. This amount is classified as a non-current asset in the Company's Consolidated Balance Sheet. See Note 6 to the Consolidated Financial Statements regarding "Build-to-Suit Lease" for more information.

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
Build-to-suit property	30 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.

On October 30, 2018, the Company entered into a surrender agreement for its office space in Dún Laoghaire, Ireland. The Company paid €270,000, or \$309,000 as converted using an exchange rate as of November 28, 2018, as full and final settlement of outstanding contractual obligations of \$1.6 million in exchange for surrender and assignment to the landlord including surrender of approximately \$0.5 million of long-lived assets. There were no impairment charges recorded during the years ended December 31, 2017 and 2016.

Leases

At the inception of a lease, the Company evaluates the lease agreement to determine whether the lease is an operating, capital or build-to-suit lease using the criteria in ASC 840, Leases.

Certain lease agreements also require the Company to make additional payments for taxes, insurance, and other operating expenses incurred during the lease period, which are expensed as incurred.

Operating Leases

For operating leases, the Company recognizes rent expense on a straight-line basis over the lease term and records the difference between cash rent payments and the recognition of rent expense as a deferred liability. Where lease agreements contain rent escalation clauses, rent abatements and/or concessions, such as rent holidays, the Company applies them on a straight-line basis over the lease term. Tenant improvement allowances are recorded as a deferred rent liability and are amortized over the term of the lease as a reduction to rent expense.

Build-to-Suit Leases

In certain lease arrangements, the Company is involved in the construction of the building. To the extent the Company is involved with the structural improvements of the construction project or takes construction risk prior to the commencement of a lease, ASC 840-40, Leases – Sale-Leaseback Transactions (Subsection 05-5), requires the Company to be considered the owner for accounting purposes of these types of projects during the construction period. Therefore, the Company records an asset in property and equipment, net on the Consolidated Balance Sheets, including capitalized interest costs, for the replacement cost of the pre-existing building plus the amount of estimated construction costs and tenant improvements incurred by the landlord and the Company as of the balance sheet date. The Company records a corresponding build-to-suit lease obligation on its Consolidated Balance Sheets representing the amounts paid by the lessor.

Once construction is completed, the Company considers the requirements for sale-leaseback accounting treatment, including evaluating whether all risks of ownership have been transferred back to the landlord, as evidenced by a lack of continuing involvement in the leased property. If the arrangement does not qualify for sale-leaseback accounting treatment, the building asset remains on the Company's Consolidated Balance Sheets at its historical cost, and such asset is depreciated over its estimated useful life. The Company bifurcates its lease payments into a portion allocated to the building and a portion allocated to the parcel of land on which the building has been built. The portion of the lease payments allocated to the land is treated for accounting purposes as operating lease payments, and therefore is recorded as rent expense in the Consolidated Statements of Operations. The portion of the lease payments allocated to the building is further bifurcated into a portion allocated to interest expense and a portion allocated to reduce the build-to-suit lease obligation. The interest rate used for the build-to-suit lease obligation represents the Company's estimated incremental borrowing rate at inception of the lease, adjusted to reduce any built in loss. The initial recording of these assets and liabilities is classified as non-cash investing and financing items, respectively, for purposes of the Consolidated Statements of Cash Flows.

Revenue Recognition

Revenue is recognized only when the Company satisfies an identified performance obligation by transferring a promised good or service to a customer.

Contracts with Multiple Performance Obligations

The Company's License Agreement with Roche contains multiple performance obligations. 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 Roche and Roche's 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.

The Company does not disclose the value of unsatisfied performance obligations for (i) contracts with an original expected length of one year or less and (ii) contracts for which the Company recognize revenue at the amount to which the Company has the right to invoice for services performed.

Collaboration Revenue

Upon adoption of ASC 606, the Company recognizes research and development reimbursements as collaboration revenue earned over time as services are performed. Prior to adoption of ASC 606, the Company recorded research reimbursement as collaboration revenue and development reimbursement as an offset to R&D expense once the license revenue cap was met.

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.

In general, 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, 2018, 2017 and 2016.

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, 2018, the Company does not have such costs capitalized in its Consolidated Balance Sheet.

Research and Development

Research and development costs are expensed as incurred and include, but are not limited to, salary and benefits, share-based compensation, clinical trial activities, drug development and manufacturing prior to FDA and other regulatory approval and third-party service fees, including clinical research organizations and investigative sites. Costs for certain development activities, such as clinical trials, are recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, or information provided to the Company by its vendors on their actual costs incurred. The objective of the Company's accrual policy is to match the recording of the expenses in its Consolidated Financial Statements to the actual services received and efforts expended. As such, expense accruals related to clinical trials are recognized based on its estimate of the degree of completion of the events specified in the specific clinical study or trial contract. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the Consolidated Financial Statements as prepaid or accrued research and development. 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.

Restructuring Charges

The Company recognizes restructuring charges related to its reorganization plan. In connection with these activities, the Company records restructuring charges for contractual employee termination benefits, one-time employee termination benefits and contract termination costs. The Company accounts for its restructuring charges as a liability when the obligations are incurred and records such charges at fair value.

The recognition of restructuring charges requires the Company to make certain judgments and estimates regarding the nature, timing and amount of costs associated with the planned reorganization plan. To the extent the Company's actual results differ from its estimates and assumptions, the Company may be required to revise the estimates of future liabilities, requiring the recognition of additional restructuring charges or the reduction of liabilities already recognized. Such changes to previously estimated amounts may be material to the Consolidated Financial Statements. Changes in the estimates of the restructuring charges are recorded in the period the change is determined.

At the end of each reporting period, the Company evaluates the remaining accrued balances to ensure that no excess accruals are retained and the utilization of the provisions are for their intended purpose in accordance with developed restructuring plans. See Note 12, "Restructuring" for additional information regarding restructuring charges.

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 accounting policy for legal costs related to loss contingencies is to accrue for the probable fees that can be reasonably estimated. The Company's accounting policy for uncertain recoveries is to recognize the anticipated recovery when realization is deemed probable.

Share-based Compensation

To determine the fair value of share-based payment awards, 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. Share-based compensation expense is recognized on a straight-line basis over the requisite service period for each award. 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. 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. Through December 31, 2017, the expected volatility was based on a combination of historical volatility for the Company's stock and the historical volatilities of several of the Company's publicly traded comparable companies. 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 10 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, projected future taxable income, tax planning strategies and recent financial operations.

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 and changes in overall levels of income before 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 computed by dividing net income (loss) attributable to ordinary shareholders by the weighted average number of ordinary shares outstanding during the period. Diluted net income per ordinary share is computed by giving effect to all dilutive potential ordinary shares including options. 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. In this case, diluted net loss per share is equal to basic net loss per share.

Comprehensive Loss

Comprehensive income (loss) is comprised of net income (loss) and other comprehensive income (loss). The Company has no components of other comprehensive income (loss). Therefore net income (loss) equals comprehensive income (loss) for all periods presented and, accordingly, the Consolidated Statements of Comprehensive Income (Loss) is not presented in a separate statement.

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 and accounts receivable. The Company places its cash equivalents with high credit quality financial institutions and by policy, limits the amount of credit exposure with any one financial institution. Deposits held with banks 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 receivable from Roche are amounts due from Roche entities located in the U.S. and Switzerland under the License Agreement that became effective January 22, 2014. Revenue recorded in the Consolidated Statements of Operations consists of reimbursement from Roche for research and development services. The Company's credit risk exposure is up to the extent recorded on the Company's Consolidated Balance Sheet.

As of December 31, 2018, \$52.8 million of the Company's long-lived assets were held in the U.S. and none were in Ireland. As of December 31, 2017, \$54.4 million of the Company's long-lived assets were held in the U.S. and \$0.6 million 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 pre-clinical 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

In February 2016, the FASB issued Accounting Standards Update 2016-02 Topic 842, Leases (ASC 842), which will require lessees to recognize assets and liabilities for leases with lease terms of more than 12 months. Consistent with current GAAP, the recognition, measurement, and presentation of expenses and cash flows arising from a lease by a lessee primarily will depend on its classification as a finance or operating lease. However, unlike current GAAP, which requires only capital leases to be recognized on the balance sheet, the new guidance will require both types of leases to be recognized on the balance sheet. ASC 842 is effective for annual periods beginning after December 15, 2018, and interim periods within those years. Early adoption is permitted for all entities. The standard requires that entities use a modified retrospective approach for leases that exist or are entered into after the beginning of the earliest comparative period in the financial statements. Entities have the option to use certain relief. Full retrospective application is prohibited. The FASB approved an amendment to ASC 842 in March 2018 permitting a company to use the effective date as the date of initial application on transition. Note 7, "Commitments and Contingencies" and Note 6, "Build-to-Suit Lease" provide details on the Company's current lease arrangements. The Company expects to adopt the new standard on January 1, 2019 and use the effective date as our date of initial application. Consequently, financial information will not be updated and the disclosure required under the new standard will not be provided for dates and periods before January 1, 2019. The new standard provides a number of optional practical expedients in transition. The Company expects to elect the "package of practical expedients", which permits the Company not to reassess under the new standard its prior conclusions about lease identification, lease classification and initial direct cost. The Company does not expect to elect the use-of-hindsight or the practical expedient pertaining to land easements; the

latter not being applicable to the Company. The Company expects that this standard will have a material effect on the Consolidated Financial Statements. While the Company continues to assess all the effects of adoption, the Company currently believes the most significant effects relate to (1) a change in classification of build-to-suit lease for the Company's current office in South San Francisco, California to an operating lease and as a result the Company expects to derecognize its build-to-suit asset of \$47.9 million and related liability of \$51.5 million, and (2) the recognition of right-of-use assets of \$28.5 million and lease liabilities of \$27.7 million on the consolidated balance sheet for the Company's operating leases. The Company does not expect a significant change in our leasing activities between now and adoption.

In December 2017, the SEC staff issued Staff Accounting Bulletin (“SAB”) 118, Income Tax Accounting Implications of the Tax Cuts and Jobs Act (the “TCJA”), to provide guidance for companies that are not able to complete their accounting for the income tax effects of the Act in the period of enactment. In doing so, the SEC staff acknowledged the challenges companies may face in accounting for the effects of the Act by their financial reporting deadlines and said the guidance is intended to help companies provide investors with timely, decision-useful information. The TCJA was effective in the first quarter of 2018 and, among other things, lowered the Company’s U.S. federal income tax rate from 34% to 21%. The Company recorded a provisional tax benefit of \$0.4 million during the year ended December 31, 2017 related to the remeasurement of its U.S. deferred tax assets to reflect the lower statutory tax rate. As of December 31, 2018, the Company has completed its accounting for the tax effects of TCJA and no adjustments were made to the provisional net tax benefit reported as of the year ended December 31, 2017.

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.

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

Level 2 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 \$306.2 million and \$319.7 million in money market funds included in cash and cash equivalents at December 31, 2018 and December 31, 2017, respectively.

4. Composition of Certain Balance Sheet Items

Property and Equipment, net

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

	December 31,	
	2018	2017
Machinery and equipment	\$9,693	\$9,078
Leasehold improvements	98	579
Purchased computer software	1,303	1,316
Build-to-suit property	52,245	51,760
	63,339	62,733
Less: accumulated depreciation and amortization	(10,504)	(7,743)
Property and equipment, net	\$52,835	\$54,990

Depreciation expense was \$3.2 million, \$3.1 million and \$2.4 million for the years ended December 31, 2018, 2017 and 2016, respectively.

Other Current Liabilities

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

	December 31,	
	2018	2017
Payroll and related expenses	\$4,507	\$7,342
Professional services	1,097	438
Deferred rent	44	49
Other	278	1,356
Other current liabilities	\$5,926	\$9,185

5. Net 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, 2018, 2017 and 2016, and therefore diluted net loss per share is equal to basic net loss per share.

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

	Year Ended December 31,		
	2018	2017	2016
Numerator:			
Net loss	\$(155,645)	\$(153,237)	\$(160,108)
Denominator:			
Weighted-average ordinary shares outstanding	39,559	37,654	34,351
Net loss per share:			
Basic and diluted net loss per share	\$(3.93)	\$(4.07)	\$(4.66)

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

	Year Ended		
	December 31,		
	2018	2017	2016
Stock options to purchase ordinary shares	6,727	4,407	4,064

6. Build-to-Suit Lease

In March 2016, the Company entered into a noncancelable operating sublease (the "Lease") to lease 128,751 square feet of office and laboratory space in South San Francisco, California, U.S. (the "Current SSF Facility"). Subsequently, in April 2016, the Company took possession of the Current SSF Facility. The Lease includes a free rent period and escalating rent payments and has a term that expires on December 31, 2023, unless terminated earlier. The Company's obligation to pay rent commenced on August 1, 2016. The Company is obligated to make lease payments totaling approximately \$39.2 million over the lease term. The Lease further provides that the Company is obligated to pay to the sublandlord and master landlord certain costs, including taxes and operating expenses. Expected future lease payments under the build-to-suit lease as of December 31, 2018 are included in Note 7, "Commitments and Contingencies."

In connection with this Lease, the Company received a tenant improvement allowance of \$14.2 million from the sublandlord and the master landlord, for the costs associated with the design, development and construction of tenant improvements for the Current SSF Facility. The Company is obligated to fund all costs incurred in excess of the tenant improvement allowance. The scope of the tenant improvements did not qualify as "normal tenant improvements" under the lease accounting guidance.

Accordingly, for accounting purposes, the Company is the deemed owner of the building during the construction period and the Company capitalized \$36.5 million within property and equipment, net, including \$1.2 million for capitalized interest and recognized a corresponding build-to-suit obligation in other non-current liabilities in the Consolidated Balance Sheets as of December 31, 2018. The Company has also recognized structural and non-structural tenant improvements totaling \$15.8 million as of December 31, 2018 as an addition to the build-to-suit lease property for amounts incurred by the Company during the construction period, of which \$14.2 million were reimbursed by the landlord during the year ended December 31, 2016 through the tenant improvement allowance. The Company increased its financing obligation for the additional building costs reimbursements received from the landlord during the construction period. In addition, for the years ended December 31, 2018, 2017 and 2016, respectively, the Company recorded rent expense associated with the ground lease of \$0.5 million, \$0.5 million and \$0.4 million, respectively, in its Consolidated Statements of Operations. Total interest, which represents the cost of financing obligation under the Lease agreement, was \$3.7 million, \$3.7 million and \$2.0 million for the years ended December 31, 2018, 2017 and 2016, respectively, of which \$3.7 million, \$3.7 million and \$0.9 million, respectively, was recognized within the Consolidated Statement of Operations.

During the fourth quarter of 2016, construction on the build-to-suit lease property was substantially completed and the build-to-suit lease property was placed in service. As such, the Company evaluated the Lease to determine whether it had met the requirements for sale-leaseback accounting, including evaluating whether all risks of ownership have been transferred back to the landlord, as evidenced by a lack of continuing involvement in the build-to-suit lease property. The Company determined that the construction project did not qualify for sale-leaseback accounting and will instead be accounted for as a financing lease, given the Company's expected continuing involvement after the conclusion of the construction period. The build-to-suit lease property remains on the Company's Consolidated Balance Sheets as of December 31, 2018 at its historical cost of \$52.3 million and is being depreciated over its estimated useful life. As of December 31, 2018, the total amount of the build-to-suit lease obligation was \$51.5 million, of which \$1.6 million and \$49.9 million were classified as current and non-current liability, respectively, on the Company's Consolidated Balance Sheets. The Company expects to derecognize the build-to-suit lease property and financing lease obligation upon the adoption of ASC 842.

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. As of December 31, 2018, none of the standby letter of credit amount has been used.

7. Commitments and Contingencies

Lease Commitments

The Company recognizes rent expense for its operating leases on a straight-line basis over the noncancelable lease term and records the difference between cash rent payments and the recognition of rent expense as a deferred rent liability. Where leases contain escalation clauses, rent abatements and/or concessions, such as rent holidays and landlord or tenant incentives or allowances, the Company applies them in the determination of straight-line rent expense over the lease term. The Company records the tenant improvement allowance for operating leases as deferred rent and associated expenditures as leasehold improvements that are being amortized over the shorter of their estimated useful life or the term of the lease. Rent expense was \$0.7 million, \$0.9 million and \$2.2 million for the years ended December 31, 2018, 2017 and 2016, respectively.

Dublin

In August 2015, the Company entered into an agreement to lease 6,258 square feet of office space in Dún Laoghaire, Ireland. This lease had a term of 10 years from commencement and provides for an option to terminate the lease at the end of the fifth year of the term. It was also subject to a rent review every five years. On October 30, 2018, the

Company entered into a surrender agreement for this office space in Dún Laoghaire, Ireland. The Company paid €270,000, or \$309,000 as converted using an exchange rate as of November 28, 2018, as full and final settlement of outstanding contractual obligations of \$1.6 million in exchange for surrender and assignment to the landlord including surrender of approximately \$0.5 million of long-lived assets.

In September 2018, the Company entered into an agreement to lease 133 square feet of office space in Dublin, Ireland. The lease term expires on November 30, 2019. As of December 31, 2018, the Company is obligated to make lease payments over the term of the lease of approximately €22,000, or \$25,000 as converted using an exchange rate as of December 31, 2018.

Future minimum payments under the above-described noncancelable operating leases as of December 31, 2018 are as follows (in thousands):

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Year Ended December 31,	Operating Lease
2019	\$ 23
2020	—
2021	—
2022	—
2023	—
Total	\$ 23

Current SSF Facility

In March 2016, the Company entered into a noncancelable operating sublease (the “Lease”) of the Current SSF Facility which expires in December 31, 2023. The Company is considered the “accounting owner” of the Current SSF Facility as a build-to-suit property and has recorded a build-to-suit lease obligation on its consolidated balance sheet. Additional information regarding the build-to-suit lease is included in Note 6, “Build-To-Suit Lease.”

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”) for Sub-Subtenant to sub-sublease from the Company approximately 46,641 square feet of office and laboratory space of the Company’s Current SSF Facility.

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 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 Master Lease or the Sublease 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.

Future minimum payments under build-to-suit lease obligation and future minimum rentals to be received under the Sub-Sublease as of December 31, 2018 are as follows (in thousands):

Year Ended December 31,	Expected Cash Payments Under Build-To-Suit Lease Obligation	Sub-Sublease Rental
2019	\$ 5,803	\$ 2,746
2020	5,979	2,843
2021	6,165	2,944

2022	6,350	3,047
2023	6,535	3,019
Total	\$ 30,832	\$ 14,599

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, 2018 and December 31, 2017.

Other Commitments

In April 2018, the Company decided to discontinue all development of NEOD001. The commitments table below includes the obligations under the Company's restructuring plan following the discontinuation of the NEOD001 program.

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, 2018, the Company had non-cancelable purchase commitments to suppliers for \$1.2 million of which \$1.0 million is included in accrued current liabilities, and contractual obligations under license agreements of \$1.3 million of which \$0.2 million 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, 2018 (in thousands):

	Total	2019	2020	2021	2022	2023	Thereafter
Purchase Obligations ⁽¹⁾	\$1,218	\$1,218	\$ —	\$ —	\$ —	\$ —	\$ —
Contractual obligations under license agreements ⁽²⁾	1,300	415	95	95	80	80	535
Obligations under restructuring plan	461	461	—	—	—	—	—
Total	\$2,979	\$2,094	\$ 95	\$ 95	\$ 80	\$ 80	\$ 535

⁽¹⁾ Purchase obligations consist of non-cancelable purchase commitments to suppliers.

⁽²⁾ Excludes future obligations pursuant to the cost-sharing arrangement under the Company's License Agreement with Roche. Amounts of such obligations, if any, cannot be determined at this time.

On July 16, 2018, a purported class action lawsuit entitled Granite Point Capital v. Prothena Corporation plc, et al., Civil Action No. 18-cv-06425, was filed in the U.S. District Court for the Southern District of New York against the Company and certain of its current and former officers. The plaintiff seeks compensatory damages, costs and expenses in an unspecified amount on behalf of a putative class of persons who purchased the Company's ordinary shares between October 15, 2015 and April 20, 2018, inclusive. The complaint alleges that the defendants violated federal securities laws by allegedly making false and misleading statements and omitting certain material facts in certain public statements and in the Company's filings with the U.S. Securities and Exchange Commission during the putative class period, regarding the clinical trial results and prospects for approval of the Company's NEOD001 drug development program. On October 31, 2018, the Court issued an order naming Granite Point Capital and Simon James, an individual, as the lead plaintiffs in the purported class action, which is now entitled In re Prothena Corporation plc Securities Litigation. Because the Company is in the early stages of this proceeding, the Company is not able to estimate a reasonably possible loss or range of loss, if any, that could result from the proceeding.

8. 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 (PRX002/RG7935), 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; and 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.

For prasinezumab, Roche is also obligated to pay:

- up to \$350.0 million upon the achievement of development, regulatory and various first commercial sales milestones;
- up to an additional \$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 on ex-U.S. annual net sales, subject to certain adjustments.

Roche bears 100% of the cost of conducting the research activities under the License Agreement. In the U.S., the parties share all development and commercialization costs, as well as profits, all of which will be allocated 70% to Roche and 30% to the Company, for PRX002/RG7935 in the Parkinson's disease indication, as well as any other Licensed Products and/or indications for which the Company opts in to participate in co-development and co-funding. After the completion of specific clinical trial activities, the Company may opt out of the co-development and cost and profit sharing on any co-developed Licensed Products and instead receive U.S. commercial sales milestones totaling up to \$155.0 million and tiered, single-digit to high double-digit royalties in the teens based on U.S. annual net sales, subject to certain adjustments, with respect to the applicable Licensed Product.

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 study, 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.

While Roche will record product revenue from sales of the Licensed Products, the Company and Roche will share in the net profits and losses of sales of the PRX002/RG7935 for the Parkinson's disease indication in the U.S. on a 70%/30% basis with the Company receiving 30% of the profit and losses provided that the Company has not exercised its opt-out right.

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 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.

Adoption of ASC 606, Revenue from Contracts with Customers

The Company adopted ASC 606, Revenue from Contracts with Customers, as of January 1, 2018 using the modified retrospective transition method. The Company recognized the cumulative effect of applying the new revenue standard as an adjustment to the opening balance of the accumulated deficit as of January 1, 2018. Prior period amounts are not adjusted and continue to be reported in accordance with the Company's historical accounting under ASC 605, Revenue Recognition.

As of January 1, 2018, the Company did not record any changes to the opening balance of the accumulated deficit since the cumulative effect of applying the new revenue standard was the same as applying ASC 605. The impact of the adoption of ASC 606 to revenues for the year ended December 31, 2018 was an increase of \$1.0 million, which represents the revenue recognized for the development services provided by the Company during the period that is reimbursable by Roche. Historically, the Company recorded such reimbursement as an offset against its R&D expenses under ASC 605. Upon the adoption of ASC 606, the reimbursement for development services is now included as part of the Company's collaboration revenue.

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 β -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 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, 2018 and 2017, 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.

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 include, among other things, estimated selling price of the license and costs for clinical supply and development costs.

The initial transaction price under the License Agreement, pursuant to ASC 606, was \$55.1 million, including \$45.0 million for the Royalty Bearing License, \$9.1 million for the IND and Development Services Obligations, and \$1.1 million for the Supply Services Obligation. The \$45.0 million for the Royalty Bearing License included the upfront payment of \$30.0 million and the clinical milestone payment of \$15.0 million upon initiation of the Phase 1 clinical trial of prasinezumab, both of which were made in 2014. The remaining transaction price amounts the Company expected to receive as reimbursements were based on costs expected to be paid to third parties and other costs to be incurred by the Company in order to satisfy its performance obligations. They are considered to be variable considerations not subject to constraint. The Company did not incur any incremental costs, such as commissions, to obtain or fulfill the License Agreement.

Under ASC 606, the transaction price was allocated to the performance obligations as follows: \$48.9 million to the Royalty Bearing License; \$4.6 million to the IND and Development Services Obligations; \$1.1 million to the Clinical Product Supply Obligation; and \$0.6 million to the Supply Services Obligation. As of December 31, 2018, the aggregate amount of the transaction price allocated to the performance obligations that are unsatisfied is \$nil. Prior to the adoption of ASC 606, the transaction price was allocated to the deliverables as follows: \$35.6 million to the Royalty Bearing License; \$3.3 million to the IND and Development Services Obligations; \$0.8 million to the Clinical Product Supply Obligation; and \$0.4 million to the Supply Services Obligation.

The Company allocated the initial transaction price to the Royalty Bearing License and other performance obligations using the relative selling price method based on its best estimate of selling price for the Royalty Bearing License and third party evidence for the remaining performance obligations. The best estimate of selling price for the Royalty Bearing License 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 Royalty Bearing License included the market opportunity for commercialization of PRX002/RG7935 in the U.S. and the royalty territory (for licensed products that are jointly funded the royalty territory is worldwide except for the U.S., and for all licensed products that are not jointly funded the Royalty Territory is worldwide), the probability of successfully developing and commercializing prasinezumab, the estimated remaining development costs for PRX002/RG7935, and the estimated time to commercialization of prasinezumab. The Company concluded that a change in the assumptions used to determine the best estimate of selling price (“BESP”) of the license deliverable would not have a significant effect on the allocation of arrangement consideration.

The Company’s discounted cash flow model included several market conditions and entity-specific inputs, including the likelihood that clinical trials for prasinezumab will be successful, the likelihood that regulatory approval will be obtained and the product commercialized, the appropriate discount rate, the market locations, size and potential market share of the product, the expected life of the product, and the competitive environment for the product. The market assumptions were generated using a patient-based forecasting approach, with key epidemiological, market penetration, dosing, compliance, length of treatment and pricing assumptions derived from primary and secondary market research, referenced from third-party sources.

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.

Optional Goods and Services

An option for additional goods or services exists when a customer has a present contractual right that allows it to choose the amount of additional distinct goods or services that are purchased. Prior to the customer's exercise of that right, the vendor is not presently obligated to provide those goods or services. ASC 606-10-25-18(j) requires recognition of an option as a distinct performance obligation when the option provides a customer with a material right.

In addition to the distinct performance obligations noted above, the Company was obligated to provide indeterminate research services for up to three years ending in 2017 at rates that were not significantly discounted and fully reimbursable by Roche (the “Research Services”). The amount for any such Research Services was not fixed and determinable and was not at a significant incremental discount. There were no refund rights, concessions or performance bonuses to consider.

The Company evaluated the obligation to perform Research Services under ASC 606-10-55-42 and 55-43 to determine whether it gave Roche a “material right”. According to ASC 606-10-55-43, if a customer has the option to acquire an additional good or services at a price that would reflect the standalone selling price for that good or service, that option does not provide the customer with a material right even if the option can be exercised only by entering into a previous contract.

The Company concluded that Roche’s option to have the Company perform Research Services did not represent a “material right” to Roche that it would not have received without entering into the License Agreement. As a result, Roche’s option to acquire additional Research Services was not considered a performance obligation at the outset of the License Agreement under ASC 606. Accordingly, this deliverable will become new performance obligation for Prothena when Roche asks Prothena to conduct such Research Services. As of December 31, 2018, there were no remaining Research Services performance obligations. Prior to the adoption of ASC 606, the Company recognized Research Services as collaboration revenue as earned.

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 and upon the adoption of ASC 606, the Company recognizes the reimbursements for Additional Development Services as collaboration revenue as earned.

Revenue and Expense Recognition

The Company recognized \$1.0 million as collaboration revenue for the year ended December 31, 2018 for Additional Development Services and \$nil for Research Services, as compared to \$0.9 million and \$1.1 million of Research Services as collaboration revenue for the years ended December 31, 2017 and 2016, respectively. The Company recorded \$1.7 million and \$3.6 million of reimbursement for Additional Development Services from Roche for the years ended December 31, 2017 and 2016, respectively, as offset to R&D expenses. Cost sharing payments to Roche are recorded as R&D expenses. The Company recognized \$13.0 million in R&D expenses for payments made to Roche during the year ended December 31, 2018, as compared to \$7.2 million and \$3.1 million for the years ended December 31, 2017 and 2016, 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. In June 2017, the Company achieved a \$30.0 million clinical milestone under the License Agreement as a result of dosing of first patient in Phase 2 study for PRX002. The milestone was accounted for under ASC 605 and was allocated to the units of

accounting based on the relative selling price method for income statement classification purposes. As such, the Company recognized \$26.6 million of the \$30.0 million milestone as collaboration revenue and \$3.4 million as an offset to R&D expenses during the year ended December 31, 2017. The Company did not achieve any clinical and regulatory milestones under the License Agreement during the year ended December 31, 2018.

Celgene Collaboration Agreement

Overview

On March 20, 2018, the Company, through its wholly owned subsidiary Prothena Biosciences Limited, entered into a Master Collaboration Agreement (the “Collaboration Agreement”) with Celgene Switzerland LLC (“Celgene”), a subsidiary of Celgene Corporation, 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, Celgene has an exclusive right to license clinical candidates in the U.S. at the IND filing and if exercised, would also have a right to expand the license to global rights at the completion of Phase 1. Following the exercise for U.S. rights, Celgene would have decision making authority over development activities and all regulatory, manufacturing and commercialization activities in the U.S. The Company would be responsible for certain of those activities through completion of Phase 1 clinical studies of products in each such program, for which Celgene exercises its US Rights unless Celgene elects otherwise to do so at its cost.

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.

Celgene U.S. and Global Rights and Licenses

On a program-by-program basis, following the Company’s filing of an IND application for any of the Company’s three collaboration programs to Celgene, Celgene may elect in its sole discretion to exercise its US Rights to receive an exclusive license to develop and commercialize antibodies targeting the applicable Collaboration Target in the U.S. If Celgene 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 Phase 1, Celgene 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 Celgene has previously exercised its US Rights, Celgene 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 and commercialize antibodies targeting the applicable Collaboration Target. If Celgene exercises its Global Rights, Celgene 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 Celgene would have decision making authority over developing, obtaining and maintaining regulatory approval for, manufacturing and commercializing the Collaboration Products worldwide.

After Celgene’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. For obtaining either US Rights or Global Rights for such collaboration program by Celgene, 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 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.

Celgene 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 Celgene 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 Celgene 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 Celgene challenges a patent licensed by Prothena to Celgene 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, Celgene 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 the 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, Celgene will be entitled to request the registration of the Shares with the U.S. Securities and Exchange Commission 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 (the “Securities Act”).

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 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 concluded that it does not have material distinct performance obligation as the Company is not obligated to transfer the US or Global license to Celgene unless Celgene exercises its US Right or Global Right, 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 therefore are not considered distinct performance obligations under ASC 606. 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. The Company is solely responsible for any and all costs and expenses in connection with the performance, in its discretion, of any program prior to the exercise of the Global Right for such program. 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 Celgene unless Celgene exercises its right to participate in the Phase 1 development.

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.

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 evaluated the potential obligations to transfer the U.S. and global licenses to Celgene under ASC 606-10-55-42 and 55-43 to determine whether it gave Celgene a “material right” and concluded that Celgene’s options to exercise its US Rights or Global Rights represented a “material right” to Celgene that it would not have received without entering into the Collaboration Agreement. However, the obligations to transfer the U.S. and Global licenses to Celgene were not considered performance obligations at the outset of the Collaboration Agreement under ASC 606, and will become performance obligations only if and when Celgene chooses to exercise its options. In addition, the Company did not include the option fees in the initial transaction price because such fees are variable consideration that 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, the Company will have the obligation to deliver the U.S. and global licenses, respectively. The Company will include the option fees in the transaction price at a point in time when the Company can conclude that it is probable that a significant revenue reversal will not occur. In addition, the Company did not include in the initial transaction price certain clinical and regulatory milestone payments since these variable considerations are constrained due to high likelihood of a revenue reversal.

At the inception of the Collaboration Agreement, the Company did not transfer any goods or services to Celgene that are material. Accordingly, the Company has concluded that the initial transaction price will be recognized as contract liability and will be deferred until the Company transfers control of goods or services to Celgene (which would be when Celgene exercises the US Right and receives control of the US license for at least one of the programs) or at the termination of the Collaboration Agreement, whichever occurs first. At such point that the Company transfers control of goods or services to Celgene, the total transaction price will be allocated by first applying the fair value for each program, relative to the other programs, on the assumption that each program processes to the point that Celgene could exercise its US Rights, to arrive at a transaction price per program, and then allocating each such transaction price per program to each of the Company’s performance obligations on a relative standalone selling price basis.

The relative selling price method is based on the Company’s best estimate of the selling price of the respective US or Global licenses for that program. The best estimate of selling price for the US and Global licenses by program 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 US and Global license 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, and the estimated time to commercialization of the drug for that program.

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 Celgene or receipt by Celgene 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 Celgene to the Company is variable 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 Celgene or the Company. Variable considerations related to clinical and regulatory milestone payments and option fees are constrained due to high likelihood of a revenue reversal.

Milestone and Royalties Accounting

Under the Collaboration Agreement, 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.

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 year ended December 31, 2018.

9. Shareholders' Equity

Ordinary Shares

As of December 31, 2018, the Company had 100,000,000 ordinary shares authorized for issuance with a par value of \$0.01 per ordinary share and 39,863,711 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, 2018, 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, 2018. 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.

January 2016 Offering

In January 2016, the Company completed an underwritten public offering of an aggregate of 2,587,500 of its ordinary shares at a public offering price of \$53.00 per ordinary share. The Company received aggregate net proceeds of approximately \$128.6 million, after deducting the underwriting discount and estimated offering costs.

March 2017 Offering

In March 2017, the Company completed an underwritten public offering of an aggregate of 2,700,000 of its ordinary shares at a public offering price of \$57.50 per ordinary share. The Company received aggregate net proceeds of approximately \$150.3 million, after deducting the underwriting discount and offering costs.

Celgene Share Subscription Agreement

In connection with the Celgene 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, of which the fair value of \$39.8 million was recorded in shareholders' equity and the premium of \$10.2 million was recorded as deferred revenue from Celgene.

Under the SSA, Celgene 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 the 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, Celgene 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 Securities Act.

10. Share-Based Compensation

2018 Long Term Incentive Plan ("2018 LTIP")

In May 2018, the Company's shareholders approved the 2018 Long Term Incentive Plan (the "2018 LTIP"), which provides for the grant 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 under the 2018 LTIP may be granted for periods up to ten years. All options issued to date have had a ten year life. Under the 2018 LTIP, the number of ordinary shares authorized for issuance under the 2018 LTIP is equal to the sum of (a) 1,800,000 shares, (b) 1,177,933 shares that were available for issuance under the 2012 LTIP as of the May 15, 2018 effective date of the 2018 LTIP, and (c) any shares subject to issued and outstanding awards under the 2012 Long Term Incentive Plan (the "2012 LTIP") that expire, are cancelled or otherwise terminate following the effective date of

the 2018 LTIP; provided, that no more than 2,500,000 shares may be issued pursuant to the exercise of ISOs.

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Amended and Restated 2012 Long Term Incentive Plan

Prior to the effective date of the 2018 LTIP, employees and consultants of the Company, its subsidiaries and affiliates, as well as members of the Company's Board of Directors, received equity awards under the 2012 LTIP. Options under the 2012 LTIP were granted for periods up to ten years. All options issued to date have had a ten year life.

Shares Available for Grant

The Company granted 4,140,800, 1,566,800 and 1,508,725 options during the year ended December 31, 2018, 2017 and 2016, respectively, in aggregate under the 2012 LTIP and the 2018 LTIP. The Company's option awards generally vest over four years. As of December 31, 2018, 1,535,371 ordinary shares remained available for grant under the 2018 LTIP, and options to purchase 6,726,715 ordinary shares in aggregate under the 2012 LTIP and the 2018 LTIP were outstanding with a weighted-average exercise price of approximately \$26.82 per share.

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. Since the Company does not have sufficient historical employee share option exercise data, 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. Through December 31, 2017, the expected volatility was based on a combination of historical volatility for the Company's stock and the historical volatilities of several of the Company's publicly traded comparable companies due to insufficient historical employee share option exercise data. 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.

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 2022 related to unvested share-based payment awards at December 31, 2018 is \$58.3 million. The weighted-average period over which the unearned share-based compensation is expected to be recognized is 3.12 years. If there are any modifications or cancellations of the underlying unvested securities, the Company may be required to accelerate and/or increase any remaining unearned share-based compensation expense. Future share-based compensation expense and unearned share-based compensation will increase to the extent that the Company grants additional equity awards.

Share-based compensation expense recorded in these Consolidated Financial Statements for the years ended December 31, 2018, 2017 and 2016 was based on awards granted under the 2012 LTIP and the 2018 LTIP. The following table summarizes share-based compensation expense for the periods presented (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Research and development	\$9,830	\$10,914	\$7,094
General and administrative ⁽²⁾	16,232	15,850	17,835
Restructuring costs ⁽¹⁾	948	—	—
Total share-based compensation expense	\$27,010	\$26,764	\$24,929

(1) Restructuring costs for the year ended December 31, 2018 includes \$0.9 million of share-based compensation expense related to the contractual acceleration of vesting of certain stock options granted to executive officers.

Includes \$nil, \$nil and \$6.5 million for the years ended December 31, 2018, 2017 and 2016, respectively, of (2) share-based compensation expense related to the accelerated vesting of stock options to the Company's former CEO upon his death.

For the years ended December 31, 2018, 2017 and 2016, the Company recognized tax benefits from share-based awards of \$4.7 million, \$4.2 million and \$4.3 million, respectively.

The fair value of the options granted to employees and non-employee directors during the years ended December 31, 2018, 2017 and 2016 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,		
	2018	2017	2016
Expected volatility	79.5%	72.4%	75.2%
Risk-free interest rate	2.8%	2.0%	1.5%
Expected dividend yield	—%	—%	—%
Expected life (in years)	6.0	6.0	6.0
Weighted average grant date fair value	\$13.70	\$35.71	\$26.41

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, 2018:

	Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2017	4,406,752	\$ 38.93	7.60	\$ 30,455
Granted	4,140,800	20.20		
Exercised	(206,411)	22.70		
Canceled	(1,614,426)	43.42		
Outstanding at December 31, 2018	6,726,715	\$ 26.82	7.39	\$ 2,169
Vested and expected to vest at December 31, 2018	6,213,727	\$ 27.26	7.26	\$ 2,169
Vested at December 31, 2018	2,516,207	\$ 32.47	5.21	\$ 2,169

The total intrinsic value of options exercised was \$2.4 million, \$39.9 million and \$12.8 million during the years ended December 31, 2018, 2017 and 2016, respectively, determined as of the date of exercise.

The following table summarizes information about the Company's options outstanding as of December 31, 2018:

Range of Exercise Prices	Options Outstanding				Options Exercisable		
	Number of Options	Weighted - Average Contractual Life (Years)	Weighted Average Exercise Price	Number of Options	Weighted Average Exercise Price		
\$6.41 \$13.05	666,565	4.84	\$ 7.29	572,065	\$ 6.51		
15.04 15.04	2,605,200	8.99	15.04	—	—		
16.42 29.81	807,356	5.66	25.95	671,213	27.44		
33.06 33.06	2,500	9.16	33.06	—	—		
33.10 33.10	718,400	8.29	33.10	15,000	33.10		
34.04 42.50	716,345	6.73	35.78	525,616	36.08		
43.40 55.00	951,955	6.37	53.02	536,948	52.76		
55.15 62.10	172,144	7.35	56.60	129,195	56.73		
63.27 63.27	25,000	8.75	63.27	7,291	63.27		
67.64 67.64	61,250	1.82	67.64	58,879	67.64		
\$6.41 \$67.64	6,726,715	7.39	\$ 26.82	2,516,207	\$ 32.47		

11. 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,		
	2018	2017	2016
Ireland	\$(163,653)	\$(162,865)	\$(164,797)
Switzerland	384	480	—
U.S.	7,154	4,782	5,833
Loss before provision for income taxes	\$(156,115)	\$(157,603)	\$(158,964)

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

	Year Ended December 31,		
	2018	2017	2016
Current:			
U.S. Federal	\$1,320	\$(2,478)	\$4,464
U.S. State	1	1	1
Switzerland	(197)	306	—
Ireland	(5)	5	—
Total current provision	\$1,119	\$(2,166)	\$4,465
Deferred:			
U.S. Federal	\$(1,589)	\$(2,200)	\$(3,321)
U.S. State	—	—	—
Switzerland	—	—	—
Ireland	—	—	—
Total deferred benefit	(1,589)	(2,200)	\$(3,321)
Total provision for (benefit from) income taxes	\$(470)	\$(4,366)	\$1,144

The Company adopted ASU 2016-09 on January 1, 2017. Pursuant to the adoption of ASU 2016-09, tax attributes previously tracked off balance sheet have been recorded as deferred tax assets, offset by a valuation allowance. Further, excess benefits of stock compensation have been recorded as a benefit to the tax provision for all periods presented. For the year ended December 31, 2018, the Company recorded a net tax shortfall of \$1.7 million as compared to excess tax benefits of \$5.3 million for the year ended December 31, 2017 all of which were recorded as part of its income tax provision in the Consolidated Statements of Operations. The Company's income tax expense will continue to be impacted by fluctuations in stock price between the grant dates and the exercise dates of its option awards.

The provision for income taxes differs from the statutory tax rate of 12.5% applicable to Ireland primarily due to Irish net operating losses for which a tax provision benefit is not recognized, U.S. income taxed at different rates, and excess tax benefits from stock options. 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):

	Years Ended December 31,		
	2018	2017	2016
Taxes at the Irish statutory tax rate of 12.5%	\$(19,514)	\$(19,700)	\$(19,870)
Income tax at rates other than applicable statutory rate	(458)	678	813
Change in valuation allowance	26,747	28,967	25,200
Share-based payments	2,215	(8,242)	422
Tax credits	(10,351)	(5,857)	(5,384)
Other	891	(212)	(37)
Provision for (benefit from) income taxes	\$(470)	\$(4,366)	\$1,144

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.

On December 22, 2017, the U.S. Tax Cuts and Jobs Act (the "TCJA") was signed into law. It contains many significant changes to the U.S. income tax laws. The TCJA was effective in the first quarter of 2018 and, among other things, lowered the Company's U.S. federal income tax rate from 34% to 21%. The Company recorded a provisional tax benefit of \$0.4 million during the year ended December 31, 2017 related to the remeasurement of its U.S. deferred tax assets to reflect the lower statutory tax rate. As of December 31, 2018, the Company has completed its accounting for the tax effects of TCJA and no adjustments were made to the provisional net tax benefit reported as of the year ended December 31, 2017.

Due to the repeal of alternative minimum taxes, the Company anticipates that its future U.S. taxes will decrease due to its ability to use additional tax credits previously limited by the alternative minimum tax. However, the Company also expects an increase to its taxable income due to additional limitations imposed by the TCJA on the deductibility of compensation of certain of its executive officers.

Significant components of the Company's net deferred tax assets as of December 31, 2018 and 2017 are as follows (in thousands):

	December 31,	
	2018	2017
Deferred tax assets:		
Net operating losses	\$88,626	\$67,653
Tax credits	22,339	16,308
Accruals	1,521	1,285
Share-based compensation	9,322	7,444
Gross deferred tax assets	121,808	92,690
Valuation allowance	(111,429)	(83,972)
Net deferred tax assets	10,379	8,718
Deferred tax liability:		
Fixed Assets	(677)	(605)
Net deferred tax assets	\$9,702	\$8,113

The Company's deferred tax assets are composed primarily of its Irish subsidiaries' net operating loss carryovers, state net operating loss carryforwards available to reduce future taxable income of the Company's U.S. subsidiary, federal and state tax credit carryforwards, share-based compensation 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. 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 the deferred tax assets will be fully realizable. Accordingly, the Company has provided a valuation allowance of \$111.4 million against its deferred tax assets as of December 31, 2018 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, \$9.7 million as of December 31, 2018, consist of U.S. federal temporary differences. Due to consistent U.S. operating income, the Company expects to realize such deferred tax assets. The net increase of \$27.5 million in the valuation allowance during the year ended December 31, 2018 was primarily due to net operating losses of the Company and its Irish entities, and to a lesser extent from U.S. federal and state tax credits.

As of December 31, 2018, certain of the Company's Irish entities had trading loss carryovers of \$652.1 million and non-trading loss carryovers of \$11.6 million, each of which can be carried forward indefinitely but are limited to the same trade/trades. In addition, as of December 31, 2018, the Company had state net operating loss carryforwards of approximately \$47.6 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 \$18.7 million and \$10.5 million, respectively, at December 31, 2018. The federal research and development credit carryforwards will expire starting in 2035 if not utilized. The California tax credits can be carried forward indefinitely.

Cumulative unremitted earnings of the Company's U.S. and Swiss subsidiaries total approximately \$32.2 million and \$0.8 million, respectively, at December 31, 2018. The Company's U.S. subsidiary's cash balances at December 31, 2018 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. and Swiss subsidiaries. The Company considers the U.S. earnings to be indefinitely reinvested. The Company expects to distribute the remaining cash from its Swiss subsidiary to its Irish parent in 2019 however, the Company considers any potential tax associated with the distribution of Swiss earnings to be insignificant. Unremitted earnings may be subject to withholding taxes (potentially at 5% in the U.S. and 5% in Switzerland) and Irish taxes (potentially at a rate of 12.5%) if they were to be distributed as dividends. However, Ireland allows a credit against Irish taxes for U.S. and Swiss taxes withheld, and as of December 31, 2018 the Company's current year net operating losses in Ireland are sufficient to offset any potential dividend income received from its overseas subsidiaries.

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

	2018	2017
Gross Unrecognized Tax Benefits at January 1	\$4,268	\$2,406
Additions for tax positions taken in the current year	2,589	1,464
Additions for tax positions taken in the prior year	32	398
Reductions for tax positions taken in the prior year	(34)	—
Gross Unrecognized Tax Benefits at December 31	\$6,855	\$4,268

If recognized, none of the Company's unrecognized tax benefits as of December 31, 2018 would reduce its annual effective tax rate, primarily due to corresponding adjustments to its deferred tax valuation allowance. As of December 31, 2018, 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 2018 remain subject to examination by the U.S. taxing authorities and the tax years 2013 to 2018 remain subject to examination by the Irish taxing authorities.

12. Restructuring

In May 2018, the Company commenced a reorganization plan to reduce its operating costs and better align its workforce with the needs of its business following the Company's April 23, 2018 announcement of its decision to discontinue further

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development of NEOD001.

The Company incurred aggregate restructuring and impairment charges of approximately \$16.1 million for the year ended December 31, 2018. Restructuring charges incurred under this plan primarily consisted of employee termination benefits and contract termination costs primarily associated with exit fees relating to third-party manufacturers that we contracted with for NEOD001 clinical and commercial supplies. Employee termination benefits include severance costs, employee-related benefits, supplemental one-time termination payments and non-cash share-based compensation expense related to the acceleration of stock options. Charges and other costs related to the workforce reduction and structure realignment are presented as restructuring costs in the Consolidated Statements of Operations. Substantially all of the cash payments are expected to be paid out by the end of the first quarter of 2019. The Company may also incur additional costs not currently contemplated due to events that may occur as a result of, or that are associated with, the restructuring.

The following table summarizes the restructuring liability and utilization by cost type associated with the restructuring activities during the year ended December 31, 2018 (in thousands):

	Restructuring Liability					Total
	Termination Benefits	Contract Termination Costs	Assets Impairment (1)	Other(2)		
Balance at January 31, 2018	\$—	\$ —	\$ —	\$ —	\$ —	\$ —
Restructuring charges	8,187	5,922	—	613		14,722
Non cash charges	948	(23)	498	—		1,423
Reduction in non cash charges	(948)	23	(498)	—		(1,423)
Reductions for cash payments	(7,716)	(5,655)	—	(613)		(13,984)
Foreign Exchange	(10)	(267)	—	—		(277)
Balance at December 31, 2018	\$461	\$ —	\$ —	\$ —		\$ 461

(1) Includes \$0.5 million of long-lived assets surrendered to the landlord as part of the full and final settlement of our office lease in Dún Laoghaire, Ireland as discussed in Note 7, "Commitments and Contingencies".

(2) Includes \$0.6 million of costs incurred related to the sub-sublease of the Current SSF Facility as discussed in Note 7, "Commitments and Contingencies".

The total amount expected to be incurred in connection with the restructuring plan is \$16.1 million. The cumulative amount incurred to date is \$16.1 million as of December 31, 2018. As of December 31, 2018, the restructuring liability is included in current liabilities on the Consolidated Balance Sheets.

13. 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 \$0.7 million, \$0.7 million and \$0.6 million for the years ended December 31, 2018, 2017 and 2016, respectively.

In Europe, the Company recorded total expense for employer contribution of \$247,000, \$352,000 and \$92,000, in the years ended December 31, 2018, 2017 and 2016, respectively. In Ireland, the Company operates a defined contribution plan in which it contributes up to 7.5% of an employee's eligible earnings. In Switzerland, the Company contributed to an employee pension fund up to 19.0% of an employee's two-third eligible earnings. The percentage paid by the Company in Switzerland depended on the employee's age, gender, and employee classification. In Germany, Belgium and Spain, the Company contributed at a fixed rate of 8.0%, 7.5% and 7.5%, respectively, of an

employee's eligible earnings.

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14. Related Parties

Consulting Agreement

Carol D. Karp commenced employment with the Company as its Chief Regulatory Officer on December 14, 2016. Prior to that, Ms. Karp provided consulting services to the Company under a written Consulting Agreement. That Consulting Agreement terminated as of December 13, 2016, before Ms. Karp joined the Company. There were no consulting fees paid to Ms. Karp for the years ended December 31, 2018 and 2017. During fiscal year 2016 through December 13, 2016, the Company paid to Ms. Karp a total of \$304,150 (not including expense reimbursements) under the Consulting Agreement.

15. Selected Quarterly Financial Information (Unaudited)

The following table presents selected unaudited consolidated financial data for each of the eight quarters in the two-year period ended December 31, 2018. In the Company's opinion, this unaudited information has been prepared on the same basis as the audited information and includes all adjustments (consisting of only normal recurring adjustments) necessary for a fair statement of the financial information for the period presented. Net loss per share - basic and diluted, for the four quarters of each fiscal year may not sum to the total for the fiscal year because of the different number of shares outstanding during each period (in thousands, except per share data):

	Quarter			
	First	Second	Third	Fourth
Year Ended December 31, 2018				
Revenues	\$227	\$279	\$255	\$194
Operating expenses	\$48,935	\$63,348	\$24,578	\$22,949
Net loss	\$(48,743)	\$(59,882)	\$(24,559)	\$(22,461)
Net loss per share - basic	\$(1.26)	\$(1.50)	\$(0.62)	\$(0.56)
Net loss per share - diluted	\$(1.26)	\$(1.50)	\$(0.62)	\$(0.56)
Year Ended December 31, 2017				
Revenues	\$259	\$26,812	\$219	\$229
Operating expenses	\$36,530	\$44,944	\$53,753	\$47,546
Net income (loss)	\$(35,384)	\$(17,701)	\$(52,394)	\$(47,758)
Net income (loss) per share - basic	\$(0.99)	\$(0.46)	\$(1.37)	(1.24)
Net income (loss) per share - diluted	\$(0.99)	\$(0.46)	\$(1.37)	\$(1.24)

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS

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, 2018, 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, 2018, 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, 2018, our internal control over financial reporting was effective. The effectiveness of our internal control over financial reporting as of December 31, 2018 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, 2018 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.

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ITEM 9B. OTHER INFORMATION

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 21, 2019 (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:

Election of Directors

Section 16(a) Beneficial Ownership Reporting Compliance

Executive Officers of the Registrant

Following is certain information regarding our executive officers as of March 11, 2019.

Name	Age	Position(s)	Since
Gene G. Kinney	50	President and Chief Executive Officer, Director	2016
A. W. Homan	59	Chief Legal Officer	2014
		Company Secretary	2018
Carol D. Karp	66	Chief Regulatory Officer	2016
Tran B. Nguyen	45	Chief Financial Officer	2013
		Chief Operating Officer	2018
Radhika Tripuraneni	39	Chief Development Officer	2018
Karin L. Walker	55	Chief Accounting Officer and Controller	2013
Wagner M. Zago	46	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) for Elan Pharmaceuticals, Inc; 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.

A. W. Homan has served as our Chief Legal Officer since 2014 and as Company Secretary since 2018. Prior to joining Prothena, he was Senior Vice President, General Counsel and Secretary of Complete Genomics, Inc. (a laboratory services company), a position he held from 2012 until its sale in 2013. Mr. Homan was Senior Vice President, General Counsel and Secretary of Varian, Inc. (a scientific instruments company), from 1999 until it was acquired in 2010. Prior to that, he was Associate General Counsel at Varian Associates, Inc., and also worked at a leading San Francisco law firm. Mr. Homan earned BA from Virginia Tech and his JD (law degree) from the University of Virginia.

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. (a biotechnology company), 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 (a biopharmaceutical company). Previously, Ms. Karp held senior regulatory positions at Janssen Alzheimer Immunotherapy, 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 a member of the Board of Trustees.

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Tran B. Nguyen has served as our Chief Financial Officer since 2013 and as our Chief Operating Officer since 2018. Prior to joining Prothena in 2013, he was Vice President, Chief Financial Officer (from 2010 to 2011) and then Senior Vice President, Chief Financial Officer of Somaxon Pharmaceuticals, Inc. (a biopharmaceutical company), from 2011 until its sale in 2013. Mr. Nguyen was Vice President, Chief Financial Officer at Metabasis Therapeutics, Inc. (a biopharmaceutical company) 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 on the board of directors of Sierra Oncology, Inc. (a publicly-traded clinical-stage oncology company) and Rain Therapeutics Inc. (a privately-held clinical-stage oncology 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.

Radhika Tripuraneni, M.D., M.P.H., has served as our Chief Development Officer since 2018. Prior to that, she was our Vice President, Medical Affairs and Development Operations. Prior to joining Prothena in 2018, Dr. Tripuraneni was Vice President, Medical Affairs and Chief of Staff to the Chief Medical Officer of MyoKardia Inc. (a biotechnology company), positions she held from 2017 to 2018. From 2012 to 2017, she was Vice President, Medical Affairs at Synageva BioPharma Corp. (a biopharmaceutical company) and then Alexion Pharmaceuticals (a pharmaceutical company), which acquired Synageva in 2015. Dr. Tripuraneni held various medical director positions at Gilead Sciences, Inc. and Genzyme Corporation (both biopharmaceutical companies) from 2007 to 2012, and prior to that worked at Summer Street Research Partners (an equity research firm). She earned her BAs in business and liberal arts and her MD from the University of Missouri, and her Master in Public Health from Harvard University. Dr. Tripuraneni did her clinical training in general surgery at Harvard - Beth Israel Deaconess Medical Center.

Karin L. Walker has served as our Chief Accounting Officer and Controller since 2013. Prior to joining Prothena, she was Vice President, Finance and Chief Accounting Officer of Affymax, Inc. (a biopharmaceutical company), a position she held from 2012 to 2013. From 2009 to 2012, Ms. Walker was Vice President, Finance and Corporate Controller at Amyris Inc. (a biotechnology company). From 2006 to 2009, she was Vice President, Finance and Corporate Controller for CV Therapeutics, Inc. (a biopharmaceutical company). Ms. Walker also held senior financial leadership positions at Knight Ridder Digital, Accellion, Niku Corporation, Financial Engines, Inc. and NeoMagic Corporation. 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 (a biopharmaceutical 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>. 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 T804, 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>.

ITEM 11. EXECUTIVE COMPENSATION

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

Executive Compensation

Director Compensation

Report of the Compensation Committee of the Board of Directors

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:

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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

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

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 - Fees Paid to KPMG

• Proposal No. 2 - Ratification of Appointment of Independent Registered Public Accounting Firm - Pre-Approval Policies and Procedures

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. EXHIBITS, 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	<u>Demerger Agreement, dated as of November 8, 2012, between Elan Corporation, plc and Prothena Corporation plc</u>	10/A	001-35676	11/30/2012	2.1
2.2(a)	<u>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.</u>	8-K	001-35676	12/21/2012	2.1
2.2(b)	<u>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</u>	S-1/A	333-191218	9/30/2013	2.2(b)
2.3	<u>Intellectual Property License and Conveyance Agreement, dated as of December 20, 2012, among Neotope Biosciences Limited, Elan Pharma International Limited and Elan Pharmaceuticals, Inc.</u>	8-K	001-35676	12/21/2012	2.2
3.1	<u>Amended and Restated Memorandum and Articles of Association (Constitution) of Prothena Corporation plc</u>	8-K	001-35676	5/25/2016	3.1
4.1	<u>Amended and Restated Memorandum and Articles of Association (Constitution) of Prothena Corporation plc</u>	8-K	001-35676	5/25/2016	3.1
10.1(a)	<u>Tax Matters Agreement, dated as of December 20, 2012, between Elan Corporation, plc and Prothena Corporation plc</u>	8-K	001-35676	12/21/2012	10.1
10.1(b)	<u>Amendment No. 1 to Tax Matters Agreement, dated as of June 25, 2013, between Elan Corporation, plc and Prothena Corporation plc</u>	10-Q	001-35676	8/13/2013	10.2
10.2	<u>License Agreement, dated as of December 31, 2008, between the University of Tennessee Research Foundation and Elan Pharmaceuticals, Inc.</u>	10/A	001-35676	11/30/2012	10.14
10.3(a)†	<u>License Agreement, dated as of November 4, 2013, between The Regents of the University of California and Neotope Biosciences Limited</u>	10-Q/A	001-35676	8/17/2018	10.1(a)

10.3(b)†	<u>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</u>	10-Q/A 001-35676 8/17/2018	10.1(b)
10.4†	<u>Exclusive License Agreement, dated as of July 25, 2016, between University Health Network and Prothena Biosciences Limited</u>	10-Q/A 001-35676 8/17/2018	10.2
10.5†	<u>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.</u>	10-K/A 001-35676 6/6/2014	10.4
10.6†	<u>Master Collaboration Agreement, dated as of March 20, 2018, between Prothena Biosciences Limited and Celgene Switzerland LLC</u>	10-Q/A 001-35676 8/17/2018	10.3

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Exhibit No.	Description	Previously Filed			Filed Herewith
		Form	File No.	Filing Date	
10.7	<u>Share Subscription Agreement, dated as of March 20, 2018, between Celgene Switzerland LLC and Prothena Corporation plc</u>	10-Q	001-35676	5/9/2018	10.4
10.8†	<u>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</u>	10-Q	001-35676	8/13/2013	10.3
10.9†	<u>Letter Agreement, dated April 5, 2017, among Prothena Therapeutics Limited, Prothena Biosciences Limited and Boehringer Ingelheim Biopharmaceuticals GmbH</u>	10-Q	001-35676	8/9/2017	10.4
10.10†	<u>Commercial Supply Contract, dated as of November 9, 2016, between Prothena Therapeutics Limited and Rentschler Biotechnologie GmbH</u>	10-K	001-35676	2/27/2017	10.6
10.11	<u>Termination and Release Agreement, dated July 20, 2018, between Prothena Biosciences Limited and Rentschler Biopharma SE</u>	10-Q	001-35676	11/6/2018	10.1
10.12(a)	<u>Sublease, dated as of March 22, 2016, between Prothena Biosciences Inc and Amgen Inc.</u>	10-Q	001-35676	5/4/2016	10.2(a)
10.12(b)	<u>Consent to Sublease Agreement, dated as of March 28, 2016, among Prothena Biosciences Inc, Amgen Inc. and HCP BTC, LLC</u>	10-Q	001-35676	5/4/2016	10.2(b)
10.13(a)	<u>Sub-Sublease, dated as of July 18, 2018, between Prothena Biosciences Inc and Assembly Biosciences, Inc.</u>	10-Q	001-35676	11/6/2018	10.2(a)
10.13(b)	<u>Consent to Sub-Sublease, dated as of September 19, 2018, among Prothena Biosciences Inc, Assembly Biosciences, Inc., Amgen Inc. and HCP BTC, LLC</u>	10-Q	001-35676	11/6/2018	10.2(b)
10.14#	<u>Prothena Corporation plc Amended and Restated 2012 Long Term Incentive Plan</u>	8-K	001-35676	5/23/2017	10.1
10.15#	<u>Prothena Corporation plc 2018 Long Term Incentive Plan</u>	8-K	001-35676	5/18/2018	10.1
10.16#	<u>Prothena Corporation plc Amended and Restated Incentive Compensation Plan</u>	10-Q	001-35676	5/9/2017	10.1
10.17#	<u>Prothena Biosciences Inc Amended and Restated Severance Plan</u>	8-K	001-35676	12/15/2015	10.1

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10.18#	<u>Form of Deed of Indemnification between Prothena Corporation plc and its Directors and Officers</u>	8-K	001-35676	12/11/2014	10.1
10.19#	<u>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)</u>	S-8	333-196572	6/6/2014	99.2
10.20#	<u>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)</u>	10-Q	001-35676	8/7/2018	10.2
10.21#	<u>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)</u>	S-8	333-196572	6/6/2014	99.3

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Exhibit No.	Description	Previously Filed		Filed Herewith
		Form	File No. Filing Date	
10.22#	<u>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)</u>	10-K	001-356763/13/2015	10.11
10.23#	<u>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)</u>	10-Q	001-356768/7/2018	10.3
10.24#	<u>Offer letter, dated March 20, 2013, between Prothena Biosciences Inc and Tran B. Nguyen</u>	8-K	001-356763/28/2013	10.1
10.25#	<u>Employment Agreement, dated September 30, 2016, between Prothena Biosciences Inc and Gene G. Kinney</u>	8-K	001-356761/1/4/2016	10.1
10.26#	<u>Offer letter, dated December 14, 2012, between Prothena Biosciences Inc and Tara Nickerson</u>	10-K	001-356763/29/2013	10.20
10.27#	<u>Promotion letter, dated February 5, 2014, between Prothena Biosciences Inc and Tara Nickerson</u>	8-K	001-356763/3/2014	10.1
10.28#	<u>Separation Agreement, dated May 23, 2018, between Prothena Biosciences Inc and Tara Nickerson</u>	10-Q	001-356768/7/2018	10.1
10.29#	<u>Offer letter, dated April 19, 2013, between Prothena Biosciences Inc and Karin L. Walker</u>	8-K	001-356765/22/2013	10.1
10.30#	<u>Offer letter, dated April 11, 2014, between Prothena Biosciences Inc and A. W. Homan</u>	10-Q	001-356768/5/2014	10.5
10.31#	<u>Retirement transition letter, dated December 11, 2018, between Prothena Biosciences Inc and A. W. Homan</u>			X
10.32#	<u>Offer letter, dated December 5, 2016, between Prothena Biosciences Inc and Carol D. Karp</u>	10-K	001-356762/27/2017	10.28
10.33#	<u>Offer letter, dated April 2, 2017, between Prothena Biosciences Inc and Sarah B. Noonberg</u>	10-Q	001-356768/9/2017	10.2
10.34#	<u>Promotion letter, dated June 9, 2017, between Prothena Biosciences Inc and Wagner M. Zago</u>	10-Q	001-356768/9/2017	10.3
10.35#	<u>Promotion letter, dated December 11, 2018, between Prothena Biosciences Inc and Radhika Tripuraneni</u>			X

21.1 List of Subsidiaries X

23.1 Consent of KPMG LLP, independent registered public
accounting firm X

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Exhibit No.	Description	Previously Filed			Filed Herewith
		Form	File No.	Filing Date	
24.1	<u>Power of Attorney (see signature page hereto)</u>				X
31.1	<u>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</u>				X
31.2	<u>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</u>				X
32.1*	<u>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</u>				X
101.INS+	XBRL Instance Document				X
101.SCH+	XBRL Taxonomy Extension Schema Document				X
101.CAL+	XBRL Taxonomy Extension Calculation Linkbase Document				X
101.DEF+	XBRL Taxonomy Extension Definition Linkbase Document				X
101.LAB+	XBRL Taxonomy Extension Label Linkbase Document				X
101.PRE+	XBRL Taxonomy Extension Presentation Linkbase Document				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, 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, 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 SEC.

XBRL information is furnished and not filed for purposes of Sections 11 and 12 of the Securities Act of 1933, as amended, and Section 18 of the Securities Exchange Act of 1934, as amended, and is not subject to liability under those sections, is not part of any registration statement or prospectus to which it relates and is not incorporated or deemed to be incorporated by reference into any registration statement, prospectus or other document.

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: March 15, 2019 Prothena
Corporation
plc
(Registrant)

/s/ Gene G.
Kinney
Gene G.
Kinney
President
and Chief
Executive
Officer

/s/ Tran B.
Nguyen
Tran B.
Nguyen
Chief
Operating
Officer and
Chief
Financial
Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose individual signature appears below hereby authorizes and appoints Gene G. Kinney and Tran B. Nguyen, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

Name	Title	Date
/s/Gene G. Kinney Gene G. Kinney, Ph.D.	President and Chief Executive Officer (Principal Executive Officer) and Director	March 15, 2019
/s/Tran B. Nguyen Tran B. Nguyen	Chief Operating Officer and Chief Financial Officer (Principal Financial Officer)	March 15, 2019
/s/Karin L. Walker Karin L. Walker	Chief Accounting Officer and Controller (Principal Accounting Officer)	March 15, 2019
/s/Lars G. Ekman Lars G. Ekman, M.D., Ph.D.	Chairman of the Board	March 15, 2019
/s/Richard T. Collier Richard T. Collier	Director	March 15, 2019
/s/Shane M. Cooke Shane M. Cooke	Director	March 15, 2019
/s/K. Anders O. Härfstrand K. Anders O. Härfstrand, M.D., Ph.D.	Director	March 15, 2019
/s/Christopher S. Henney Christopher S. Henney, Ph.D., D.Sc.	Director	March 15, 2019
/s/Dennis J. Selkoe Dennis J. Selkoe, M.D.	Director	March 15, 2019