

Prothena Corp plc
Form 10-K
March 13, 2015

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the year ended December 31, 2014

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

For the transition period from _____ to _____

Commission file number: 001-35676

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

| | |
|--|---|
| Ireland | 98-1111119 |
| (State or other jurisdiction of incorporation or organization) | (I.R.S. Employer Identification Number) |

Alexandra House
The Sweepstakes, Ballsbridge
Dublin 4, Ireland

(Address of principal executive offices including Zip Code)
Registrant's telephone number, including area code: 011-353-1-902-3519

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

| Title of Each Class | Name of Each Exchange on Which Registered |
|---|---|
| Ordinary Shares, par value \$0.01 per share | The Nasdaq Global Select Market |

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

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

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

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

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Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post such files). Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K 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. See definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer Accelerated filer

Non-accelerated filer (Do not check if a smaller reporting company) Smaller reporting company

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

As of June 30, 2014, 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 \$600.7 million, based on the last reported sale of the registrant's ordinary shares on the Nasdaq Global Market on such date. 27,399,535 of the Registrant's ordinary shares, par value \$0.01 per share, were outstanding as of February 27, 2015.

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, 2015 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, 2014.

PROTHENA CORPORATION PLC
 Annual Report on Form 10-K
 For the Year Ended December 31, 2014
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PART I
ITEM 1. BUSINESS

Overview

We are a late-stage clinical biotechnology company focused on the discovery, development and commercialization of novel protein immunotherapy programs for the potential treatment of diseases that involve amyloid or cell adhesion. We are developing antibody-based product candidates that target a number of potential indications including AL amyloidosis (NEOD001), Parkinson's disease and other related synucleinopathies (PRX002) and psoriasis and other inflammatory diseases (PRX003).

We are conducting The VITAL Amyloidosis Study, a Phase 3 global registrational trial, and a concurrent Phase 1/2 trial for our lead antibody, NEOD001, for the potential treatment of patients with AL amyloidosis. NEOD001 received Fast Track designation from the U.S. Food and Drug Administration (the "FDA") in December 2014.

In collaboration with Roche, we are developing PRX002 for the treatment of Parkinson's disease and other related synucleinopathies. During 2014, we advanced PRX002 into clinical development with the initiation of two Phase 1 studies. Results for the first Phase 1 study, a single ascending dose trial in healthy volunteers, are expected in March 2015. We continue to enroll patients with Parkinson's disease in the second Phase 1 multiple ascending dose study, with results expected in first half of 2016.

For PRX003, we expect to initiate a Phase 1 single ascending dose study in healthy volunteers during the first half of 2015, with a multiple ascending dose study in patients with psoriasis beginning in 2016 to establish potential clinical proof-of-biology in Phase 1. Beyond psoriasis, we may further develop PRX003 for the potential treatment of orphan and/or other inflammatory diseases.

We are a public limited company formed under the laws of Ireland. On December 20, 2012, we separated from Elan Corporation, plc ("Elan"). Our ordinary shares began trading on The Nasdaq Global Market under the symbol "PRTA" on December 21, 2012 and currently trade on The Nasdaq Global Select Market.

Our Strategy

Our goal is to be a leading biotechnology company focused on the discovery, development and commercialization of novel protein immunotherapy programs for the treatment of diseases that involve amyloid or cell adhesion. Key elements of our strategy to achieve this goal are to:

• Continue to discover antibodies directed against novel targets related to amyloid or cell adhesion.

We leverage our core scientific expertise and proprietary technology to develop innovative antibody-based therapeutics for the potential treatment of major unmet medical needs. Once we formulate a novel hypothesis or approach to a known target, we generate antibodies against that target. Specific and selective antibodies are characterized in vitro, then used to test the initial hypothesis in vivo using animal models of disease. We often rely on the use of animal models that have been extensively developed by external laboratories, as we have already done with our programs for AL amyloidosis, Parkinson's disease and psoriasis.

• Quickly translate our research discoveries into clinical development.

Once we establish in vivo proof of concept for our antibody candidates, we use animal models to identify potential clinical candidates and to rapidly advance these candidates into manufacturing and preclinical testing. In 2012, we filed an Investigational New Drug Application ("IND") with the FDA for NEOD001 for AL and AA amyloidosis and less than two years later, in December 2014, we initiated The VITAL Amyloidosis Study, a Phase 3 global registrational clinical trial in patients with AL amyloidosis and cardiac dysfunction.

• Establish early clinical proof of concept with our therapeutic antibodies.

We leverage our insight of disease pathology related to amyloid or cell adhesion to employ biomarker endpoints as a way to detect signals of biological activity early in the clinical development process. We may elect to start clinical testing of our antibodies in indications that have well-established endpoints in order to demonstrate proof of concept as a basis for further investment in clinical trials, by us or potential partners.

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Focus on diseases that lack effective therapies.

We focus on the development and commercialization of therapies for serious and/or life-threatening diseases that lack effective therapies. NEOD001 received Fast Track designation in December 2014, and has received orphan drug designation in both the U.S. and Europe for the treatment of AL amyloidosis. We have initiated The VITAL Amyloidosis Study, a Phase 3 clinical trial for NEOD001 for the treatment of newly-diagnosed, treatment-naïve patients with AL amyloidosis and cardiac dysfunction. To date, there are no approved therapies for the treatment of AL amyloidosis.

In collaboration with Roche, we are developing PRX002 as a potential disease-modifying treatment of Parkinson's disease and other related synucleinopathies. During 2014, we advanced PRX002 into clinical development with the initiation of two Phase 1 studies. Results for the first Phase 1 study, a single ascending dose trial in healthy volunteers, are expected in March 2015. We continue to enroll patients with Parkinson's disease in the second Phase 1 multiple ascending dose study, with results expected in the first half of 2016. To date, all approved therapies for patients with Parkinson's disease focus on the alleviation of disease symptoms.

We expect to initiate a Phase 1 single ascending dose study for PRX003 in healthy volunteers in the first half of 2015, with a multiple ascending dose trial enrolling patients with psoriasis in 2016. While therapies exist today that treat psoriasis and other inflammatory disorders, we believe our antibody has the potential to improve the outcome for patients who do not receive adequate benefit from existing therapies.

Moving forward, we intend to advance new discovery-stage monoclonal antibody therapeutics that show promise in orphan disease indications.

Strategically collaborate or out-license select programs.

Our robust discovery engine generates monoclonal antibodies that may be useful in treating unmet medical needs. For therapeutic antibody programs targeting broad patient populations that may require large clinical trials and development investment, we may seek to collaborate or license these potential antibody therapeutics to biotechnology or pharmaceutical companies for development and/or commercialization. In line with our strategy, in December 2013, we entered into the License, Development and Commercialization Agreement with Roche (described below), to develop and commercialize certain antibodies that target alpha-synuclein, including PRX002 for the potential treatment of Parkinson's disease and other related synucleinopathies.

Highly leverage external talent and resources.

Although we plan to maintain strong talent internally having expertise in our core areas of focus and as needed to execute efficiently on our clinical development and business objectives, we will leverage external resources to meet our operational and business needs while maintaining flexibility as those needs may change over time. We plan to continue to rely on the very extensive experience of our management team to execute on our objectives.

Collaborate with scientific and clinical experts in disease areas of interest.

We collaborate with highly regarded scientists having expertise in our disease areas of interest to test and characterize our potential therapeutic antibody candidates. We also collaborate with leading clinical experts in our disease areas of interest for feedback and guidance on our programs. In addition, we engage a number of consultants having specific functional and/or disease area expertise to help us execute on our preclinical and clinical development programs.

Evaluate commercialization strategies in order 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 options for each drug candidate's commercialization strategy. These options include building our own internal sales force; entering into a joint marketing partnership with another pharmaceutical or biotechnology company, 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 terms of potential offers from other pharmaceutical and biotechnology

companies.

Research and Development Pipeline

Our research and development pipeline includes three therapeutic antibody programs that we intend to advance: NEOD001 for the potential treatment of AL amyloidosis; PRX002 in collaboration with Roche, for the potential treatment of Parkinson's disease and other related synucleinopathies; and PRX003 for the potential treatment of psoriasis and other inflammatory diseases.

The following table summarizes the status of our research and development pipeline for our lead programs:
Our Lead Programs

NEOD001 for AL Amyloidosis

Our most advanced product development program, NEOD001, targets AL amyloidosis. Systemic amyloidoses, including AL, AA and ATTR amyloidosis, are a complex group of diseases caused by tissue deposition of amyloid proteins that result in progressive organ damage. The most common type, AL amyloidosis or primary systemic amyloidosis, results from hematological disorder involving abnormal plasma cells. 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. A subset of plasma cells begin overproducing a single light chain in great abundance. These light chains then misfold in blood and eventually aggregate into tissues, such as heart and kidneys, causing extensive organ damage and fatigue.

AL amyloidosis is a grievous disease and there are no approved treatments that directly target the toxic forms of the AL protein that build up in the organs. AL amyloidosis is a rare disorder with about 15,000 patients in the U.S. and Europe, however, we believe this disease is significantly underdiagnosed. Both the cause and origins of AL amyloidosis remain poorly understood.

Current treatment for patients with AL amyloidosis include organ transplants or the administration of off-label chemotherapeutic and/or oncologic therapies targeted at killing plasma cells to decrease the production of light chain circulating in the blood, called the hematologic burden. These chemotherapeutic and/or oncologic agents are associated with a known adverse event profile and patients often become refractory to their hematologic effect and/or relapse. In addition, the target of these therapies remains the plasma cells responsible for production of light chain, rather than the toxic light chain in circulation or built up in the organs. There remains a significant unmet need to directly target and remove the insoluble amyloid deposited on organs, to improve organ function and mortality, without increasing adverse events.

NEOD001 is a humanized monoclonal antibody that specifically targets the circulating misfolded soluble light chain and deposited insoluble amyloid that accumulates in AL amyloidosis. NEOD001 received Fast Track designation from the FDA in December 2014. The purpose of the Fast Track designation is to make important new drugs available to patients earlier. The Fast Track program also provides a company with the ability to submit sections of the Biologics License Applications ("BLA") for review before the company submits the complete BLA. This enables the FDA to review sections of the BLA as they are received, rather than waiting until every section of the application is completed, and also allows for Priority Review, which can shorten the standard review of the final BLA to six months. A drug program with Fast Track designation permits the company to have

early and frequent communications with the FDA in the development and review of the product candidate, potentially leading to faster drug approval.

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.

The VITAL Amyloidosis Study, a Phase 3 Clinical Trial

In December 2014, we initiated The VITAL Amyloidosis Study, a Phase 3 clinical trial for NEOD001 in patients with AL amyloidosis. The trial is designed to support global regulatory approvals. We intend to enroll approximately 230 newly-diagnosed, treatment-naïve patients with AL amyloidosis and cardiac dysfunction. Patients will be 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 is event-based, with all-cause mortality or cardiac hospitalizations as qualifying events. Secondary endpoints of the study include evaluation of the cardiac biomarker NT-proBNP, renal biomarker proteinuria, six-minute walk test, and multiple quality of life evaluations including the Short Form-36 and the Kansas City Cardiomyopathy Questionnaire. Prothena designed the study with 90% power to detect a 30% change in the event rate between the treatment and placebo groups with a two-sided alpha of 0.05. The trial allows for an interim analysis to assess the primary endpoint for efficacy and futility.

Cardiac and Renal Biomarker Responses in Phase 1/2 Study

The VITAL Amyloidosis Study, a Phase 3 clinical trial, was initiated following report of positive data in the ongoing Phase 1/2 clinical trial. In December 2014, we reported results from the ongoing Phase 1/2 study that showed 7 of 14 cardiac-evaluable patients (50%) treated with NEOD001 demonstrated a cardiac response, defined as more than 30% and 300 pg/mL decrease in levels of NT-proBNP from baseline (a validated cardiac biomarker associated with mortality). Cardiac responders, on average, showed more NT-proBNP decline with added monthly NEOD001 infusions. The 50% cardiac response rate compares favorably with the expected results of a 26.5% cardiac response rate from historical data in patients treated solely with standard of care that is not approved specifically for AL amyloidosis (Comenzo, et al., *Leukemia*. 2012;26:2317-2325). As noted in numerous peer-reviewed publications, increasing levels of NT-proBNP predicts higher mortality rates in patients with AL amyloidosis. Conversely, decreasing levels of NT-proBNP predicts lower mortality rates.

In a best response analysis of renal-evaluable patients treated with NEOD001, 6 of 14 renal-evaluable patients (42.9%) demonstrated a response, defined as more than 30% decrease in proteinuria in the absence of greater than 25% worsening of estimated glomerular filtration rate ("eGFR"). The 42.9% renal response rate compares favorably with the expected results of an approximately 24% renal response rate from historical data in patients treated solely with standard of care that is not approved specifically for AL amyloidosis (Palladini, et al., *Blood*. 2014 124: 2325-2332). Increased levels of proteinuria and decreased eGFR predicts faster progression to dialysis where decreased levels of proteinuria and increased eGFR predicts delayed time to dialysis.

Safety, Tolerability, Pharmacokinetics and Immunogenicity

Data from the Phase 1/2 study also continued to demonstrate that chronic monthly infusions of NEOD001 are safe and well-tolerated in patients with AL amyloidosis and persistent organ dysfunction. A database analysis as of September 30, 2014 showed a total of 27 patients in seven dosing cohorts received 209 infusions, with each patient treated on average for approximately eight months. No hypersensitivity reactions or drug-related serious adverse events were reported and no anti-NEOD001 antibodies were detected. NEOD001 demonstrated excellent pharmacokinetic

properties, supporting a dose level of 24 mg/kg every 28 days. The most frequently reported adverse events (more than 10% of subjects) were fatigue, cough, dyspnea, diarrhea, upper respiratory infection, anemia, headache, hyponatremia, nausea and edema. All adverse events were mild to moderate and no dose limiting toxicities have been observed. As of September 30, 2014, 19 patients continued on therapy (eight patients discontinued). No patient discontinued due to drug-related adverse events. Following selection of 24 mg/kg as the Phase 3 recommended dose, in consultation with their treating physician, all 14 eligible patients continuing in the dose escalation portion of the Phase 1/2 study have chosen to escalate to 24 mg/kg.

Expansion Portion of Phase 1/2 Study

Concurrent with The VITAL Amyloidosis Study, a Phase 3 clinical trial, we are enrolling up to an additional 25 patients, with AL amyloidosis and selected persistent organ dysfunction, in an open-label expansion portion of the Phase 1/2 study. We plan to enroll 10 patients with cardiac dysfunction, 10 patients with renal dysfunction and five patients with peripheral neuropathy,

all of whom will receive 24 mg/kg intravenously every 28 days. The expansion phase will continue to evaluate safety, tolerability, pharmacokinetics and immunogenicity of NEOD001 as well as the specific clinical activity against cardiac, renal and neuropathy endpoints.

PRX002 for Parkinson's Disease

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 alpha-synuclein, including PRX002. Together, we and Roche aim to develop PRX002 as a disease-modifying treatment for Parkinson's disease and potentially other synucleinopathies. For more information on the License Agreement, see the information below.

Alpha-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 synuclein is not well understood, the protein normally occurs in a soluble form. In synucleinopathies, the 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 synuclein in Parkinson's disease. In rare cases of familial forms of Parkinson's disease, there are mutations in the synuclein gene, or duplication and triplications of the gene that may cause synuclein protein to form amyloid-like fibrils that contribute to the disease. There is also increasing evidence that this disease-causing synuclein can be propagated and transmitted from neuron to neuron, resulting in an infection-like spread of neuronal death. Recent studies in cellular and animal models suggest that the spread of synuclein-associated neurodegeneration can be disrupted by targeting aberrant forms of synuclein.

Parkinson's disease is a degenerative disorder of the central nervous system that affects one in 100 people over age 60. Current treatments for Parkinson's disease are only effective at managing the early motor symptoms of the disease, mainly through the use of levodopa and dopamine agonists. As the disease progresses and dopaminergic neurons continue to be lost, these drugs eventually become less effective at treating the symptoms. The goal of our approach is to slow down the progressive neurodegenerative consequences of disease, a current unmet need. PRX002 targets alpha-synuclein and may slow or reduce the neurodegeneration associated with synuclein misfolding and/or transmission.

During 2014, we and Roche advanced PRX002 into clinical development with the initiation of two Phase 1 studies. The first study, a Phase 1 double-blind, placebo-controlled, single ascending dose trial, enrolled 40 healthy volunteers, all of which were randomized 3:1 into five escalating dose cohorts to receive PRX002 or placebo every 28-days. Results for this trial are expected in March 2015.

In addition, we are enrolling patients with Parkinson's disease in a Phase 1 multiple ascending dose study. The Phase 1 randomized, double-blind, placebo-controlled, multiple ascending dose study of PRX002 is expected to enroll up to 60 patients with Parkinson's disease at multiple centers across the U.S. and is designed to evaluate the safety, tolerability, pharmacokinetics and immunogenicity of PRX002. The multiple ascending dose study will also evaluate multiple clinical and exploratory biomarker endpoints. Patients will be enrolled in escalating dose cohorts of PRX002 or placebo and will be observed for up to 6 months.

Prior to initiating clinical trials, we tested the efficacy of PRX002 in various cellular and animal models of synuclein-related disease. In transgenic mouse models of Parkinson's disease, passive immunization with 9E4, the murine version of PRX002, reduced the appearance of synuclein pathology, protected synapses and improved performance by the mice in behavioral testing.

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 alpha-synuclein, including PRX002, which are referred to in this report collectively as “Licensed Products.” The License Agreement became effective following the expiration of the applicable Hart-Scott-Rodino waiting period on January 17, 2014, which triggered an upfront payment to us of \$30.0 million from Roche, which we received in February 2014.

Pursuant to the License Agreement, we and Roche are collaborating to research and develop antibody products targeting alpha-synuclein. Roche is providing funding for a research collaboration between us and Roche focused on optimizing early stage antibodies targeting alpha-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 PRX002. Roche will also become 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 a clinical milestone payment of \$15.0 million paid in 2014, Roche is also obligated to pay:

- up to \$380.0 million upon the achievement of 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., the parties will share all development and commercialization costs, as well as profits, all of which will be allocated 70% to Roche and 30% to us, for PRX002 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 PRX002 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. Outside the U.S., Roche will have 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.

PRX003 for Psoriasis and Other Inflammatory Diseases

We are developing PRX003, a monoclonal antibody targeting melanoma cell adhesion molecule ("MCAM") for the potential treatment of psoriasis and other inflammatory diseases, and expect to initiate a Phase 1 single ascending dose study in the first half of 2015. Beyond psoriasis, we may further develop this antibody for the potential treatment of orphan and/or other inflammatory diseases.

Within the immune system, white blood cells play an important role. T-cells are a subset of white blood cells that express either CD4 glycoprotein (CD4+) or CD8 glycoprotein (CD8+) on their surface. CD4+ T-cells are called "helper"

cells as they do not neutralize the infection, but rather initiate the body's response to infections. Th-17 cells are a subset of CD4+ T-cells characterized by the production of IL-17, and are known to be key participants in inflammatory reactions and various autoimmune diseases.

MCAM is a cell adhesion molecule that allows certain cells traveling in the blood stream to leave the circulation and enter tissues. MCAM is expressed on pathogenic Th-17 immune cells. These immune cells are believed to underlie many inflammatory diseases. MCAM functions like VELCRO™ hook-and-loop fasteners, allowing these cells to stick to the blood vessel wall, so that they can migrate into the surrounding tissues to initiate and/or maintain their pathogenic process.

Our research in the area of cell adhesion has uncovered unique insights into MCAM function, allowing us to develop specific and novel antibodies that block MCAM's VELCRO™-like function and may serve as therapeutics to prevent disease causing cells from spreading into tissue.

Anti-MCAM antibodies may be useful for treating a variety of inflammatory diseases such as psoriasis, psoriatic arthritis, rheumatoid arthritis, multiple sclerosis, sarcoidosis, uveitis, and Behcet's disease. Autoimmune and/or autoinflammatory diseases arise from the body's inappropriate immune response against substances and tissues normally present in the body. In other words, the immune system mistakes some part of the body as a foreign pathogen and attacks its own cells. A substantial portion of the population suffers from these diseases, which are often chronic, debilitating, and life-threatening.

Current treatment for many types of inflammatory diseases may entail the use of broad acting immunosuppressive agents that weaken the body's ability to fight infection. Only 3 to 5% of CD4+ T-cells in the circulation express MCAM, yet these cells appear to be disproportionately involved in the propagation of inflammatory diseases. Hence, anti-MCAM based therapy may provide a more specific way to target the disease-causing immune cells while not interfering with normal function of the majority of the immune system.

We have generated monoclonal antibodies that selectively block MCAM-mediated cell adhesion and have been shown to delay relapse and severity of relapse in a mouse model of autoimmune inflammation.

We expect to initiate a Phase 1 single ascending dose trial of PRX003 in the first half of 2015, with a multiple ascending dose study beginning in 2016. Our clinical strategy is to pursue psoriasis initially to allow for potential rapid feedback on the biological activity of our therapeutic agent and establish a solid clinical foundation to inform our decisions as we explore the full development potential of this antibody in psoriasis and other inflammatory indications. We may elect to license or partner PRX003 for disease areas that would require larger clinical trials and investment.

Our Discovery Programs

Our pipeline also includes several late discovery-stage programs for which we are testing the efficacy of antibodies in preclinical models of diseases related to amyloid or cell adhesion. If promising, we expect that these antibodies will advance to preclinical development. New target discovery will focus on the potential treatment of orphan indications involving amyloidosis or cell-adhesion where we can bring these therapies to patients expeditiously through our internal expertise and resources. Existing late discovery-stage programs with non-orphan indications may be partnered or out-licensed.

Regulation

We anticipate that if we commercialize any products, the U.S. market will 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 and comparable regulatory authorities in other countries, regulate the design, development, testing, manufacturing, safety, efficacy, labeling, storage, record-keeping, advertising, promotion and marketing of pharmaceutical products, including biologics, under the Federal Food, Drug, and Cosmetic Act and its implementing regulations, and the 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 product approval applications until manufacturing or other alleged deficiencies are brought into compliance. The FDA also has the authority to cause the withdrawal of approval of a marketed product or to impose 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 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 Federal Food, Drug and Cosmetics Act, Public Health Safety 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 IND, which must become effective before human clinical trials may begin and must be

updated annually;

• completion of extensive preclinical laboratory tests and preclinical animal studies, all performed in accordance with the FDA's Good Laboratory Practice ("GLP") regulations;

• performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the product for each proposed indication, all performed in accordance with FDA's current good clinical practices ("cGCP") regulations;

• submission to the FDA of a BLA for a new biologic, after completion of all pivotal 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 current good manufacturing practices ("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.

Preclinical tests assess the potential safety and efficacy of a product candidate in animal models. 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 administer an investigational drug or biologic product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for human studies. The IND also includes results of animal studies or other human studies, as appropriate, as well as manufacturing information, analytical data and any available clinical data or literature to support the use of the investigational new drug. An IND must become effective before human clinical trials may begin. 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 the proposed clinical trials. 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 clinical trials can begin. Accordingly, submission of an IND may or may not result in the FDA allowing clinical trials 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 monitor the study until completed. There are also requirements governing the reporting of ongoing clinical trials and clinical trial results to public registries.

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

Phase 1. Phase 1 includes the initial introduction of an investigational product into humans. Phase 1 clinical trials are typically 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, dosage tolerance, 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 and

scientifically valid 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 effectiveness of the investigational product for a particular indication(s) in patients with the disease or condition under study, to determine dosage tolerance and optimal dosage, 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 of the product has been obtained, and are intended to further evaluate dosage, clinical effectiveness 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 three to ten years or more 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 preclinical and clinical testing, along with information regarding the manufacturing 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 pertinent preclinical and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators.

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 or, in the case of Priority Review, six months from the 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, pure and potent, which includes determining whether it is 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 review, 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 program designations - Fast Track, Breakthrough Therapy, Accelerated Approval and Priority Review - to facilitate and expedite development and review of new drugs to address unmet medical needs in the treatment of serious or life-threatening conditions. The Fast Track designation provides pharmaceutical manufacturers with opportunities for frequent interactions with FDA reviewers during the product's development and the ability for the manufacturer to do a rolling submission of the BLA. A rolling submission allows completed portions of the application to be submitted and reviewed by the FDA on an ongoing basis. The Breakthrough Therapy designation provides manufacturers 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 manufacturer to conduct required post-approval confirmatory trials to verify the clinical benefit. The Priority Review designation means that the FDA's goal is to take action on the BLA within six months, compared to ten months under standard review.

After the FDA evaluates the BLA and conducts inspections of manufacturing facilities where the candidate product and/or its API will be produced, 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 pivotal Phase 3 clinical trial(s), and/or other significant, expensive and time-consuming requirements related to clinical trials, preclinical 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 condition approval on, among other things, changes to proposed labeling, development of adequate controls and specifications, or a commitment to conduct one or more post-market studies or clinical trials. Such post-market testing may include Phase 4 clinical trials and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

There can be no marketing in the U.S. of a biologic until a BLA has been submitted and approved by the FDA. Until an application is actually approved, there can be no assurance that the information requested and submitted will be considered adequate by the FDA.

European Union. In Europe, there are several tracks for marketing approval, depending on the type of product for which approval is sought. Under the centralized procedure, a company submits a single application to the EMA. The marketing application is similar to the NDA 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 quality, safety, and efficacy, 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 member states.

In addition to the centralized procedure, the EC also has: (i) a nationalized procedure, which requires a separate application to 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 other countries may accept or reject the initial decision. Regardless of the approval process employed, various parties 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 experiences with the biologic, 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.

Manufacturers 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 and impose reporting and documentation requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers 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 and treatment 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, recently have increased their scrutiny of the promotion and marketing of drugs.

The FDA also enforces the requirements of the 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 Federal Anti-Kickback Statute, the False Claims Act, and similar state laws. Pricing and rebate programs must comply with the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990, as amended. We may also be subject to the Physician Payment Sunshine Act ("Sunshine Act") which regulates disclosure of payments to healthcare professionals and providers.

The Foreign Corrupt Practices Act (the "FCPA") and U.K. Bribery Act prohibit companies and their representatives from offering, promising, authorizing or making payments to foreign officials (and certain private individuals under the U.K. Bribery Act) for the purpose of obtaining or retaining business abroad. In many countries, the healthcare professionals we interact with may meet the definition of a foreign government official for purposes of the FCPA. Failure to comply with domestic or foreign 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 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 a showing 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 foreign 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 foreign 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 foreign jurisdictions in which we conduct our business. Such laws include, without limitation, state and federal 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 foreign patents and pending Patent Cooperation Treaty applications and foreign counterparts. As of February 27, 2015, our patent portfolio included the following patents or patent applications that we own or have exclusively licensed from other parties:

- ◆ Approximately 57 patent and patent applications related to AL or AA amyloidosis, including our NEOD001 program;
- ◆ Approximately 133 patents and patent applications related to Parkinson's disease and other synucleinopathies,

including our PRX002 program;

• Approximately 20 patents and patent applications related to psoriasis and other inflammatory diseases, including our PRX003 program; and

• Approximately 77 patents and patent applications related to other potential targets of intervention.

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 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 foreign 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 2036 (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. 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 date of execution 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 alpha-synuclein. Under that sublicensable, worldwide license, we are required to pay to the University of California an amount equal to 1% of net sales of any product covered by any licensed patent, plus certain additional payments for milestones achieved and sublicense revenue. To date, we have not paid or incurred any royalties to the University of California under our

agreement. The agreement is effective until the expiration date of the last to expire licensed patent. The obligation to pay royalties continues on a country-by-country basis until the expiration of the last to expire patent containing a valid claim covering the applicable product. The agreement will terminate prior to the end of its term without prior written notice if (i) we, or third parties on our behalf or at our written urging, file a claim including an assertion that any portion of the licensed patents is invalid or unenforceable, or (ii) upon the filing of a petition for relief under the U.S. Bankruptcy Code by or against us as a debtor or alleged debtor. The University of California may terminate the agreement prior to the end of its term upon our default, if we fail to cure the default within 60 days of written notice of such default. We may terminate the agreement prior to the end of its term upon a 90 day written notice to the University of California.

Elan License Agreement: Under an Amended and Restated Intellectual Property License and Contribution Agreement with Elan and certain of its affiliates, we have exclusively licensed from Elan and those affiliates certain patents and patent applications owned by them, and exclusively sublicensed from Elan and those affiliates certain patents and patent applications owned by Janssen Alzheimer Immunotherapy. Those licenses are worldwide, fully paid, royalty-free, perpetual and irrevocable,

and relate to our program targeting alpha-synuclein.

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.

Product Supply

While supplies of raw materials and clinical supplies of our main product candidate are generally available in quantities adequate to meet the needs of our business, we are dependent on Boehringer Ingelheim to manufacture our clinical supplies for certain of our therapeutic antibody programs. An inability to obtain product supply could have a material adverse effect on our business, financial condition or results of operations.

Research and Development

Our research and development expenses totaled \$38.5 million, \$26.1 million and \$34.1 million in 2014, 2013 and 2012, respectively. For more information, see “Management’s Discussion and Analysis of Financial Condition and Results of Operations.”

Employees

As of December 31, 2014, we had 46 employees, of whom 29 were engaged in research and development activities and the remainder were working in general and administrative areas.

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 Alexandra House, The Sweepstakes, Ballsbridge, Dublin 4, Ireland, and our telephone number at that address is 011-353-1-902-3519. 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 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 our 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, Alexandra House, The Sweepstakes, Ballsbridge, Dublin 4, Ireland, 011-353-1-902-3519, 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 impact, 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 \$7.2 million, \$41.0 million and \$41.4 million for the years ended December 31, 2014, 2013 and 2012, respectively. We expect to continue to incur substantial losses for the foreseeable future as we:

- conduct our Phase 3 and Phase 1/2 clinical trials for NEOD001, conduct our Phase 1 clinical trials for PRX002, and initiate additional clinical trials for these and other programs;

- develop and commercialize our product candidates, including NEOD001, PRX002 and PRX003;

- complete preclinical development of other product candidates and initiate clinical trials, if supported by positive preclinical 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, 2014, we had cash and cash equivalents of \$293.6 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 eventually 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 our Phase 3 and Phase 1/2 clinical trials for NEOD001, our Phase 1 clinical trials for PRX002, and our contemplated Phase 1 clinical trial for PRX003;

- the timing, initiation, progress, results and costs of these and our other research, development and commercialization activities, including in connection with PRX002 under our License Agreement with Roche;

- the results of our research and preclinical studies;

- the costs of clinical manufacturing and of establishing commercial manufacturing arrangements and other commercialization needs;

- 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 costs to satisfy our obligations under 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 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 a 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 you 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 for one or more of our drug candidates;
- delay arrangements for activities that may be necessary to commercialize our drug candidates;
- curtail or eliminate our drug research and development programs that are designed to identify new drug candidates; or
- cease operations.

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

Our historical financial information is not necessarily representative of the results we would have achieved as a separate, publicly traded company and may not be a reliable indicator of our future results.

Prior to our separation from Elan on December 20, 2012, our financial results previously were included within the consolidated results of Elan; however, we were not directly subject to the reporting and other requirements of the Exchange Act until our separation from Elan, which we refer to in this Form 10-K as the "Separation and Distribution." The historical financial information we have included or incorporated by reference in this report may not reflect what our financial condition, results of operations and cash flows would have been had we been an independent, publicly traded company during the periods presented or what our results of operations, financial position and cash flows will be in the future. This is primarily because:

- our historical financial information reflects allocations for services historically provided to us by Elan, which allocations may not reflect the costs we will incur for similar services in the future as an independent company;
- subsequent to the completion of the Separation and Distribution, the cost of capital for our business has been and may continue to be higher than Elan's cost of capital prior to the Separation and Distribution because Elan's cost of debt was lower than ours has been and will likely continue to be; and
- our historical financial information does not reflect changes that we have incurred as a result of the separation of our business from Elan, including changes in the cost structure, personnel needs, financing and operations of the contributed business as a result of the separation from Elan and from reduced economies of scale.

We are also responsible for the additional costs associated with being an independent, public company, including costs related to corporate governance and compliance with the rules of The Nasdaq Stock Market ("Nasdaq") and the SEC. In addition, we incur costs and expenses, including professional fees, to comply with Irish corporate and tax laws and financial reporting requirements and costs and expenses incurred in connection with holding the meetings of

our board of directors, or our Board, in Ireland. Prior to the Separation and Distribution, our business was operated by Elan as part of its broader corporate organization, rather than as an independent company. Elan or one of its affiliates performed various corporate functions for us, including, but

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not limited to, legal, treasury, accounting, auditing, risk management, information technology, human resources, corporate affairs, tax administration, certain governance functions and external reporting. Our historical financial results include allocations of corporate expenses from Elan for these and similar functions. These allocations of cash and non-cash expenses are less than the comparable expenses we have incurred thus far as a separate publicly traded company. Therefore, our consolidated Financial Statements may not be indicative of our future performance as an independent company.

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. Dale B. Schenk, our President and Chief Executive Officer. There can be no assurance that we will be able to retain Dr. Schenk or any of our key personnel. The loss of the services of Dr. Schenk or any other person on which we become highly dependent might impede the achievement of our research and development objectives. Recruiting and retaining qualified scientific personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific personnel from universities and research institutions.

We announced on December 2, 2014 that Dr. Schenk has been diagnosed with pancreatic cancer. He is undergoing treatment for that cancer.

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

We have entered into certain agreements with Elan in connection with the Separation and Distribution, which set forth the main terms of the separation and provide 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.

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 ongoing Phase 3 and Phase 1/2 clinical trials for NEOD001 and Phase 1 clinical trials for PRX002, there is no assurance that these clinical 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, and, with respect to approval in the U.S., to the satisfaction of the U.S. Food and Drug Administration (the "FDA") or, with respect to approval in other countries, similar regulatory authorities in those countries, that the drug candidate is safe and effective for use for that target indication. 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, comparable products;
- be proven safe and effective in clinical trials; or
- meet applicable regulatory standards.

Positive results in preclinical 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 preclinical studies and clinical trials for our drug candidates may not be predictive of the results we may obtain in later stage trials or studies. Our preclinical studies or clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional preclinical 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;
- collaborating with pharmaceutical companies or contract sales organizations to market and sell any approved drug; or
- acceptance of any approved drug in the medical community and by patients and third-party payors.

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.

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 our Phase 3 or Phase 1/2 clinical trials for NEOD001, our Phase 1 clinical trials for PRX002, or any 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 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 or any foreign regulatory authority 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 retention rate of subjects in clinical trials for a variety of reasons, including size of patient population, nature of trial protocol, the availability of other treatments for the relevant disease and competition from other clinical trial programs for similar indications;
- serious and unexpected drug-related side effects experienced by patients in clinical trials; or
- failure of our third-party contractors to meet their contractual obligations to us in a timely manner.

Clinical trials may also be delayed or terminated as a result of ambiguous or negative interim results. In addition, a clinical trial may be suspended or terminated by us, the FDA, the IRBs at the sites where the IRBs are overseeing a trial, or a data safety monitoring board ("DSMB") overseeing the clinical trial at issue, or other regulatory authorities 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 or other regulatory authorities resulting in the imposition of a clinical hold;
- varying interpretation of data by the FDA or other regulatory authorities;
- requirement by the FDA or other regulatory authorities to perform additional studies;
- failure to achieve primary or secondary endpoints or other failure to demonstrate efficacy;
- 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 harmed and our ability to generate product revenues will be 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 and comparable foreign 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 and comparable foreign 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 or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign 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 or comparable foreign 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 or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our drug candidates may not be sufficient to support the submission of a Biologics License Application ("BLA") or other submission or to obtain regulatory approval in the U.S. or elsewhere;
- the FDA or comparable foreign 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 or comparable foreign 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 not approve the price we intend to charge for our products, 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.

We rely on obtaining and maintaining orphan drug exclusivity for NEOD001, if approved, but cannot ensure that we will enjoy market exclusivity in a particular market.

NEOD001 has been granted orphan drug designation by the FDA for the treatment of AL and AA amyloidosis and by the European Medicines Agency (the "EMA") for the treatment of AL amyloidosis. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, defined as a disease or condition that affects a patient population of fewer than 200,000 in the U.S., or a patient population greater than 200,000 in the U.S. where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the U.S. In the European Union (the "EU"), the EMA's Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention, or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the EU. Additionally, designation is granted for products intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition when, without incentives, it is unlikely that sales of the drug in the EU would be sufficient to justify the necessary investment in developing the drug or biological product or where there is no satisfactory method of diagnosis, prevention, or treatment, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition.

In the 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. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity. In the EU, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity following drug or biological product approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Even though we have obtained orphan drug designation for NEOD001 in the U.S. and the EU, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products. Further, even if we obtain orphan drug designation for a product, that exclusivity may not effectively protect the product from competition from different drugs with different active moieties which may be approved for the same condition. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. Even if one of our drug candidates receives orphan exclusivity, the FDA may still approve other drugs that have a different active ingredient for use in treating the same indication or disease, or may approve an application to market the same drug for the same indication that shows clinical superiority over our product. Furthermore, the FDA may waive orphan exclusivity if we are unable to manufacture sufficient supply of our product.

Even if our drug candidates receive regulatory approval in the United States, we may never receive approval or commercialize our products outside of the United States.

In order to market any products outside of the U.S., we must establish and comply with numerous and varying regulatory requirements of other countries regarding 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 FDA approval. The regulatory approval process in other countries may include all of the risks detailed above regarding FDA approval in the U.S. as well as other risks. Regulatory approval in one country does not ensure regulatory approval in another, 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 other countries or any delay or setback in obtaining such approval would impair our ability to develop foreign markets for our drug candidates.

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, the manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion, distribution and record keeping related to the product are subject to extensive, ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, 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 with our third-party manufacturers or manufacturing processes, or failure to comply with the regulatory requirements of the FDA and other applicable U.S. and foreign regulatory authorities could subject us to administrative or judicially imposed sanctions, including:

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

The FDA's 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 or other comparable foreign authorities. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the 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 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;

we may be required to change the way the product is administered, conduct additional clinical trials or change the labeling of the product;

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 federal, state, local and international 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 payors, 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 and severity of adverse side effects;

- availability of coverage and adequate reimbursement from managed care plans and other third-party payors;

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 PRX002 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 commercialize PRX002 and our business. Furthermore, if we opt out of profit and loss sharing with Roche, our revenues from PRX002 will be reduced.

The success of sales of PRX002 in the U.S. will be dependent on the ability of Roche to successfully develop in collaboration with us, and launch and commercialize PRX002, 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 PRX002, 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 commercialization of PRX002 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 PRX002 in the U.S. In addition, Roche may under some circumstances independently

develop products that compete with PRX002, or Roche may decide to not commit sufficient resources to the marketing and distribution of PRX002. If we are not able to collaborate effectively with Roche on plans and efforts to develop and commercialize PRX002, 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 PRX002 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 PRX002 could be substantially harmed as we will be required to develop our own sales and marketing organization or enter into another strategic collaboration in order to commercialize PRX002 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 PRX002, including the timing of launch and potential pricing, will have a significant impact on the ultimate success of PRX002 in the U.S., and the success of the overall commercial arrangement with Roche. If launch of commercial sales of PRX002 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 PRX002 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 PRX002 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 PRX002 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 PRX002 will be reduced.

Our right to co-develop PRX002 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 PRX002 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 PRX002 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 PRX002 as diligently as we would like. We could also become involved in disputes with Roche, which could lead to delays in or termination of commercialization programs 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 or marketing PRX002 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 commercialize PRX002. If Roche's efforts are unsuccessful, our ability to generate future product sales from PRX002 outside the United States would be significantly reduced.

Under our License Agreement, outside of the U.S., Roche has responsibility for developing and commercializing PRX002 and any future Licensed Products targeting alpha-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 PRX002 outside of the U.S., or under some circumstances independently develop products that compete with PRX002, or decide not to commit sufficient

resources to the marketing and distribution of PRX002.

In the event that Roche does not diligently commercialize PRX002, 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 PRX002, 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 commercialize PRX002 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 PRX002 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 an organization for the sales, marketing and distribution of pharmaceutical products. In order to market any products that may be approved by the FDA, 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 PRX002 and may develop our own sales force and marketing infrastructure to co-promote PRX002 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 PRX002 or other Licensed Products, our ability to generate additional revenue from potential sales of PRX002 or such products in the U.S. may be harmed. In addition, our right to co-promote PRX002 and other Licensed Products will terminate if we commence a Phase 3 study for a competitive product that treats Parkinson's disease. For our other approved products, 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 payors 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 domestic and foreign markets, our sales of any future products will depend in part upon the availability of reimbursement from third-party payors. Such third-party payors 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 payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Third-party payors 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 payors' 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 foreign markets, 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 foreign 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 Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the “Healthcare Reform Law”), was enacted. The Healthcare Reform Law substantially changes 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:

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- 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 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 False Claims Act and the Anti-Kickback Statute, new government investigative powers and enhanced penalties for non-compliance;
- a new Medicare Part D coverage gap discount program, under which manufacturers must 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 on April 1, 2013 and will stay in effect through 2024 unless additional congressional action is taken. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, 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 payors. 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 payors, that coverage or an adequate level of reimbursement will be available, or that third-party payors' 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 preclinical testing and clinical trials, obtaining regulatory approvals and manufacturing and marketing pharmaceutical products;
- drug candidates that have been approved or are in late-stage clinical development; and/or
- collaborative arrangements in our target markets with leading companies and research institutions

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

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

Our 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 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 may be subject, directly or indirectly, to federal and state anti-kickback, fraud and abuse, false claims, physician payment transparency, health information privacy and security, and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.

If we obtain FDA approval for any of our drug candidates and begin commercializing those products in the U.S., our operations may be directly, or indirectly through our customers, subject to various federal and state fraud and abuse and other healthcare laws and regulations, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act, which may constrain the business or financial arrangements and relationships through which we sell, market and distribute any drugs for which we obtain marketing approval. In addition, we may be subject to physician payment transparency laws and patient privacy regulation by both the federal government and the states and foreign jurisdictions in which we conduct our business. The laws that may affect our ability to operate include:

the federal 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; federal civil and criminal false claims laws and civil monetary penalty laws, including the federal 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 payors 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 federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which created new federal criminal statutes that impose criminal and civil liability for executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;

the federal Physician Payment Sunshine Act, which requires 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, which is defined to include doctors, dentists, optometrists, podiatrists and chiropractors, and teaching hospitals and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by the physicians and their immediate family members. The period between August 1, 2013 and December 31, 2013 was the first reporting period, and manufacturers were required to report aggregate payment data by March 31, 2014, and were required to report detailed payment data and submit legal attestation to the accuracy of such data during Phase 2 of the program (which began in May 2014). Thereafter, manufacturers must submit reports by the 90th day of each subsequent calendar year;

HIPAA, as amended by the Health Information Technology and Clinical Health Act, and its implementing regulations, which impose obligations on covered healthcare providers, health plans, and healthcare clearinghouses, as well as their business associates that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity, with respect to safeguarding the privacy, security and transmission of individually identifiable health information; and

analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Further, the Healthcare Reform Law, among other things, amended the intent requirements of the federal 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 federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations may involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to significant civil, criminal, and administrative penalties, including, without limitation, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, imprisonment, damages, fines and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business, including our collaborators, is found not to be in compliance with applicable laws, it may be subject to criminal, civil or administrative sanctions, including exclusions from participation in government healthcare programs, which could also adversely affect our business.

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, health care 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 in the aggregate amount of \$10.0 million for all of our clinical trials in all jurisdictions; we have an additional \$5.0 million in coverage for certain clinical trials in certain jurisdictions. 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 perform this function. 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 requires 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, EMA or comparable foreign 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 similar entities 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, nonclinical and preclinical 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 a third-party manufacturer to produce our pre-clinical and clinical trial drug supplies.

We do not currently operate manufacturing facilities for pre-clinical or clinical production of any of our drug candidates. We have limited experience in drug manufacturing, and we lack the resources and the capabilities to manufacture any of our drug candidates on a clinical or commercial scale. As a result, we rely on a single third-party manufacturer to supply, store, and distribute pre-clinical and clinical supply of our drug candidates, and plan to continue to do so until we increase the number of manufacturers with whom we contract. Any performance failure or capacity limitation on the part of our existing or future manufacturers could delay clinical development or regulatory approval of our drug candidates or commercialization of any approved products, producing additional losses and depriving us of potential product revenue.

Our drug candidates require precise, high quality manufacturing. Failure by our contract manufacturer to achieve and maintain high manufacturing standards could result in patient injury or death, product recalls or withdrawals, delays or failures in testing or delivery, cost overruns, or other problems that could seriously hurt our business. Contract manufacturers may encounter difficulties involving production yields, quality control, and quality assurance. These manufacturers are subject to ongoing periodic and unannounced inspections by the FDA and corresponding state and foreign agencies to ensure strict compliance with cGMPs and other applicable government regulations and corresponding foreign standards; however, we do not have control over third-party manufacturers' compliance with these regulations and standards.

If a contract manufacturer cannot perform as agreed, we may be required to replace it. Although we believe there are a number of potential replacements as our manufacturing processes are not manufacturer specific, we may incur added costs and delays in identifying and qualifying any such replacements because the FDA must approve any replacement manufacturer prior to manufacturing our drug candidates. Such approval would require new testing and compliance inspections. In addition, a new manufacturer would have to be educated in, or develop substantially equivalent processes for, production of our drug candidates after receipt of FDA approval.

We anticipate continued reliance on third-party manufacturers if we are successful in obtaining marketing approval from the FDA and other regulatory agencies for any of our drug candidates, and our commercialization of any of our drug candidates may be halted, delayed or made less profitable if those third parties fail to obtain or maintain necessary regulatory approvals, fail to provide us with sufficient quantities of drug product or fail to do so at acceptable quality levels or prices.

To date, our drug candidates have been manufactured in small quantities for preclinical and clinical testing by third-party manufacturers. If the FDA or other regulatory agencies approve any of our drug candidates for commercial sale, we expect that we would continue to rely, at least initially, on third-party manufacturers to produce commercial

quantities of approved drug candidates. These manufacturers may not be able to successfully increase the manufacturing capacity for any approved drug candidates in a timely or economic manner, or at all. Significant scale-up of manufacturing may require additional validation studies, which the FDA must review and approve. If third party manufacturers are unable to successfully increase the manufacturing capacity for a drug candidate, or we are unable to establish our own manufacturing capabilities, the commercial launch of any approved products may be delayed or there may be a shortage in supply, which in turn could have a material adverse effect on our business. In addition, the facilities used by our contract manufacturers to manufacture our drug candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit a BLA to the FDA. We do not control the manufacturing

process of, and are completely dependent on, our contract manufacturing partners for compliance with cGMPs, for manufacture of both active drug substances and finished drug products. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other regulatory authorities, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our drug candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our drug candidates, if approved.

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 foreign 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 foreign 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. On September 16, 2011, the 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 recently developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first-to-file provisions, only became effective on March 16, 2013. 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 foreign 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 foreign jurisdictions. If we encounter such difficulties in protecting or are otherwise precluded from effectively protecting our intellectual property rights in foreign 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;
- 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 clinical trials;
- our collaboration with Roche pursuant to the License Agreement to develop and commercialize PRX002, as well as any future Licensed Products targeting alpha-synuclein;
- failure or delays in advancing our preclinical 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;

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- regulatory developments or enforcement in the U.S. and foreign 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; 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. In the past, when the market price of a stock has been volatile, some holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our shareholders brought a lawsuit against us, we could incur substantial costs defending the lawsuit. Such a lawsuit could also divert the time and attention of our management.

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

As with any publicly traded company, your percentage ownership in us may be diluted in the future because of equity issuances for acquisitions, capital raising transactions 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, 2014, the number of ordinary shares available for issuance pursuant to outstanding and future equity awards under our equity plan was 2,868,676.

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 Securities Exchange Act of 1934, as amended, including the requirements of Section 404 of the Sarbanes-Oxley Act of 2002, which require annual management assessments of the effectiveness of our internal control over financial reporting. However, our auditors will not be required to formally attest to the effectiveness of our internal control over financial reporting pursuant to Section 404 until we are no longer an “emerging growth company” as defined in the Jumpstart Our Business Startups Act (the “JOBS Act”) if we continue to take advantage of the exemptions available to us through the JOBS Act.

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 of 2002. 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 Financial Statements for external purposes in accordance with accounting principles generally accepted in the U.S. Any failure to maintain effective internal controls could have an adverse effect on our business, financial position and results of operations.

For as long as we are an emerging growth company, we will be exempt from certain reporting requirements, including those relating to accounting standards and disclosure about our executive compensation, that apply to other public companies.

The JOBS Act contains provisions that, among other things, relax certain reporting requirements for emerging growth companies, including certain requirements relating to accounting standards and compensation disclosure. We are classified as an emerging growth company, which is defined as a company with annual gross revenues of less than \$1 billion, that has been a public reporting company for a period of less than five years, and that does not have a public float of \$700 million or more in securities held by non-affiliated holders. We will remain an emerging growth company until the earliest of (i) the end of the fiscal year in which the market value of our ordinary shares that are held by non-affiliates exceeds \$700 million as of the end of the second fiscal quarter, (ii) the end of the fiscal year in which we have total annual gross revenues of \$1 billion or more during such fiscal year, (iii) the date on which we issue more than \$1 billion in non-convertible debt in a three-year period or (iv) the end of the fiscal year following the fifth anniversary of the date of the first sale of our ordinary shares pursuant to an effective registration statement filed under the Securities Act of 1933, as amended.

For as long as we are an emerging growth company, unlike other public companies, we are eligible to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not “emerging growth companies.” These include, but are not limited to, (i) reduced obligations with respect to the disclosure of selected financial data in registration statements filed with the Securities and Exchange Commission, (ii) reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, (iii) an exception from compliance with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, and (iv) exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and the requirement to obtain shareholder approval of any golden parachute payments not previously approved.

As noted above, under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards that have different effective dates for public and private companies until such time as those standards apply to private companies. We intend to take advantage of such extended transition period. Since we would then not be required to comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies, our Consolidated Financial Statements may not be comparable to the financial statements of companies that comply with public company effective dates. If we were to elect to comply with these public company effective dates, such election would be irrevocable pursuant to Section 107 of the JOBS Act.

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 its income constitutes passive income (the “income test”) or (ii) 50% or more of our assets produce passive income (the “asset test”). In general, the total value of our assets for purposes of the asset test is determined based on the market price of our ordinary shares. As a result, fluctuations in the market price of our ordinary shares may cause us to become a PFIC. In addition, changes in the composition of our income or assets 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, 2014 and 2013. In addition, we do not expect to be a PFIC for U.S. federal income tax purposes for any future taxable year. However, we cannot assure you the Internal Revenue Service (the "IRS") will not successfully challenge this position.

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 Acts 1963-2013, 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.

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

Transfers of our ordinary shares effected by means of the transfer of book entry interests in DTC should not be subject to Irish stamp duty. However, if a shareholder holds our ordinary shares directly rather than beneficially through DTC any transfer of those ordinary shares could be subject to Irish stamp duty (currently at the rate of 1% of the higher of the price paid or the market value of the ordinary shares acquired). Payment of Irish stamp duty is generally a legal obligation of the transferee. The potential for stamp duty could adversely affect the price of your ordinary 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. At the date hereof, children have a tax-free threshold of €225,000 in respect of taxable gifts or inheritances received from their parents. 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

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Our corporate headquarters are located in Dublin, Ireland and our U.S. operations are located in South San Francisco, California. In South San Francisco, California, we occupy approximately 50,400 square feet of office and laboratory space under a lease which expires in November 2020, 14,000 square feet of which is occupied by a third party under a sublease which we entered into in December 2014. This sublease commenced in January 2015 and expires in December 2017. We believe that our facilities are sufficient to meet our current needs.

ITEM 3. LEGAL PROCEEDINGS

We are not currently a party to any material legal proceedings. We may at times be involved in litigation and other legal claims in the ordinary course of business. When appropriate in management's estimation, we may record reserves in our financial statements for pending litigation and other claims.

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 2014 | | |
| Fourth quarter | \$24.67 | \$17.00 |
| Third quarter | \$24.31 | \$16.71 |
| Second quarter | \$41.33 | \$18.52 |
| First quarter | \$49.24 | \$24.42 |
| Fiscal 2013 | | |
| Fourth quarter | \$30.55 | \$18.93 |
| Third quarter | \$22.48 | \$12.14 |
| Second quarter | \$14.00 | \$6.49 |
| First quarter | \$7.50 | \$5.64 |

On February 27, 2015, the closing price of our ordinary shares was \$26.58.

Holders

There were approximately 1,396 shareholders of record of our ordinary shares as of February 27, 2015. 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 less accumulated realized losses and includes reserves created by way of capital reduction. 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 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 accounts" of Prothena. The "relevant accounts" are either the last set of unconsolidated annual audited financial statements or other financial statements properly prepared in accordance with the Companies Acts, which give a "true and fair view" of our unconsolidated financial position and accord with accepted accounting practice. The relevant accounts 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 21, 2012 through December 31, 2014 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 25 MONTH CUMULATIVE TOTAL RETURN

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

| Cumulative Total Return as of | 12/21/2012 | 12/31/2012 | 6/30/2013 | 12/31/2013 | 6/30/2014 | 12/31/2014 |
|-------------------------------|------------|------------|-----------|------------|-----------|------------|
| Prothena Corporation plc | \$100 | \$102 | \$179 | \$ 368 | \$ 313 | \$ 288 |
| Nasdaq Composite Index | \$100 | \$100 | \$113 | \$ 138 | \$ 146 | \$ 157 |
| Nasdaq Biotechnology Index | \$100 | \$99 | \$126 | \$ 164 | \$ 186 | \$ 220 |

⁽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 Financial Transfers Act, 1992 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 Financial Transfers Act, 1992 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, 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 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 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).

Shares Held Through DTC

A transfers 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.

Shares Held Outside of DTC or Transferred Into or Out of DTC

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.

Our historical results of operations presented below may not be reflective of our financial position, results of operations and cash flows had we operated as a stand-alone public company for all periods prior to December 21, 2012. Prior to December 21, 2012, the Prothena Business operated as part of Elan and not as a separate stand-alone entity. Our Combined Financial Statements prior to December 21, 2012 have been prepared on a "carve-out" basis from the consolidated financial statements of Elan to represent our financial position and performance as if we had existed on a stand-alone basis during each of the fiscal years presented in the Consolidated Financial Statements. Central support costs have been allocated to us for the purposes of preparing the Consolidated Financial Statements based on our estimated usage of the resources. Our estimated usage of the central support resources was determined by estimating our portion of the most appropriate driver for each category of central support costs such as headcount or labor hours, depending on the nature of the costs. We believe that such allocations have been made on a reasonable basis, but may not necessarily be indicative of all of the costs that would have been incurred if we had operated on a standalone basis.

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, | | | | |
|---|-------------------------|-------------|-------------|-------------|-------------|
| | 2014 | 2013 | 2012 | 2011 | 2010 |
| Consolidated Statement of Operations Data: | | | | | |
| Collaboration revenue | \$50,320 | \$— | \$— | \$— | \$— |
| Revenue—related party | 534 | 676 | 2,658 | 507 | 1,243 |
| Total revenue | 50,854 | 676 | 2,658 | 507 | 1,243 |
| Operating expenses: | | | | | |
| Research and development | 38,452 | 26,052 | 34,139 | 24,172 | 9,787 |
| General and administrative | 19,051 | 15,051 | 9,929 | 5,579 | 3,618 |
| Total operating expenses | 57,503 | 41,103 | 44,068 | 29,751 | 13,405 |
| Loss from operations | (6,649) | (40,427) | (41,410) | (29,244) | (12,162) |
| Other income (expense): | | | | | |
| Interest income | 79 | 71 | 5 | — | — |
| Other income (expense), net | 231 | (225) | — | — | — |
| Total other income (expense) | 310 | (154) | 5 | — | — |
| Loss before income taxes | (6,339) | (40,581) | (41,405) | (29,244) | (12,162) |
| Provision for income taxes | 811 | 415 | 6 | 426 | 320 |
| Net loss | \$(7,150) | \$(40,996) | \$(41,411) | \$(29,670) | \$(12,482) |
| Basic and diluted net loss per share ⁽¹⁾ | \$(0.29) | \$(2.20) | \$(2.84) | \$(2.05) | \$(0.86) |
| Shares used to compute basic and diluted net loss per share | 24,672 | 18,615 | 14,593 | 14,497 | 14,497 |

| | December 31, | | | | |
|---|--------------|-----------|-----------|----------|-------|
| | 2014 | 2013 | 2012 | 2011 | 2010 |
| Consolidated Balance Sheet Data: | | | | | |
| Cash and cash equivalents ⁽¹⁾ | \$293,579 | \$176,677 | \$124,860 | \$— | \$— |
| Total assets | 304,116 | 182,410 | 129,283 | 3,618 | 3,278 |
| Other non-current liabilities | 2,188 | 1,734 | 1,055 | 1,650 | 1,384 |
| Total liabilities | 14,227 | 9,140 | 2,799 | 10,054 | 3,249 |
| Shareholders' and parent company equity (deficit) | 289,889 | 173,270 | 126,484 | (6,436) | (30) |

⁽¹⁾ Prior to the Separation and Distribution completed on December 20, 2012, we operated as part of Elan and not as a separate stand-alone entity. As a result, we did not have any ordinary shares outstanding and cash and cash equivalents prior to December 20, 2012. The calculation of basic and diluted net loss per share assumes that the 14,496,929 ordinary shares issued to Elan shareholders in connection with the separation from Elan have been outstanding for the years ended December 31, 2012 and 2011 and that the 3,182,253 ordinary shares issued to Elan upon separation have been outstanding since December 20, 2012.

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 strategy; the design and expected timing, scope, enrollment and results of our VITAL Amyloidosis Study for NEOD001; the expected enrollment and timing of reporting additional data from our ongoing Phase 1/2 study for NEOD001; the possible clinical benefit of NEOD001; the timing of reporting data from our Phase 1 single ascending dose and multiple ascending dose studies for PRX002; the possible clinical benefit of PRX002; the timing of initiating our Phase 1 single ascending dose and multiple ascending dose studies for PRX003 and the timing of proof-of-biology in Phase 1 of PRX003; research and development ("R&D") and general and administrative ("G&A") expenses in 2015; and the sufficiency of our cash and cash equivalents. Forward-looking statements may include words such as "may," "will," "should," "expect," "plan," "intend," "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "expect," "goal," "intend," "may," "objective," "plan," "predict," "potential," "positioned," "seek," "should," "target," "will," or 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 "Risk Factors" in this Form 10-K.

- our ability to obtain additional financing in future offerings;
- our operating losses;
- our ability to successfully complete research and development of our drug candidates;
- our ability to develop and commercialize products;
- our collaboration with Roche pursuant to the License Agreement;
- 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;
- restrictions on our ability to take certain actions due to tax rules and covenants with Elan;
- 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 the "Risk Factors" section 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

We are a late-stage clinical biotechnology company focused on the discovery, development and commercialization of novel protein immunotherapy programs for the potential treatment of diseases that involve amyloid or cell adhesion. We are developing antibody-based product candidates that target a number of potential indications including AL amyloidosis (NEOD001), Parkinson's disease and other related synucleinopathies (PRX002) and psoriasis and other inflammatory diseases (PRX003).

We are a public limited company formed under the laws of Ireland. We separated from Elan Corporation Limited (formerly Elan Corporation, plc ("Elan")), which subsequently became a wholly owned subsidiary of Perrigo Company plc ("Perrigo"), on December 20, 2012. After the separation from Elan, and the related distribution of the Company's ordinary shares to Elan's

shareholders (the "Separation and Distribution"), 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 business consists of a substantial portion of Elan's former drug discovery business platform, including Neotope Biosciences Limited and its wholly owned subsidiaries Onclave Therapeutics Limited and Prothena Biosciences Inc (which for the period prior to the Separation and Distribution we collectively refer to herein as the "Prothena Business"). Prior to December 21, 2012, the Prothena Business operated as part of Elan and not as a separate stand-alone entity. Our Financial Statements for the periods prior to December 21, 2012 have been derived from Elan's historical accounting records and reflect significant allocations of direct costs and expenses. All of the allocations and estimates in these Financial Statements are based on assumptions that we believe are reasonable. However, the Financial Statements do not necessarily represent our financial position or results of operations had we been operating as a separate independent entity. See "Critical Accounting Policies and Estimates" below as well as Note 2 of the "Notes to the Consolidated Financial Statements" included in Item 8 of this Form 10-K.

Recent Developments

NEOD001

In December 2014, we initiated The VITAL Amyloidosis Study, a Phase 3 clinical trial for NEOD001 in patients with AL amyloidosis. The trial is designed to support global regulatory approvals. We intend to enroll approximately 230 newly-diagnosed, treatment-naïve patients with cardiac dysfunction. Patients will be 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 is event-based, with all-cause mortality or cardiac hospitalizations as qualifying events. Secondary endpoints of the study include evaluation of the cardiac biomarker NT-proBNP, renal biomarker proteinuria, six-minute walk test, and multiple quality of life evaluations including the Short Form-36 and the Kansas City Cardiomyopathy Questionnaire. Prothena designed the study with 90% power to detect a 30% change in the event rate between the treatment and placebo groups with a two-sided alpha of 0.05. The trial allows for an interim analysis to assess the primary endpoint for efficacy and futility.

Concurrent with The VITAL Amyloidosis Study, a Phase 3 clinical trial, we are enrolling up to an additional 25 patients, with AL amyloidosis and selected persistent organ dysfunction, in an open-label expansion portion of the Phase 1/2 study. We plan to enroll 10 patients with cardiac dysfunction, 10 patients with renal dysfunction and five patients with peripheral neuropathy, all of whom will receive 24 mg/kg intravenously every 28 days. The expansion phase will continue to evaluate safety, tolerability, pharmacokinetics and immunogenicity of NEOD001 as well as the specific clinical activity against cardiac, renal and neuropathy endpoints.

NEOD001 received Fast Track designation from the U.S. Food and Drug Administration (the "FDA") in December 2014. The purpose of the Fast Track designation is to make important new drugs available to patients earlier.

PRX002

In April 2014, together with Roche, we initiated a Phase 1 clinical trial of PRX002. Results for this study are expected in March 2015. The study is a randomized, double-blind, placebo-controlled, single ascending dose study in healthy subjects designed to assess PRX002 for safety, tolerability, pharmacokinetics and immunogenicity. We received a \$15.0 million milestone payment from Roche upon initiation of this study under the License Agreement, as described below. In July 2014, together with Roche, we initiated a randomized, double-blind, placebo-controlled multiple ascending dose Phase 1 clinical trial of PRX002 in patients with Parkinson's disease. This multiple ascending dose study is designed to assess PRX002 for safety, tolerability, pharmacokinetics and immunogenicity and builds upon the Phase 1 single ascending dose study initiated in April 2014.

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 alpha-synuclein, including PRX002, which are referred to collectively as

“Licensed Products.” The License Agreement became effective following the expiration of the applicable Hart-Scott-Rodino waiting period on January 17, 2014, which triggered an upfront payment to us of \$30.0 million from Roche, which we received in February 2014.

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

We filed an Investigational New Drug Application ("IND") with the FDA for PRX002 and subsequently initiated a Phase 1 study in April 2014. In May 2014, we received a \$15.0 million milestone payment from Roche related to the initiation of the Phase 1 study for PRX002 in the clinic.

Following the Phase 1 study, Roche will be primarily responsible for developing, obtaining and maintaining regulatory approval for, and commercializing Licensed Products. Roche will also become 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 the \$15.0 million clinical milestone payment, Roche is also obligated to pay to us the following:

- up to \$380.0 million upon the achievement of 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., the parties will share all development and commercialization costs, as well as profits, all of which will be allocated 70% to Roche and 30% to us, for PRX002 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 PRX002 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. Outside the U.S., Roche will have responsibility for developing and commercializing the Licensed Products.

October 2013 Offering

In October 2013, we completed an underwritten public offering of an aggregate of 6,796,500 of our ordinary shares at a public offering price of \$22.00 per share, which consisted of 4,177,079 newly issued ordinary shares sold by us and 2,619,421 ordinary shares sold by Janssen Pharmaceutical, a wholly-owned subsidiary of Johnson & Johnson, as the selling shareholder. We received aggregate net proceeds of approximately \$84.5 million, after deducting the underwriting discount and estimated offering costs. We did not receive any proceeds from the sale of 2,619,421 ordinary shares sold, which represented Janssen Pharmaceutical's entire shareholding in Prothena.

During the year ended December 31, 2013 we recorded underwriting discounts and offering costs of \$7.4 million as an offset to the proceeds in additional paid in capital.

February 2014 Offering

In February 2014, Elan Science One Limited ("ESOL"), an indirect wholly owned subsidiary of Perrigo, sold 3,182,253 ordinary shares of Prothena. The ordinary shares were sold at a price to the public of \$26.00 per ordinary share, before the underwriting discount. As a result, ESOL and Perrigo no longer owned any ordinary shares of Prothena as of such sale.

We did not receive any of the proceeds from the offering. We paid the costs associated with the sale of these ordinary shares (other than the underwriting discount, fees and disbursements of counsel for the selling shareholder) pursuant to a Subscription and Registration Rights Agreement dated November 8, 2012 by and among us, Elan (acquired by Perrigo) and ESOL.

June 2014 Offering

In June 2014, we completed an underwritten public offering of an aggregate of 4,750,000 of our ordinary shares at a public offering price of \$22.50 per ordinary share. We received aggregate net proceeds of approximately \$102.5 million, after deducting the underwriting discount and estimated offering costs. In July 2014, the underwriters exercised their right to subscribe for and purchase an additional 712,500 ordinary shares, pursuant to which we received net proceeds of approximately \$14.9 million, after deducting the underwriting discount.

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For the year ended December 31, 2014 underwriting discount and offering expense of \$5.5 million were classified as an offset to the proceeds and recorded in additional paid in capital on the balance sheet.

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Basis of Presentation and Preparation of the Financial Statements

Our business consists of a substantial portion of Elan's former drug discovery business platform, including Neotope Biosciences Limited (now named Prothena Biosciences Limited) and its wholly owned subsidiaries Onclave Therapeutics Limited (now named Prothena Therapeutics Limited) and Prothena Biosciences Inc, and related tangible assets and liabilities.

Prior to December 21, 2012, the Prothena business operated as part of Elan and not as a separate stand-alone entity.

Our consolidated financial statements for the periods prior to December 21, 2012 have been prepared on a "carve-out" basis from the consolidated financial statements of Elan to represent our financial performance as if we had existed on a stand-alone basis during those periods.

Prior to the Separation and Distribution on December 20, 2012, centralized support costs were allocated to us for the purposes of preparing the consolidated financial statements based on our estimated usage of the resources. Our estimated usage of the centralized support resources was determined by estimating our portion of the most appropriate driver for each category of centralized support costs such as headcount or labor hours, depending on the nature of the costs. We believe that such allocations were made on a reasonable basis, but may not necessarily be indicative of the costs that would have been incurred if we had operated on a standalone basis. For additional information regarding the basis of preparation, refer to Note 2 of the "Notes to the Consolidated Financial Statements" included in Item 8 of this report.

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.

Carve-out of the Results of Operations, Financial Condition and Cash Flows of the Prothena Business

Prior to December 21, 2012, the Prothena Business operated as part of Elan and not as a separate stand-alone entity.

Our consolidated financial statements for the periods prior to December 21, 2012 have been prepared on a "carve-out" basis from the consolidated financial statements of Elan to represent the financial position and performance of Prothena as if we had existed on a stand-alone basis during those periods, and as if Financial Accounting Standards Board ("FASB") Accounting Standard Codification ("ASC") Topic 810, "Consolidation" ("ASC 810") had been applied throughout. The consolidated financial statements have been prepared in conformity with GAAP, by aggregating financial information from the components of Prothena described in Note 2 to the Consolidated Financial Statements.

The accompanying Consolidated Financial Statements include allocations of direct costs and indirect costs attributable to our operations for the periods prior to December 21, 2012. Indirect costs relate to certain support functions that were provided on a centralized basis within Elan. The support functions provided to us by Elan included, but were not limited to: accounting, information technology, taxation, legal, corporate strategy, investor relations, corporate governance and other professional services, employee benefit administration, including equity award and pension services, and cash and treasury management. Central support costs of our business for the year ended December 31, 2012 was \$7.7 million. These costs have been allocated to us for the purposes of preparing the consolidated financial statements based on our estimated usage of the resources. Our estimated usage of the central support resources was determined by estimating our portion of the most appropriate driver for each category of central support costs such as headcount or labor hours, depending on the nature of the costs. We believe that such allocations have been made on a reasonable basis, but may not necessarily be indicative of the costs that would have been incurred if we had operated on a standalone basis.

Revenue Recognition

Revenue is recognized when earned and non-refundable, when payment is reasonably assured, and when there is no future obligation with respect to the revenue, in accordance with the terms prescribed in the applicable contract.

Multiple Element Arrangements

Our revenues are generated primarily through our license, development and commercialization agreement. These types of agreements generally contain multiple elements, or deliverables, which may include (i) licenses to our

technology, (ii) R&D activities to be performed on behalf of the collaborative partner, and (iii) in certain cases, services or obligations in connection with the manufacturing or supply of pre-clinical and clinical material. Payments to us under these arrangements typically include

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one or more of the following: non-refundable, upfront license fees; funding of research and/or development efforts; milestone payments; and royalties on future product sales.

Revenue under license, development and commercialization agreements is recognized based on the performance requirements of the contract. Determinations of whether persuasive evidence of an arrangement exists and whether delivery has occurred or services have been rendered are based on management's judgments regarding the fixed nature of the fees charged for deliverables and the collectability of those fees. Should changes in conditions cause management to determine that these criteria are not met for any new or modified transactions, revenue recognized could be adversely affected.

We recognize revenue related to license, development and commercialization agreements in accordance with the provisions of FASB ASC Topic 605-25, "Revenue Recognition - Multiple-Element Arrangements." We evaluate all deliverables within an arrangement to determine whether or not they provide value on a stand-alone basis. Based on this evaluation, the deliverables are separated into units of accounting. The arrangement consideration that is fixed or determinable at the inception of the arrangement is allocated to the separate units of accounting based on their relative selling prices. We may exercise significant judgment in determining whether a deliverable is a separate unit of accounting, as well as in estimating the selling prices of such unit of accounting. A change in such judgment could result in a significant change in the period in which revenue is recognized.

To determine the selling price of a separate deliverable, we use the hierarchy as prescribed in ASC Topic 605-25 based on vendor-specific objective evidence ("VSOE"), third-party evidence ("TPE") or best estimate of selling price ("BESP"). VSOE is based on the price charged when the element is sold separately and is the price actually charged for that deliverable. TPE is determined based on third party evidence for a similar deliverable when sold separately and BESP is the estimated selling price at which we would transact a sale if the elements of collaboration and license arrangements were sold on a stand-alone basis to the buyer. We may not be able to establish VSOE or TPE for the deliverables within collaboration and license arrangements, as we may not have a history of entering into such arrangements or selling the individual deliverables within such arrangements separately. In addition, there may be significant differentiation in these arrangements, which indicates that comparable third party pricing may not be available. We may determine that the selling price for the deliverables within collaboration and license arrangements should be determined using BESP. The process for determining BESP involves significant judgment on our part and includes consideration of multiple factors such as estimated direct expenses and other costs, and available data. Payments or full reimbursements resulting from our R&D efforts for those arrangements where such efforts are considered as deliverables are recognized as the services are performed and are presented on a gross basis so long as there is persuasive evidence of an arrangement, the fee is fixed or determinable, and collection of the related receivable is reasonably assured. However, such funding is recognized as a reduction of R&D expense when we engage in a R&D project jointly with another entity, with both entities participating in project activities and sharing costs and potential benefits of the project. Accordingly, reimbursement of R&D expenses pursuant to the cost-sharing provisions of our agreements with Roche is recognized as a reduction to R&D expense.

Milestone Revenue

We account for milestones under ASU No. 2010-17, "Milestone Method of Revenue Recognition". Under the milestone method, contingent consideration received from the achievement of a substantive milestone is recognized in its entirety in the period in which the milestone is achieved. A milestone is defined as an event (i) that can only be achieved based in whole or in part on either the entity's performance or on the occurrence of a specific outcome resulting from the entity's performance, (ii) for which there is substantive uncertainty at the date the arrangement is entered into that the event will be achieved, and (iii) that would result in additional payments being due to the entity. At the inception of an agreement that includes milestone payments, we evaluate whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether (a) the consideration is commensurate with either (1) the entity's performance to achieve the milestone, or (2) the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the entity's performance to achieve the milestone, (b) the consideration relates solely to past performance, and (c) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. We evaluate factors such as the scientific, regulatory, commercial and other risks that must be overcome to achieve the respective

milestone, the level of effort and investment required to achieve the respective milestone and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement in making this assessment. The conclusion as to whether milestone payments are substantive involves management judgment regarding the factors noted above.

We generally classify each of our milestones into one of three categories: (i) clinical milestones, (ii) regulatory and development milestones, and (iii) commercial milestones. Clinical milestones are typically achieved when a product candidate advances or completes a defined phase of clinical research. For example, a milestone payment may be due to us upon the initiation of a clinical trial for a new indication. Regulatory and development milestones are typically achieved upon acceptance of the submission for marketing approval of a product candidate or upon approval to market the product candidate by the FDA or other

regulatory authorities. For example, a milestone payment may be due to us upon filing of a Biologics License Application ("BLA") with the FDA. Commercial milestones are typically achieved when an approved pharmaceutical product reaches certain defined levels of net royalty sales by the licensee of a specified amount within a specified period.

Commercial milestone payments and milestone payments that are not deemed to be substantive will be accounted for as a contingent revenue payment with revenue recognized when all contingencies are lifted, which is expected to be upon achievement of the milestone, assuming all revenue recognition criteria are met.

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 collectability is reasonably assured. If profit sharing estimates are materially different from actual results it could impact the amount of revenue recognized in future periods. If the profit share cannot be reasonably estimated or collectability of the profit share amount is not reasonably assured, our portion of the profit share it could impact the amount of revenue recognized in future periods.

Royalty Revenue

We will recognize revenue from royalties based on licensees' sales of our products or products using its technologies. Royalties are recognized as earned in accordance with the contract terms when royalties from licensees can be reasonably estimated and collectability is reasonably assured. If we can no longer estimate royalty revenue or our estimates are materially different from actual results it could impact the amount of revenue recognized in future periods.

Research and Development

We expense R&D costs as incurred. R&D expenses include, but are not limited to, salary and benefits, share-based compensation, clinical trial activities, drug development and manufacturing, prior to FDA approval and third-party service fees, including clinical research organizations 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.

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. 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 base our assumptions on historical data when available or when not available, on a peer group of companies. Since we do not have a long trading history to use the volatility of our ordinary shares, the expected volatility was based on historical stock volatilities of peer group of companies over a period equal to the expected life of the options. 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.

However, 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 year ended December 31, 2014, 2013 and 2012 was \$5.6 million, \$3.1 million and \$7.5 million, respectively.

The expense for periods prior to December 21, 2012 was allocated to us based on awards from Elan equity plans granted to Elan employees who have, directly or indirectly, provided services to Prothena. Share-based compensation expense for restricted stock units was measured based on the closing fair market value of Elan's ordinary shares on the date of grant. We did not recognize any expense after December 20, 2012 in relation to the existing Elan equity-based awards as our employees were not required to provide service after the Separation and Distribution in order to receive the benefits of the awards. The share-based compensation expense relating to the changes described above is a non-recurring charge that is directly attributable to Elan as part of the Separation and Distribution of the Prothena Business, therefore it was not recorded in the Company's Consolidated Financial Statements after December 20, 2012.

Recent Accounting Pronouncements

As an emerging growth company under the Jumpstart Our Business Startups Act (the "JOBS Act"), unlike other public companies, we are eligible to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies. We have an extended transition period for adopting new or revised accounting standards that have different effective dates for public and private companies until such time as those standards apply to private companies.

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, 2014, 2013 and 2012

Revenue

| | Year Ended December 31, | | | Percentage Change | | |
|-----------------------|-------------------------|-------|---------|-------------------|-----------|------|
| | 2014 | 2013 | 2012 | 2014/2013 | 2013/2012 | |
| | (Dollars in thousands) | | | | | |
| Collaboration revenue | \$50,320 | \$— | \$— | nm | nm | |
| Revenue—related party | 534 | 676 | 2,658 | (21) |)% | (75) |
| Total revenue | \$50,854 | \$676 | \$2,658 | 7,423 | % | (75) |

nm = not meaningful

Total revenue was \$50.9 million, \$0.7 million and \$2.7 million for the years ended December 31, 2014, 2013 and 2012, respectively. Collaboration revenue includes reimbursements under our License Agreement with Roche, which became effective January 22, 2014.

Collaboration revenue for the year ended December 31, 2014 consisted of the following amounts from Roche under the License Agreement: a one-time, non-refundable, non-creditable upfront payment of \$30.0 million (which was recognized as collaboration license revenue), a clinical milestone of \$15.0 million (of which \$13.3 million was recognized as collaboration revenue), reimbursement for development costs of \$6.0 million (of which \$5.3 million was recognized as collaboration license revenue) and reimbursement for research services of \$1.7 million. The portion of the amounts recognized as collaboration revenue for the milestone and the development reimbursements were based on the relative selling price method in applying multiple element accounting, see Note 7 to the Consolidated Financial Statements "Roche License Agreement" for more information.

Related-party revenue for the years ended December 31, 2014, 2013 and 2012 was comprised of fees earned from the provision of research and development services to Elan (acquired by Perrigo). Total related-party revenue decreased by \$142,000, or 21%, during the year ended December 31, 2014, compared to the corresponding periods of the prior year, and decreased by \$2.0 million, or 75%, during the year ended December 31, 2013 compared to the prior year, due to a reduction in the scope of the R&D services provided to Elan. Since our research and development services agreement with Elan terminated in December 2014, we do not expect any related-party revenue in 2015.

Operating Expenses

| | Year Ended December 31, | | | Percentage Change | | |
|----------------------------|-------------------------|----------|----------|-------------------|-----------|----|
| | 2014 | 2013 | 2012 | 2014/2013 | 2013/2012 | |
| | (Dollars in thousands) | | | | | |
| Research and development | \$38,452 | \$26,052 | \$34,139 | 48 | % (24 |)% |
| General and administrative | 19,051 | 15,051 | 9,929 | 27 | % 52 | % |
| Total operating expenses | \$57,503 | \$41,103 | \$44,068 | 40 | % (7 |)% |

Total operating expenses consist of research and development ("R&D") expenses and general and administrative ("G&A") expenses. Our operating expenses for the years ended December 31, 2014, 2013 and 2012 were \$57.5 million, \$41.1 million and \$44.1 million, respectively.

Our R&D expenses primarily consisted of personnel costs and related expenses, including share-based compensation, external costs associated with preclinical activities and drug development related to our drug programs, including NEOD001, PRX002, PRX003 and our discovery programs, and costs of providing research services to Elan. Pursuant to our License Agreement with Roche, in 2014 we began making payments to Roche for our share of the development expenses incurred by Roche related to PRX002 program, which is included in our R&D expense. We recorded reimbursements from Roche for development and supply services based on the relative percentages as an offset to R&D expense.

Our G&A expenses primarily consist of professional services expenses and personnel costs and related expenses, including share-based compensation and, for the year ended December 31, 2012, certain centralized support costs that had been allocated to us by Elan based on our estimated usage of the resources. Share-based compensation expense during the year ended December 31, 2012 was also allocated to us by Elan. Additional information regarding the allocation of centralized G&A expenses is discussed above under the caption "Carve-out of the Results of Operations, Financial Condition and Cash Flows of the Prothena Business".

Research and Development Expenses

Our R&D expenses increased by \$12.4 million, or 48%, for the year ended December 31, 2014, compared to the prior year. The increase for the year ended December 31, 2014 compared to the prior year was primarily due to an increase in external expenses related to product manufacturing primarily associated with our PRX003 and NEOD001 programs offset in part by a reduction in PRX002 product manufacturing expense, increased external expenses for drug development including clinical trial cost associated with PRX002 and to a lesser extent NEOD001 programs, higher personnel costs including share-based compensation expenses, and \$1.4 million in expense reimbursements to Roche offset in part by \$2.4 million in expense reductions from reimbursements from Roche (including \$1.7 million for a portion of the \$15.0 million milestone received from Roche in the quarter ended June 30, 2014).

Our R&D expenses decreased by \$8.1 million, or 24%, for the year ended December 31, 2013 compared to the prior year. The decrease for the year ended December 31, 2013 was primarily due to a decrease in share-based compensation expense, lower personnel costs and lower external expenses related to the ELND005, discovery and NEOD001 programs, partially offset by increases in external expenses attributable to our PRX002 and PRX003 programs.

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 preclinical and drug development, 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 and PRX002) and other R&D expenses for the years ended December 31, 2014, 2013 and 2012, and the cumulative amounts to date (in thousands):

| | Year Ended December 31, | | | Cumulative to Date |
|--------------------------|-------------------------|---------|---------|--------------------|
| | 2014 | 2013 | 2012 | |
| NEOD001 ⁽¹⁾ | \$8,203 | \$3,763 | \$8,029 | \$35,439 |
| PRX002 ⁽²⁾ | 9,373 | 11,677 | 6,887 | 30,310 |
| Other R&D ⁽³⁾ | 20,876 | 10,612 | 19,223 | |

\$38,452

\$26,052

\$34,139

Cumulative R&D costs to date for NEOD001 include the costs incurred from the date when the program has been (1) 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.

Cumulative R&D costs to date for PRX002 and related antibodies 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. PRX002 cost include (2) payments to Roche for our share of the development expenses incurred by Roche related to PRX002 programs and 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, 2014, \$2.4 million was recorded as an offset to R&D expenses including \$1.7 million for a portion of the \$15.0 million milestone received from Roche in the quarter ended June 30, 2014.

Other R&D is comprised of preclinical development and discovery programs that have not had successful first (3) patient dosing in a Phase 1 clinical trial, including PRX003, and research costs we incurred in providing research services to Elan.

We expect our R&D expenses to increase in 2015 primarily due to increased spending for the NEOD001 program with the initiation of a Phase 3 clinical trial and to a lesser extent higher costs associated with development and manufacturing costs incurred under our cost-sharing arrangement with Roche including the continuation of the Phase 1 clinical trial for PRX002.

General and Administrative Expenses

Our G&A expenses increased by \$4.0 million, or 27%, for the year ended December 31, 2014 compared to the prior year, primarily due to higher personnel costs, including share-based compensation expenses, and higher external consulting expenses.

Our G&A expenses increased by \$5.1 million, or 52%, for the year ended December 31, 2013 compared to the prior year. G&A expenses during the year ended December 31, 2013 consisted primarily of professional services fees (including payments to Elan under a transitional services agreement), internal personnel costs and share-based compensation expense of \$2.1 million. G&A expenses during the year ended December 31, 2012 were presented on a "carve-out" basis and consisted of \$2.2 million of direct expense incurred by the Prothena Business and \$7.7 million of indirect expenses which was based on an allocation to the Prothena Business by Elan.

We expect our G&A expenses to increase moderately in 2015 over the prior year as the result of increases in personnel, legal and other administrative expenses associated with being a growing public company.

Other Income (Expense)

| | Year Ended December 31, | | | Percentage Change | | |
|------------------------------|-------------------------|---------|------|-------------------|------------|----|
| | 2014 | 2013 | 2012 | 2014/2013 | 2013/2012 | |
| | (Dollars in thousands) | | | | | |
| Interest income | \$79 | \$71 | \$5 | 11 | % 1,320 | % |
| Other income (expense), net | 231 | (225) | — | (203) |)% nm | |
| Total Other Income (Expense) | \$310 | \$(154) | \$5 | (301) |)% (3,180) |)% |

nm = not meaningful

Interest income increased by \$8,000, or 11%, for the year ended December 31, 2014 compared to the prior year, primarily due to higher balances in our cash and money market accounts. Other income (expense), net for the year ended December 31, 2014 was higher primarily due to foreign exchange income from transactions with vendors denominated in Euros.

Interest income increased by \$66,000 for the year ended December 31, 2013 compared to the prior year primarily due to interest earned on our cash and money market accounts. For the year ended December 31, 2012, no interest income was allocated to the Prothena Business by Elan. Other income (expense), net for the year ended December 31, 2013 was primarily made up of foreign exchange losses from transactions with vendors denominated in Euros.

Provision for Income Taxes

| | Year Ended December 31, | | | Percentage Change | |
|--|-------------------------|------|------|-------------------|-----------|
| | 2014 | 2013 | 2012 | 2014/2013 | 2013/2012 |

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(Dollars in thousands)

| | | | | | | | |
|----------------------------|-------|-------|-----|----|---|-------|---|
| Provision for income taxes | \$811 | \$415 | \$6 | 95 | % | 6,817 | % |
|----------------------------|-------|-------|-----|----|---|-------|---|

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The tax provisions were \$811,000, \$415,000 and \$6,000 for the years ended December 31, 2014, 2013 and 2012, respectively. The tax provisions for all periods presented reflect U.S. federal taxes associated with nominal, recurring profits attributable to intercompany services that the Company's U.S. subsidiary performs for the Company. No tax benefit has been recorded related to tax losses recognized in Ireland and any deferred tax assets for those losses are offset by a valuation allowance.

Subsequent to our separation from Elan, we began to file our 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. Prior to the separation from Elan, income taxes as presented in the consolidated financial statements represented current and deferred income taxes of Elan attributed to us in a manner that is systematic, rational and consistent with the asset and liability method prescribed by the accounting guidance for income taxes. Our income tax provision prior to the separation from Elan was prepared under the "separate return method." The separate return method applies the accounting guidance for income taxes to the standalone financial statements as if we were a separate taxpayer and a stand-alone enterprise.

Liquidity and Capital Resources

Overview

| | December 31, 2014 | December 31, 2013 |
|-------------------------------|----------------------|----------------------|
| Working capital | \$287,236 | \$170,816 |
| Cash and cash equivalents | 293,579 | 176,677 |
| Total assets | 304,116 | 182,410 |
| Other non-current liabilities | 2,188 | 1,734 |
| Total liabilities | 14,227 | 9,140 |
| Total shareholders' equity | 289,889 | 173,270 |

Working capital was \$287.2 million at December 31, 2014, an increase of \$116.4 million from working capital of \$170.8 million as of December 31, 2013. This increase was principally attributable to a higher net cash and cash equivalents balance resulting from the net proceeds of \$117.3 million from our June 2014 public offering, as well as the \$45.0 million in upfront and milestone payments from Roche.

As of December 31, 2014, we had \$293.6 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, 2014, \$16.6 million of our outstanding cash and cash equivalents related to U.S. operations that management asserted was permanently reinvested. 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 preclinical studies; the costs of clinical manufacturing and of establishing commercial manufacturing arrangements; the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims; the costs and timing of capital asset purchases; our ability to establish research collaborations, strategic collaborations, licensing or other arrangements; the costs to satisfy our obligations under current and potential future collaborations; and the timing, receipt, and amount of revenues or royalties, if any, from any approved drug candidates. Pursuant to the License Agreement with Roche, in the U.S., we and Roche will share all development and commercialization costs, as well as profits, all of which will be allocated 70% to Roche and 30% to us, for PRX002 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. 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.

Prior to the Separation and Distribution, our operating and capital resource requirements were funded by Elan. As part of the Separation and Distribution, Elan made a cash investment in us of \$99.0 million, which we have been using to fund working

capital expenses and for other general corporate purposes. Additionally, a wholly-owned subsidiary of Elan made a cash payment of \$26.0 million to subscribe for 18% of our outstanding ordinary shares (as calculated immediately following the subscription).

June 2014 Offering

In June 2014, the Company completed an underwritten public offering of an aggregate of 4,750,000 of its ordinary shares at a public offering price of \$22.50 per ordinary share. The Company received aggregate net proceeds of approximately \$102.5 million, after deducting the underwriting discount and estimated offering costs.

In July 2014, the underwriters exercised their option to subscribe for and purchase an additional 712,500 ordinary shares, pursuant to which the Company received net proceeds of approximately \$14.9 million, after deducting the underwriting discount of approximately \$1.1 million.

October 2013 Equity Financing

In October 2013, we completed an underwritten public offering of an aggregate of 6,796,500 of our ordinary shares at a public offering price of \$22.00 per share, which consisted of 4,177,079 newly issued ordinary shares sold by us and 2,619,421 shares sold by Janssen Pharmaceutical, a wholly-owned subsidiary of Johnson & Johnson, as the selling shareholder. We received aggregate net proceeds of approximately \$84.5 million, after deducting the underwriting discount and estimated offering costs. We did not receive any proceeds from the sale of 2,619,421 ordinary shares sold, which represented Janssen Pharmaceutical's remaining shareholding in Prothena.

Cash Flows for the Year Ended December 31, 2014, 2013 and 2012

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

| | Year Ended December 31, | | |
|---|-------------------------|-------------|-------------|
| | 2014 | 2013 | 2012 |
| Net cash used in operating activities | \$(683) | \$(32,098) | \$(42,072) |
| Net cash used in investing activities | (499) | (535) | (1,301) |
| Net cash provided by financing activities | 118,084 | 84,450 | 168,233 |
| Net increase in cash and cash equivalents | \$116,902 | \$51,817 | \$124,860 |

Cash Used in Operating Activities

Net cash used in operating activities was \$0.7 million for the year ended December 31, 2014, primarily due to receipt of the upfront payment of \$30.0 million, the clinical milestone payment of \$15.0 million and reimbursement for research and development costs of \$7.0 million from Roche, recognized as revenue, partially offset by \$57.5 million in expenses (adjusted to exclude non-cash charges) and increases in accrued liabilities.

Net cash used in operating activities was \$32.1 million and \$42.1 million for the years ended December 31, 2013 and 2012, respectively, in each case consisted primarily of net losses (adjusted to exclude non-cash charges) and changes in working capital accounts. The decrease in cash used in operating activities from 2012 was primarily due to fact that in the prior year more cash was used to settle liabilities at the end of 2012 with a liability balance of \$2.8 million compared to our December 31, 2013 ending liabilities balance of \$9.1 million extending cash available for operations.

Cash Used in Investing Activities

Net cash used in investing activities was \$0.5 million, \$0.5 million and \$1.3 million for the years ended December 31, 2014, 2013 and 2012, respectively, consisting primarily of purchases of property and equipment.

Cash Provided by Financing Activities

Net cash provided by financing activities for the year ended December 31, 2014 was \$118.1 million, primarily from net proceeds from our June 2014 public offering and to a lesser extent from issuance of common stock upon exercise of stock options and excess tax benefit from stock option exercises. Net cash provided by financing activities was \$84.5 million for the year ended December 31, 2013 primarily consisting of net proceeds from our October 2013 equity financing. Net cash provided by financing activities was \$168.2 million for the year ended December 31, 2012, primarily consisting of funding provided by Elan and the issuance of ordinary shares to a wholly owned subsidiary of Elan.

Off-Balance Sheet Arrangements

At December 31, 2014, 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 main contractual obligations as of December 31, 2014 consist of operating leases of \$12.1 million, contractual obligations under license agreements of \$1.5 million and purchase obligations of \$3.2 million (of which \$3.1 million is included in the accrued current liabilities). Purchase obligations represent our non-cancelable purchase commitments to suppliers. Operating leases represent our future minimum rental commitments under our operating leases. In December 2014, we entered into a sublease agreement with a third party to sublease a portion of our leased facility. This sublease agreement has a three-year term (with options to extend for another year) which commenced in January 2015. The Company expects to receive future minimum payments from this sublease of \$0.5 million, \$0.5 million and \$0.3 million in 2015, 2016 and 2017, respectively, which is an offset to the lease payments below.

The following is a summary of our contractual obligations as of December 31, 2014 (in thousands):

| | Total | 2015 | 2016 | 2017 | 2018 | 2019 | Thereafter |
|---|-----------|----------|----------|----------|----------|----------|------------|
| Operating leases | \$ 12,109 | \$ 1,821 | \$ 1,938 | \$ 2,017 | \$ 2,096 | \$ 2,180 | \$ 2,057 |
| Purchase Obligations | 3,197 | 3,197 | — | — | — | — | — |
| Contractual obligations under license agreements ⁽¹⁾ | 1,450 | 260 | 110 | 110 | 110 | 110 | 750 |
| Total | \$ 16,756 | \$ 5,278 | \$ 2,048 | \$ 2,127 | \$ 2,206 | \$ 2,290 | \$ 2,807 |

⁽¹⁾ 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 agreement with a contract manufacturer for clinical supplies which is denominated in Euros. We recorded a gain on foreign currency exchange rate differences of approximately \$234,000 during the year ended December 31, 2014 and a loss on foreign currency exchange rate differences of \$226,000 in during the year ended December 31, 2013. At this time, we do not believe that our foreign exchange risk is material. However, if we continue or increase our business activities that require the use of foreign currencies, we may incur losses if the Euro and other such currencies strengthen against the U.S. dollar.

Interest Rate Risk

Our exposure to interest rate risk is limited to our cash equivalents, which consist of accounts maintained in money market funds. We have assessed that there is no material exposure to interest rate risk given the nature of money market funds. In general, money market funds are not subject to interest rate risk because the interest paid on such funds fluctuates with the prevailing interest rate. Accordingly, our interest income fluctuates with short-term market conditions.

In the future, we anticipate that our exposure to interest rate risk will primarily be related to our investment portfolio. 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 accounts receivables are due from two parties, Roche our collaboration partner and Elan (acquired by Perrigo) to whom we provided R&D services. We do not believe that our credit risk is significant. As of December 31, 2014, our receivables from these customers totaled \$1.8 million.

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

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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.

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ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

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Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders

Prothena Corporation plc:

We have audited the accompanying consolidated balance sheets of Prothena Corporation plc and subsidiaries as of December 31, 2014 and 2013, and the related consolidated statements of operations, shareholders' equity, and cash flows for each of the years in the three year period ended December 31, 2014. 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 conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of Prothena Corporation plc and subsidiaries as of December 31, 2014 and 2013, and the results of their operations and their cash flows for each of the years in the three year period ended December 31, 2014, in conformity with U.S. generally accepted accounting principles.

/s/ KPMG LLP
San Francisco, California
March 12, 2015

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

| | December 31, 2014 | December 31, 2013 |
|---|----------------------|----------------------|
| Assets | | |
| Current assets: | | |
| Cash and cash equivalents | \$293,579 | \$176,677 |
| Receivable from Roche | 1,729 | — |
| Receivable from related party | 30 | 58 |
| Deferred tax assets | 167 | 81 |
| Prepaid expenses and other current assets | 3,770 | 1,406 |
| Total current assets | 299,275 | 178,222 |
| Non-current assets: | | |
| Property and equipment, net | 3,121 | 3,372 |
| Deferred tax assets, non-current | 1,720 | 816 |
| Total non-current assets | 4,841 | 4,188 |
| Total assets | \$304,116 | \$182,410 |
| Liabilities and Shareholders' Equity | | |
| Current liabilities: | | |
| Accounts payable | \$4,722 | \$1,790 |
| Accrued research and development | 2,285 | 1,542 |
| Income taxes payable | 57 | 184 |
| Other current liabilities | 4,975 | 3,890 |
| Total current liabilities | 12,039 | 7,406 |
| Non-current liabilities: | | |
| Income taxes payable, non-current | 98 | — |
| Deferred rent | 2,090 | 1,734 |
| Total non-current liabilities | 2,188 | 1,734 |
| Total liabilities | 14,227 | 9,140 |
| Commitments and contingencies (Note 6) | | |
| Shareholders' equity: | | |
| Euro deferred shares, €22 nominal value: | — | — |
| Authorized shares — 10,000 at December 31, 2014 and 2013 | | |
| Issued and outstanding shares — none at December 31, 2014 and 2013 | | |
| Ordinary shares, \$0.01 par value: | 274 | 219 |
| Authorized shares — 100,000,000 at December 31, 2014 and 2013 | | |
| Issued and outstanding shares — 27,388,005 and 21,856,261 at December 31, 2014 and 2013, respectively | | |
| Additional paid-in capital | 338,106 | 214,392 |
| Accumulated deficit | (48,491 |) (41,341) |
| Total shareholders' equity | 289,889 | 173,270 |
| Total liabilities and shareholders' equity | \$304,116 | \$182,410 |

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, | | |
|--|-------------------------|-------------|-------------|
| | 2014 | 2013 | 2012 |
| Collaboration revenue | \$50,320 | \$— | \$— |
| Revenue—related party | 534 | 676 | 2,658 |
| Total revenue | 50,854 | 676 | 2,658 |
| Operating expenses: | | | |
| Research and development | 38,452 | 26,052 | 34,139 |
| General and administrative | 19,051 | 15,051 | 9,929 |
| Total operating expenses | 57,503 | 41,103 | 44,068 |
| Loss from operations | (6,649 |) (40,427 |) (41,410 |
| Other income (expense): | | | |
| Interest income | 79 | 71 | 5 |
| Other income (expense), net | 231 | (225 |) — |
| Total other income (expense) | 310 | (154 |) 5 |
| Loss before income taxes | (6,339 |) (40,581 |) (41,405 |
| Provision for income taxes | 811 | 415 | 6 |
| Net loss | \$(7,150 |) \$(40,996 |) \$(41,411 |
| Basic and diluted net loss per share attributable to holders of ordinary shares | \$(0.29 |) \$(2.20 |) \$(2.84 |
| Shares used to compute basic and diluted net loss per share attributable to holders of ordinary shares | 24,672 | 18,615 | 14,593 |

See accompanying Notes to Consolidated Financial Statements.

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

| | Year Ended December 31, | | |
|--|-------------------------|--------------|------------|
| | 2014 | 2013 | 2012 |
| Operating activities | | | |
| Net loss | \$ (7,150) | \$ (40,996) | (41,411) |
| Adjustments to reconcile net loss to cash used in operating activities: | | | |
| Depreciation and amortization | 743 | 660 | 468 |
| Share-based compensation | 5,597 | 3,128 | 6,098 |
| Excess tax benefit from share-based award exercises | (242) | — | — |
| Deferred income taxes | (990) | (538) | — |
| Gain on disposal of fixed asset | (19) | (29) | — |
| Changes in operating assets and liabilities: | | | |
| Receivable from Roche | (1,729) | — | — |
| Receivable from related party | 28 | 165 | (223) |
| Other assets | (2,352) | (721) | (467) |
| Accounts payable, accruals and other liabilities | 5,431 | 6,233 | (6,537) |
| Net cash used in operating activities | (683) | (32,098) | (42,072) |
| Investing activities | | | |
| Purchases of property and equipment | (526) | (564) | (1,301) |
| Proceeds from disposal of fixed asset | 27 | 29 | — |
| Net cash used in investing activities | (499) | (535) | (1,301) |
| Financing activities | | | |
| Proceeds from issuance of ordinary shares in public offering, net | 117,348 | 84,534 | — |
| Proceeds from issuance of ordinary shares to Elan | — | — | 26,000 |
| Proceeds from funding provided by Elan | — | — | 145,233 |
| Repayment of funding provided by Elan | — | — | (3,000) |
| Post separation adjustments to the funding provided by Elan | — | (84) | — |
| Proceeds from issuance of ordinary shares upon exercise of stock options | 494 | — | — |
| Excess tax benefit from share-based award exercises | 242 | — | — |
| Net cash provided by financing activities | 118,084 | 84,450 | 168,233 |
| Net increase in cash and cash equivalents | 116,902 | 51,817 | 124,860 |
| Cash and cash equivalents, beginning of the year | 176,677 | 124,860 | — |
| Cash and cash equivalents, end of the period | \$ 293,579 | \$ 176,677 | \$ 124,860 |
| Supplemental disclosures of cash flow information | | | |
| Cash paid for income taxes, net of refunds | \$ 1,588 | \$ 796 | \$ — |
| Supplemental disclosures of non-cash investing and financing activities | | | |
| Acquisition of property and equipment under accounts payable and accrued liabilities | \$ — | \$ 26 | \$ — |
| Offering costs in accounts payable and accrued liabilities | \$ — | \$ 82 | \$ — |
| Receivable from stock option exercises | \$ 6 | \$ — | \$ — |

See accompanying Notes to Consolidated Financial Statements.

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

| | Ordinary Shares | | Additional Paid-in Capital | Accumulated Deficit | Parent Company Equity | Total Shareholders' Equity (Deficit) |
|--|-----------------|--------|----------------------------------|------------------------|-----------------------------|---|
| | Shares | Amount | | | | |
| Balances at December 31, 2011 | — | \$— | \$— | \$— | \$(6,436) | \$(6,436) |
| Contribution of net assets to Prothena and issuance of ordinary shares | 14,496,929 | 145 | 100,684 | — | (100,829) | — |
| Issuance of ordinary shares to Elan | 3,182,253 | 32 | 25,968 | — | — | 26,000 |
| Share-based compensation | — | — | — | — | 6,098 | 6,098 |
| Net funding provided by Elan | — | — | — | — | 142,233 | 142,233 |
| Net loss | — | — | — | (345) | (41,066) | (41,411) |
| Balances at December 31, 2012 | 17,679,182 | 177 | 126,652 | (345) | — | 126,484 |
| Issuance of ordinary shares in public offering, net of issuance costs of \$7.4 million | 4,177,079 | 42 | 84,411 | — | — | 84,453 |
| Share-based compensation | — | — | 3,128 | — | — | 3,128 |
| Post separation adjustment to the funding provided by Elan | — | — | 201 | — | — | 201 |
| Net loss | — | — | — | (40,996) | — | (40,996) |
| Balances at December 31, 2013 | 21,856,261 | 219 | 214,392 | (41,341) | — | 173,270 |
| Issuance of ordinary shares in public offering, net of issuance costs of \$5.5 million | 5,462,500 | 54 | 117,375 | — | — | 117,429 |
| Share-based compensation | — | — | 5,597 | — | — | 5,597 |
| Excess tax benefit from share-based award exercises | — | — | 242 | — | — | 242 |
| Issuance of ordinary shares upon exercise of stock options | 69,244 | 1 | 500 | — | — | 501 |
| Net loss | — | — | — | (7,150) | — | (7,150) |
| Balances at December 31, 2014 | 27,388,005 | \$274 | \$338,106 | \$(48,491) | \$— | \$289,889 |

See accompanying Notes to Consolidated Financial Statements.

Notes to the Consolidated Financial Statements

1. Organization

Description of Business

Prothena Corporation plc and its subsidiaries (“Prothena” or the “Company”) is a late-stage clinical biotechnology company focused on the discovery, development and commercialization of novel protein immunotherapy programs for the potential treatment of diseases that involve amyloid or cell adhesion. The Company is developing antibody-based product candidates that target a number of potential indications including AL amyloidosis (NEOD001), Parkinson’s disease and other related synucleinopathies (PRX002) and psoriasis and other inflammatory diseases (PRX003).

The Company is a public limited company formed under the laws of Ireland. The Company separated from Elan Corporation Limited, formerly Elan Corporation, plc (“Elan”), which was subsequently acquired by Perrigo Company plc (“Perrigo”), on December 20, 2012. Prothena’s business consists of a substantial portion of Elan’s former drug discovery business platform, including Neotope Biosciences Limited and its wholly owned subsidiaries Onclave Therapeutics Limited and Prothena Biosciences Inc (which for the period prior to the separation and distribution are collectively referred to herein as the “Prothena Business”). Prior to December 21, 2012, the Prothena Business operated as part of Elan and not as a separate stand-alone entity. After the separation from Elan, and the related distribution of the Company’s ordinary shares to Elan’s shareholders (the “Separation and Distribution”), the Company’s 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.

Liquidity and Business Risks

As of December 31, 2014, the Company had an accumulated deficit of \$48.5 million and cash and cash equivalents of \$293.6 million.

In February 2014, the Company received \$30.0 million upfront payment pursuant to a License, Development, and Commercialization Agreement (the "License Agreement") with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. (collectively, "Roche"). In addition, in May 2014 the Company received a \$15.0 million payment from Roche upon achievement of a clinical milestone related to the initiation of the Phase 1 study for PRX002 in April 2014. In June and July 2014, the Company sold an aggregate of 5,462,500 ordinary shares for net proceeds of approximately \$117.4 million, after deducting the underwriting discount and offering expenses, in an underwritten public offering. Based on the Company’s business plans, management believes that the Company’s cash and cash equivalents at December 31, 2014 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 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 collaboration with Roche, 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.

The Company is dependent on Boehringer Ingelheim to manufacture clinical supplies for its therapeutic antibody programs. An inability to obtain product supply on a timely basis could have a material adverse impact on the Company’s business, financial condition and results of operations.

2. Summary of Significant Accounting Policies

Basis of Preparation and Presentation of Financial Information

The Prothena Business historically operated as part of Elan and not as a separate stand-alone entity. Prior to the separation on December 20, 2012, the consolidated financial statements of Prothena have been prepared on a “carve-out” basis from the consolidated financial statements of Elan to represent the financial position and performance of Prothena as if the Company had existed on a stand-alone basis and as if Financial Accounting Standards Board (“FASB”) Accounting Standard Codification (“ASC”)

Topic 810, "Consolidation" ("ASC 810") had been applied throughout. The accompanying Consolidated Financial Statements prior to December 21, 2012 include only those assets and liabilities that management has determined are specifically identifiable to Prothena and allocations of direct costs and indirect costs attributable to the Company's operations. The indirect costs included in the Company's Consolidated Financial Statements relate to certain centralized support functions that were provided by Elan. All intragroup transactions within the Prothena Business have been eliminated in the Consolidated Financial Statements and are not disclosed.

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. The financial information for all periods prior to the Separation and Distribution were prepared by aggregating financial information from the components of Prothena as described above. All financial information presented after December 20, 2012 includes the accounts of the Company and its wholly-owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

Prior to December 21, 2012, the centralized support functions provided to the Company by Elan included, but were not limited to, accounting, information technology, taxation, legal, corporate strategy, investor relations, corporate governance and other professional services, employee benefit administration, including equity award and pension services, and cash and treasury management. Centralized support costs allocated to the Prothena business for the year ended December 31, 2012 was \$7.7 million. These costs were allocated to the Company for the purposes of preparing the Consolidated Financial Statements based on estimated usage of the resources by the Prothena Business. The estimated usage of the central support resources allocated to the Prothena Business was determined by estimating its portion of the most appropriate driver for each category of central support costs such as headcount or labor hours, depending on the nature of the costs. The Company believes that such allocations were made on a reasonable basis, but may not necessarily be indicative of the costs that would have been incurred if the Prothena Business had operated on a standalone basis.

Elan used a centralized approach to manage substantially all of its liquid resources and to finance its operations and, as a result, no separate cash accounts for Prothena were historically maintained, and debt and liquid resources maintained at the Elan group level are not included in the accompanying Consolidated Financial Statements prior to the separation. Elan historically funded all of Prothena's operating and capital resource requirements. The parent company equity balance in the Consolidated Financial Statements constitutes Elan's investment in Prothena and represents the excess of total liabilities over total assets (or excess of total assets over total liabilities), including the netting of intercompany funding balances between Prothena and Elan. Changes in parent company equity represent Elan's net investment in Prothena, after giving effect to its net loss, contributions from Elan in the form of share-based compensation to Prothena's employees and net funding provided by Elan.

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.

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.

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:

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| | |
|-----------------------------|---|
| | Useful Life |
| Machinery and equipment | 4-7 years |
| Leasehold improvements | Shorter of expected useful life or lease term |
| Purchased computer software | 4 years |

Impairment of Long-lived Assets

Long-lived assets are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable or the estimated useful life is no longer appropriate. If circumstances require that a long-lived asset be tested for possible impairment, the Company compares the undiscounted cash flows expected to be generated by the asset to the carrying amount of the asset. If the carrying amount of the long-lived asset is not recoverable on an undiscounted cash flow basis, an impairment is recognized to the extent that the carrying amount exceeds its fair value. The Company determines fair value using the income approach based on the present value of expected future cash flows. The Company's cash flow assumptions consider historical and forecasted revenue and operating costs and other relevant factors. There were no impairment charges recorded during the years ended December 31, 2014, 2013 and 2012.

Deferred Rent

Deferred rent consists of the difference between cash payments and the recognition of rent expense on a straight-line basis for the buildings the Company occupies. The leases provide for fixed increases in minimum annual rental payments, as well as rent free periods. The total amount of rental payments due over the lease terms are being charged to rent expense ratably over the life of the leases. 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.

Revenue Recognition

Revenue is recognized when earned and non-refundable, when payment is reasonably assured, and when there is no future obligation with respect to the revenue, in accordance with the terms prescribed in the applicable contract.

Multiple Element Arrangements

The Company's revenues are generated primarily through its license, development and commercialization agreement. These types of agreements generally contain multiple elements, or deliverables, which may include (i) licenses to the Company's technology, (ii) R&D activities to be performed on behalf of the collaborative partner, and (iii) in certain cases, services or obligations in connection with the manufacturing or supply of pre-clinical and clinical material. Payments to the Company under these arrangements typically include one or more of the following: non-refundable, upfront license fees; funding of research and/or development efforts; milestone payments; and royalties on future product sales.

Revenue under license, development and commercialization agreements is recognized based on the performance requirements of the contract. Determinations of whether persuasive evidence of an arrangement exists and whether delivery has occurred or services have been rendered are based on management's judgments regarding the fixed nature of the fees charged for deliverables and the collectability of those fees.

The Company recognizes revenue related to license, development and commercialization agreements in accordance with the provisions of FASB ASC Topic 605-25, "Revenue Recognition - Multiple-Element Arrangements." The Company evaluates all deliverables within an arrangement to determine whether or not they provide value on a stand-alone basis. Based on this evaluation, the deliverables are separated into units of accounting. The arrangement consideration that is fixed or determinable at the inception of the arrangement is allocated to the separate units of accounting based on their relative selling prices.

To determine the selling price of a separate deliverable, the Company uses the hierarchy as prescribed in ASC Topic 605-25 based on vendor-specific objective evidence ("VSOE"), third-party evidence ("TPE") or best estimate of selling price ("BESP"). VSOE is based on the price charged when the element is sold separately and is the price actually charged for that deliverable. TPE is determined based on third party evidence for a similar deliverable when sold separately and BESP is the estimated selling price at which we would transact a sale if the elements of collaboration and license arrangements were sold on a stand-alone basis to the buyer.

Payments or full reimbursements resulting from our R&D efforts for those arrangements where such efforts are considered as deliverables are recognized as the services are performed and are presented on a gross basis so long as there is persuasive evidence of an arrangement, the fee is fixed or determinable, and collection of the related receivable is reasonably assured. However,

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such funding is recognized as a reduction of R&D expense when the Company engages in a R&D project jointly with another entity, with both entities participating in project activities and sharing costs and potential benefits of the project.

Milestone Revenue

The Company accounts for milestones under ASU No. 2010-17, "Milestone Method of Revenue Recognition". Under the milestone method, contingent consideration received from the achievement of a substantive milestone is recognized in its entirety in the period in which the milestone is achieved. A milestone is defined as an event (i) that can only be achieved based in whole or in part on either the entity's performance or on the occurrence of a specific outcome resulting from the entity's performance, (ii) for which there is substantive uncertainty at the date the arrangement is entered into that the event will be achieved, and (iii) that would result in additional payments being due to the entity. At the inception of an agreement that includes milestone payments, the Company evaluates whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether (a) the consideration is commensurate with either (1) the entity's performance to achieve the milestone, or (2) the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the entity's performance to achieve the milestone, (b) the consideration relates solely to past performance, and (c) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. The Company evaluates factors such as the scientific, regulatory, commercial and other risks that must be overcome to achieve a particular milestone, the level of effort and investment required to achieve such milestone and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement in making this assessment.

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 U.S. Food and Drug Administration (the "FDA") or other regulatory authorities. For example, a milestone payment may be due to the Company upon filing of a Biologics License Application ("BLA") with the FDA. Commercial milestones are typically achieved when an approved pharmaceutical product reaches certain defined levels of net royalty sales by the licensee of a specified amount within a specified period.

Commercial milestone payments and milestone payments that are not deemed to be substantive will be accounted for as a contingent revenue payment with revenue recognized when all contingencies are lifted, which is expected to be upon achievement of the milestone, assuming all revenue recognition criteria are met.

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 collectability is reasonably assured.

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 collectability is reasonably assured.

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 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.

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 bases its assumptions on historical data when available or when not available, on a peer group of 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 9 for further information).

Total share-based compensation expense recorded in the Consolidated Financial Statements for the year ended December 31, 2012 was allocated to the Company based on awards from Elan equity plans granted to Elan employees who have, directly or indirectly, provided services to the Company.

With respect to Elan options and RSUs held by Elan employees that became employees of Prothena effective upon the Separation and Distribution:

- unvested Elan options and RSUs that would otherwise have vested within twelve months following the effective date of the Separation and Distribution vested immediately upon the Separation and Distribution, with the RSUs (which by their terms are settled upon vesting) settled in Elan ordinary shares or Elan American Depository Shares ("ADSs") in accordance with their terms;

- other unvested Elan options and RSUs were forfeited; and

- all vested Elan options (including options the vesting of which were accelerated as described above) will be required to be exercised for Elan ordinary shares or Elan ADSs within twelve months of the effective date of the Separation and Distribution, or will be forfeited.

However, for Elan employees who are aged 55 or over with at least five years of service and who became employees of the Company, unvested Elan options and RSUs became fully vested and exercisable upon the Separation and Distribution, with the RSUs (which, by their terms, are settled upon vesting) settled in Elan ordinary shares or Elan ADSs in accordance with their terms, and with Elan options being exercisable for one year following the Separation and Distribution. Similarly, unvested Elan options and RSUs held by Dr. Schenk, became fully vested and exercisable upon the Separation and Distribution, with the RSUs (which, by their terms are settled upon vesting) settled in Elan ordinary shares or Elan ADSs in accordance with their terms, and with Elan options being exercisable for two years following the Separation and Distribution.

The Company did not recognize any expense after December 20, 2012 in relation to the existing Elan equity-based awards as the Company's employees are not required to provide service after the Separation and Distribution in order to receive the benefits of the awards. The share-based compensation expense relating to the changes described above is a non-recurring charge that is directly attributable to Elan as part of the Separation and Distribution of the Prothena Business, therefore it was not recorded in the Company's Consolidated Financial Statements after December 20, 2012.

Income Taxes

Subsequent to the separation from Elan, Prothena began to file 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. Prior to the separation from Elan, income taxes as presented in the Consolidated Financial Statements represented current and deferred income taxes of Elan attributed to the Company in a manner that is systematic, rational and consistent with the asset and liability method prescribed by the accounting

guidance for income taxes. The Company's income tax provision prior to the separation from Elan was prepared under the "separate return method." The separate return method applies the accounting guidance for income taxes to the standalone Consolidated Financial Statements as if the Company was a separate taxpayer and a standalone enterprise.

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.

Significant 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 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 less the weighted average number of unvested restricted ordinary shares subject to the right of repurchase. 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.

Comprehensive Loss

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

Segment and Concentration of Risks

The Company operates 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 Company’s accounts receivables are due from two parties, Roche and Elan (acquired by Perrigo) to whom the Company provided R&D services. The Company does not believe that its credit risk from accounts receivables is significant. As of December 31, 2014, receivables from these parties totaled \$1.8 million. All of the Company’s long-lived assets were held in the U.S. The Company’s accounts receivable from related party are from Elan located in Ireland for all periods presented. For the year ended December 31, 2014, receivable from Roche includes 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 Statements of Operations consists of collaboration revenue related to the upfront payment from Roche under the License Agreement, payment from Roche upon achievement of a clinical milestone and reimbursement for research and development services and fees earned from the provision of nonclinical research support to Elan, primarily in the areas of safety, toxicology and regulatory. The

fees charged to Elan were calculated based on the expenses incurred by the Company in the provision of those R&D services, plus a contractually determined mark-up of those expenses.

The Company utilizes Boehringer Ingelheim in Switzerland for its clinical drug product supply for therapeutic antibody programs. An inability to obtain drug product supply on a timely basis could have a material adverse impact on the Company's business, financial condition and results of operations.

Emerging Growth Company Status

As an Emerging Growth Company under the Jumpstart Our Business Startups Act (the “JOBS Act”), the Company is eligible to take advantage of certain exemptions from various reporting requirements that apply to other public companies that are not Emerging Growth Companies. The Company has an extended transition period for adopting new or revised accounting standards that have different effective dates for public and private companies until such time as those standards apply to private companies.

Recent Accounting Pronouncements

Except for the standards below, there have been no new accounting pronouncements or changes to accounting pronouncements during the year ended December 31, 2014, as compared to the recent accounting pronouncements described in our 2013 Form 10-K, that are of significance or potential significance to the Company.

In May 2014, the FASB issued Accounting Standards Update 2014-09 (ASU 2014-09), Revenue from Contracts with Customers. ASU 2014-09 supersedes the revenue recognition requirements in Revenue Recognition (Topic 605), and requires entities to recognize revenue in a way that depicts the transfer of promised goods and services to customers in an amount that reflects the consideration to which the entity expects to be entitled to in exchange for those goods or services. ASU 2014-09 is effective for annual reporting periods beginning after December 15, 2016, including interim periods within that reporting period, which for the Company is January 1, 2017. Early adoption is not permitted. The standard permits the use of either retrospective or cumulative effect transition method. The Company is currently evaluating the potential impact the adoption of ASU 2014-09 will have on its consolidated financial statements. The Company has not yet selected a transition method nor has it determined the effect of the standard on its ongoing financial reporting.

In July 2013, the FASB issued ASU 2013-11, "Income Taxes" (Topic 740): "Presentation of an Unrecognized Tax Benefit when a Net Operating Loss Carryforward, a Similar Tax Loss, or a Tax Credit Carryforward Exists" on the financial statement presentation of unrecognized tax benefits. The new guidance provides that a liability related to an unrecognized tax benefit would be presented as a reduction of a deferred tax asset for a net operating loss carryforward, a similar tax loss or a tax credit carryforward if such settlement is required or expected in the event the uncertain tax position is disallowed. The Company has presented in these Consolidated Financial Statements its unrecognized tax benefits as a reduction in its deferred tax assets as of December 31, 2014 and 2013.

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 consist of \$262.5 million and \$153.3 million in money market funds included in cash and cash equivalents at December 31, 2014 and

December 31, 2013, respectively.

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4. Composition of Certain Balance Sheet Items

Property and Equipment, net

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

| | December 31 | |
|---|-------------|----------|
| | 2014 | 2013 |
| Machinery and equipment | \$5,481 | \$5,649 |
| Leasehold improvements | 2,214 | 1,927 |
| Purchased computer software | 137 | 85 |
| | 7,832 | 7,661 |
| Less: accumulated depreciation and amortization | (4,711 |) (4,289 |
| Property and equipment, net | \$3,121 | \$3,372 |

Depreciation expense was \$0.7 million, \$0.7 million and \$0.5 million for the years ended December 31, 2014, 2013 and 2012, respectively.

Other Current Liabilities

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

| | December 31 | |
|------------------------------|-------------|---------|
| | 2014 | 2013 |
| Payroll and related expenses | \$3,138 | \$2,800 |
| Professional services | 1,169 | 616 |
| Deferred rent | 172 | 138 |
| Accrued offering costs | — | 82 |
| Other | 496 | 254 |
| Other current liabilities | \$4,975 | \$3,890 |

5. Net Loss Per Ordinary Share

Basic net loss per ordinary share is calculated by dividing net loss by the weighted-average number of ordinary shares outstanding during the period. Shares used in diluted net loss 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 periods presented and therefore diluted net loss per ordinary share is equal to basic net loss per ordinary share.

Prior to the Separation and Distribution, the Company operated as part of Elan and not as a separate entity. As a result, the Company did not have any ordinary shares outstanding prior to December 21, 2012. The calculation of basic and diluted net loss per ordinary share assumes that the 14,496,929 ordinary shares issued to Elan shareholders in connection with the separation from Elan were outstanding for the year ended December 31, 2012 and that the 3,182,253 ordinary shares issued to Elan upon separation have been outstanding since December 20, 2012.

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

| | Year Ended December 31, | | |
|--|-------------------------|-------------|-------------|
| | 2014 | 2013 | 2012 |
| Numerator: | | | |
| Net loss | \$(7,150) | \$(40,996) | \$(41,411) |
| Denominator: | | | |
| Weighted-average ordinary shares outstanding | 24,672 | 18,615 | 14,593 |
| Net income (loss) per share attributable to holders of ordinary shares: | | | |
| Basic and diluted net loss per share | \$(0.29) | \$(2.20) | \$(2.84) |
| 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, | | |
|---|-------------------------|-------|-------|
| | 2014 | 2013 | 2012 |
| Stock options to purchase ordinary shares | 2,612 | 1,974 | 1,005 |
| 6. Commitments and Contingencies | | | |

Operating Lease

The Company has a noncancelable operating lease agreement for office and research and development space in the U.S. that expires in November 2020 with an estimated annual rent payment of approximately \$2.0 million. The lease provides for approximately 50,400 of rentable square feet at a base rent that increases annually. In December 2014, the Company entered into a noncancelable operating sublease agreement with a third party to sublease a portion of this leased facility. This sublease agreement has a three-year term which commences in January 2015 (with options to extend for another year). The Company expects to receive future minimum payments from its sublease of \$0.5 million, \$0.5 million and \$0.3 million in 2015, 2016 and 2017, respectively, which is an offset to the lease payments below.

Future minimum payments under noncancelable operating leases and future minimum rentals to be received under the sublease as of December 31, 2014, are as follows (in thousands):

| Year Ended December 31, | Operating Lease | Sublease Rental |
|-------------------------|-----------------|-----------------|
| 2015 | \$1,821 | \$(455) |
| 2016 | 1,938 | (523) |
| 2017 | 2,017 | (316) |
| 2018 | 2,096 | — |
| 2019 | 2,180 | — |
| Thereafter | 2,057 | — |
| Total | \$12,109 | \$(1,294) |

The Company recognizes rent expense 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 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. The Company records payments received from its sublease as offset against the current period rent expense. Rent expense was \$1.8 million, \$1.3 million and \$1.3 million for the years ended December 31, 2014, 2013 and 2012, respectively.

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, 2014 and 2013.

Commitments

As of December 31, 2014, the Company had non-cancelable purchase commitments to suppliers for \$3.2 million of which \$3.1 million is included in accrued current liabilities, and contractual obligations under license agreements of \$1.5 million of which less than \$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, 2014 (in thousands):

| | Total | 2015 | 2016 | 2017 | 2018 | 2019 | Thereafter |
|---|---------|---------|-------|-------|-------|-------|------------|
| Purchase Obligations | \$3,197 | \$3,197 | \$— | \$— | \$— | \$— | \$— |
| Contractual obligations under license agreements ⁽¹⁾ | 1,450 | 260 | 110 | 110 | 110 | 110 | 750 |
| Total | \$4,647 | \$3,457 | \$110 | \$110 | \$110 | \$110 | \$750 |

⁽¹⁾ 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.

7. Roche License Agreement

Overview

In December 2013, the Company entered into the License Agreement with Roche to develop and commercialize certain antibodies that target alpha-synuclein, including PRX002, which are referred to collectively as "Licensed Products." On January 22, 2014, the License Agreement with Roche became effective following the expiration of the Hart-Scott-Rodino waiting period. Upon the effectiveness of the License Agreement, 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 PRX002 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 potentially including incorporation of Roche's proprietary Brain Shuttle™ technology to potentially increase delivery of therapeutic antibodies to the brain. The License Agreement provides that Roche would make an upfront payment to the Company of \$30.0 million, which was received in February 2014, and the clinical milestone payment of \$15.0 million triggered by the initiation of the Phase 1 study for PRX002 in the clinic, which was received in May 2014.

For PRX002, Roche is also obligated to pay:

- up to \$380.0 million upon the achievement of 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.

Roche bears 100% of the cost of conducting the research activities under the License Agreement. In the U.S., the parties will share all development and commercialization costs, as well as profits, all of which will be allocated 70% to Roche and 30% to the Company, for PRX002 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 PRX002 and subsequently initiated a Phase 1 study in 2014. Following the Phase 1 study, Roche will be primarily responsible for developing, obtaining and maintaining

regulatory approval for, and commercializing Licensed Products. Roche will also become 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, the Company has an option under the License Agreement to co-promote PRX002 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 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 contract, the Company concluded that this agreement does not qualify as a collaboration under ASC 808 because Prothena is not an active participant as a result of the opt-out provision. The Company believes that Roche is the principal in the sales transactions with third parties as it is the primary obligor, bearing inventory and credit risk. The Company will record its share of pre-tax commercial profit generated from the collaboration with Roche, as collaboration revenue when the profit share can be reasonably estimated and collectability is reasonably assured. 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 the establishment of a field sales force and other activities to support the Company's commercialization efforts, will be recorded as SG&A expense and will be factored into the computation of the profit and loss share. The Company will record the portion of the net receivable related to commercialization activities as collaboration revenue.

Multiple Element Accounting

The License Agreement was evaluated under ASC 605-25, "Multiple Element Arrangements". The License Agreement includes the following deliverables: (1) an exclusive royalty bearing license, with the right to sublicense to develop and commercialize certain antibodies that target alpha-synuclein, including PRX002 delivered at the effective date; (2) the Company's obligation to supply clinical material as requested by Roche for a period up to twelve months;

(3) the Company's obligation to provide manufacturing related services to Roche for a period up to twelve months; (4) the Company's obligation to provide development activities under the development plan including the preparation and filing of the IND and initiation of the Phase I clinical trial estimated to be carried out over the next two years; and (5) the Company's obligation to provide indeterminate research services for up to three years at rates that are not significantly discounted and fully reimbursable by Roche.

All of the deliverables were deemed to have stand-alone value and to meet the criteria to be accounted for as separate units of accounting under ASC 605-25. Factors considered in the determination included, among other things, for the license, the

research and development capabilities of Roche and Roche's sublicense rights, and for the remaining deliverables the fact that they are not proprietary and can be and have been provided by other vendors.

The amount of allocable arrangement consideration is limited to amounts that are fixed or determinable excluding refund rights, concessions or performance bonuses. As such, the Company will exclude from such allocable consideration the milestone payments and royalties regardless of the probability of receipt because such payments are not considered fixed or determinable. Such milestone payments and royalties will be evaluated separately as the related contingencies are resolved. Consideration for research services were not allocated as the amount is not fixed and determinable and is not at a significant incremental discount. There are no refund rights, concessions or performance bonuses to consider.

The Company allocated the fixed and determinable consideration to the license and other deliverables using the relative selling price method based on the best estimate of selling price for the license and third party evidence for the remaining deliverables. The best estimate of selling price for the 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 license granted to Roche under the License Agreement included the market opportunity for commercialization of PRX002 in the U.S. and the Royalty Territory (for jointly funded products the Royalty Territory is worldwide except for the U.S. for all Licensed Products that are not jointly funded the Royalty Territory is worldwide), the probability of successfully developing and commercializing PRX002, the remaining development costs for PRX002, and the estimated time to commercialization of PRX002.

The Company's discounted cash flow model included several market conditions and entity-specific inputs, including the likelihood that clinical trials 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.

The Company concluded that a change in the assumptions used to determine the BESP of the license deliverable would not have a significant effect on the allocation of arrangement consideration. Based on the relative selling price method, the amount that the Company recognized on the effective date of the agreement concurrent with the delivery of the license and know-how was limited to the lesser of the amount otherwise allocable using the relative selling price method, which based on the discounted cash flow model was determined to be \$35.6 million, or the non-contingent amount which was the \$30.0 million upfront fee. As the remaining deliverables are delivered, any consideration received will be allocated to license revenue and the other deliverables based on their relative percentages until such time as the full allocated consideration of \$35.6 million has been recognized as license revenue, and the balance of the monetary consideration will be recorded as an offset against R&D expenses. The Company recognized the \$30.0 million upfront payment as collaboration license revenue in the first quarter of 2014.

The Company recognizes the research reimbursement as collaboration revenue as earned. The Company recognized \$1.7 million as collaboration service revenue during the year ended December 31, 2014 for research reimbursement from Roche. Cost sharing payments to Roche are recorded as R&D expenses. The Company recognized \$1.4 million in R&D expense for payments made to Roche during the year ended December 31, 2014. Reimbursement for development costs from Roche under the cost-sharing arrangement are allocated between license revenue and an offset to R&D expenses based on the relative selling price method until the full allocated consideration of \$35.6 million has been recognized as license revenue, after which the full reimbursement would be recorded as an offset to R&D expenses. Reimbursement for development costs from Roche during the year ended December 31, 2014 was \$6.0 million of which \$5.3 million was recognized as collaboration license revenue and \$0.7 million was recognized as an offset to R&D expenses.

Milestone Accounting

In April 2014, the Company together with Roche initiated a Phase 1 clinical trial of PRX002. As a result of this initiation, the Company received a \$15.0 million milestone payment from Roche under the License Agreement. The Company concluded that the \$15.0 million clinical milestone triggered upon the initiation of the Phase 1 study from

PRX002 in the clinic is consistent with the definition of a substantive milestone included in ASU No. 2010-17, "Milestone Method of Revenue Recognition". 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 recognized payments related to the achievement of this milestone when the milestone was achieved. The milestone payment was allocated to the units of accounting based on the relative selling price method for income statement classification purposes. In the year ended December 31, 2014, the Company recognized \$13.3 million of the \$15.0 million milestone payment as collaboration revenue and \$1.7 million as an offset to R&D expenses.

The clinical and regulatory milestones under the License Agreement after the point at which the Company could opt-out are not considered to be substantive due to the fact that active participation in the development activities that generate the milestones is not required by the License Agreement, and the Company can opt-out of these activities. There are no refund 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 similar to the commercial milestone, which will be accounted for as contingent revenue payments with revenue recognized upon achievement of the milestone assuming all revenue recognition criteria are met. The Company did not achieve any of these other clinical and regulatory milestones under the License Agreement during the year ended December 31, 2014.

8. Shareholders' Equity

Ordinary Shares

As of December 31, 2014, the Company had 100,000,000 ordinary shares authorized for issuance with a par value of \$0.01 per ordinary share and 27,388,005 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, 2014, 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, 2014. 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.

February 2014 Offering

In February 2014, Elan Science One Limited ("ESOL"), an indirect wholly owned subsidiary of Perrigo, sold 3,182,253 ordinary shares of Prothena at a price to the public of \$26.00 per ordinary share, before the underwriting discount. As a result, ESOL and Perrigo no longer own any ordinary shares of Prothena.

The Company did not receive any of the proceeds from the offering, and the total number of the Company's ordinary shares outstanding did not change as a result of this offering. The Company paid the costs associated with the sale of these ordinary shares (other than the underwriting discount, fees and disbursements of counsel for the selling shareholder) pursuant to a Subscription and Registration Rights Agreement dated November 8, 2012 by and between the Company, Elan and ESOL.

June 2014 Offering

In June 2014, the Company completed an underwritten public offering of an aggregate of 4,750,000 of its ordinary shares at a public offering price of \$22.50 per ordinary share. The Company received aggregate net proceeds of approximately \$102.5 million, after deducting the underwriting discount and estimated offering costs.

In connection with this offering, the Company granted the underwriters the right to subscribe for and purchase, as applicable, up to an additional 712,500 ordinary shares. In July 2014, the underwriters exercised such right to subscribe for and purchase an aggregate of 712,500 ordinary shares, pursuant to which the Company received net proceeds of approximately \$14.9 million, after deducting the underwriting discount of approximately \$1.1 million.

For the year ended December 31, 2014 underwriting discount and offering expense of \$5.5 million were classified as an offset to the proceeds and recorded in additional paid in capital on the balance sheet.

October 2013 Offering

In October 2013, the Company completed an underwritten public offering of an aggregate of 6,796,500 of its ordinary shares at a public offering price of \$22.00 per share, which consisted of 4,177,079 newly issued ordinary shares sold by the Company and 2,619,421 ordinary shares sold by Janssen Pharmaceutical, a wholly-owned subsidiary of Johnson & Johnson, as the selling shareholder. The Company received aggregate net proceeds of approximately \$84.5 million, after deducting the underwriting discount and estimated offering costs. The Company did not receive any proceeds from the sale of 2,619,421 ordinary shares sold, which represented Janssen Pharmaceutical's entire shareholding in Prothena.

During the year ended December 31, 2013 underwriting discounts and offering costs of \$7.4 million were recorded as an offset to the proceeds and recorded in additional paid in capital.

9. Share-Based Compensation

The Prothena Corporation plc Amended and Restated 2012 Long Term Incentive Plan ("LTIP")

Employees and consultants of the Company, its subsidiaries and affiliates, as well as members of the Board, are eligible to receive equity awards under the LTIP. The LTIP provides for the grant of stock options, including incentive stock options and nonqualified stock options, stock appreciation rights ("SARS"), restricted shares, restricted share units ("RSUs"), cash or stock-based performance awards and other share-based awards to eligible individuals. Options under the LTIP may be granted for periods up to ten years. All options issued to date have had a ten year life. In March 2014, the Board amended the LTIP, which was subsequently approved by the shareholders on May 21, 2014 during the Company's Annual General Meeting of Shareholders. The Company's shareholders approved the increase in the aggregate number of ordinary shares authorized for issuance under the LTIP by 2,900,000 ordinary shares, to a total of 5,550,000 ordinary shares.

The Company granted 720,500 and 1,978,000 share options during the year ended December 31, 2014 and 2013, respectively, under the LTIP. The Company's option awards generally vest over four years. As of December 31, 2014, 2,868,676 ordinary shares remain available for grant and options to purchase 2,612,080 ordinary shares granted from the LTIP were outstanding with a weighted-average exercise price of approximately \$13.13 per share.

Prothena 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 highly 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 expected volatility was based on historical stock volatilities of several of the Company's publicly traded comparable companies over a period equal to the expected life of the options, as the Company does not have a long enough trading history to use the volatility of its own ordinary shares. 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 2017 related to unvested share-based payment awards at December 31, 2014 is \$16.0 million. The weighted-average period over which the unearned share-based compensation is expected to be recognized is 2.6 years. If there are any modifications or cancellations of the underlying unvested securities, the Company may be required to accelerate, increase or decrease 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, 2014 and 2013 was based on awards granted under the LTIP while the share-based compensation expense for the year ended December 31, 2012 was allocated to the Company based on awards from Elan equity plans granted to Elan employees who have, directly or indirectly, provided services to the Company. The following table summarizes share-based compensation expense for the periods presented (in thousands):

| | Year Ended December 31, | | |
|---|-------------------------|----------|----------|
| | 2014 | 2013 | 2012 |
| Research and development ⁽¹⁾ | \$ 2,270 | \$ 980 | \$ 6,093 |
| General and administrative | 3,327 | 2,148 | 5 |
| Total direct expense | \$ 5,597 | \$ 3,128 | \$ 6,098 |
| General and administrative — allocated | — | — | 1,445 |
| | \$ 5,597 | \$ 3,128 | \$ 7,543 |

(1) Includes \$108,000 and \$320,000 for the year ended December 31, 2014 and 2013, respectively, of share-based compensation expense related to options granted to a consultant.

The following table summarizes share-based compensation expense by type of award (in thousands):

| | Year Ended December 31, | | |
|--|-------------------------|----------|----------|
| | 2014 | 2013 | 2012 |
| Stock options | \$ 5,597 | \$ 3,128 | \$ 2,621 |
| Restricted stock units | — | — | 3,477 |
| Total direct | \$ 5,597 | \$ 3,128 | \$ 6,098 |
| Share-based compensation expense-allocated | — | — | 1,445 |
| | \$ 5,597 | \$ 3,128 | 7,543 |

For the years ended December 31, 2014, 2013 and 2012, the Company recognized tax benefits from share-based awards of \$1.0 million, \$0.4 and nil, respectively.

The fair value of the options granted to employees and non-employee directors during the years ended December 31, 2014 and 2013 is 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, | |
|--|-------------------------|--------|
| | 2014 | 2013 |
| Expected volatility | 84.4% | 84.0% |
| Risk-free interest rate | 1.8% | 1.2% |
| Expected dividend yield | —% | —% |
| Expected life (in years) | 6.0 | 6.0 |
| Weighted average grant date fair value | \$19.97 | \$5.22 |

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 share option activity during the year ended December 31, 2014:

| | Options | Weighted Average Exercise Price | Weighted Average Remaining Contractual Term (years) | Aggregate Intrinsic Value (in thousands) |
|--|-----------|--|---|---|
| Outstanding at December 31, 2013 | 1,973,500 | \$7.50 | 9.17 | \$37,528 |
| Granted | 720,500 | 28.02 | | |
| Exercised | (69,244) | 7.23 | | |
| Canceled | (12,676) | 15.97 | | |
| Outstanding at December 31, 2014 | 2,612,080 | \$13.13 | 8.45 | \$25,298 |
| Vested and expected to vest at December 31, 2014 | 2,535,376 | \$13.00 | 8.44 | \$24,788 |
| Vested at December 31, 2014 | 1,000,307 | \$7.35 | 8.15 | \$13,448 |

During the years ended December 31, 2014 and 2013, the total intrinsic value of options exercised was \$1.5 million and nil, respectively, determined as of the date of exercise.

The following table summarizes information about the Company's share options outstanding as of December 31, 2014:

| Range of Exercise Prices | Options Outstanding | | | Options Exercisable | | |
|--------------------------|---------------------|---|---------------------------------------|---------------------|---------------------------------------|--------|
| | Number of Options | Weighted - Average Remaining Contractual Life (Years) | Weighted Average Exercise Price | Number of Options | Weighted Average Exercise Price | |
| \$6.03 | \$6.03 | 450,937 | 8.06 | \$6.03 | 216,562 | \$6.03 |
| 6.41 | 6.41 | 807,381 | 8.08 | 6.41 | 465,271 | 6.41 |
| 6.65 | 6.65 | 50,000 | 8.21 | 6.65 | 50,000 | 6.65 |
| 6.73 | 6.73 | 366,000 | 8.25 | 6.73 | 170,478 | 6.73 |
| 8.21 | 22.14 | 336,062 | 8.89 | 17.51 | 89,246 | 15.34 |
| 22.16 | 23.11 | 37,500 | 9.74 | 22.86 | — | — |
| 24.26 | 24.26 | 30,000 | 8.84 | 24.26 | 8,750 | 24.26 |
| 29.52 | 29.52 | 25,000 | 9.09 | 29.52 | — | — |
| 29.81 | 29.81 | 479,200 | 9.09 | 29.81 | — | — |
| 37.02 | 37.02 | 30,000 | 9.25 | 37.02 | — | — |
| \$6.03 | \$37.02 | 2,612,080 | 8.45 | \$13.13 | 1,000,307 | \$7.35 |

Elan's Share-based Compensation Awards

Prior to the Separation and Distribution of the Prothena Business on December 20, 2012, the Company's employees had received share-based compensation awards under Elan's equity compensation plans and, therefore, the following disclosures pertain to share-based compensation expense that was allocated to the Prothena Business related to Elan's share-based equity awards. Elan's equity award program provided for the issuance of stock options, RSUs and other equity awards to its employees, including employees that have directly and indirectly provided service to the Prothena Business. The share-based payment compensation expense recorded in the Consolidated Financial Statements for the year ended December 31, 2012 includes all of the share-based payment expenses directly attributable to the Prothena Business and an allocation of indirect expenses that have been deemed attributable to the Prothena Business. The Company did not recognize any expense after December 20, 2012 in relation to the existing Elan equity-based awards as the Company's employees are not required to provide service after the Separation and Distribution in order to receive the benefits of the awards. The share-based compensation expense relating to the changes described below is a non-recurring charge that is directly attributable to Elan as part of the Separation and Distribution of the Prothena Business, and therefore was not recorded in the Company's Consolidated Financial Statements after December 20, 2012.

Share-based Compensation Expense

Share-based compensation expense was measured and recognized based on estimated grant date fair values. These awards include employee stock options and RSUs, and share purchases related to the Employee Equity Purchase Plan (“EEPP”). Share-based compensation cost for stock options and ordinary shares issued under Elan’s EEPP was estimated at the grant date based

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on each option's fair value as calculated using an option-pricing model. Share-based compensation expense for RSUs was measured based on the closing fair market value of Elan's ordinary shares on the date of grant. The value of awards expected to vest was recognized as an expense over the requisite service periods prior to the separation and distribution. Estimating the fair value of share-based awards as of the grant or vest date using an option-pricing model, such as the binomial model, was affected by Elan's share price as well as assumptions regarding a number of complex variables. These variables included, but were not limited to, the expected share price volatility over the term of the awards, risk-free interest rates, and actual and projected employee exercise behaviors.

Restricted Share Units

Elan granted RSUs to its employees, including employees that have directly and indirectly provided service to the Prothena Business. The RSUs generally vest between one and three years from the grant date and shares are issued to RSU holders as soon as practicable following vesting. The fair value of services received by the Prothena Business in return for the RSUs is measured by reference to the fair value of the underlying shares at grant date. The total fair value expensed over the vesting terms of RSUs that became fully vested was \$0.5 million in 2012.

Share Options

Share options are granted at the price equal to the market value at the date of grant and will expire on a date not later than 10 years after their grant. Options generally vest between one and four years from the grant date.

Equity-settled share-based payments expense recognized in the "Carve-out" Combined Financial Statements are based on the fair value of the awards measured at the date of grant. The graded-vesting attribution method is used for recognizing share-based compensation expense over the requisite service period for each separately vesting tranche of award as though the awards were, in substance, multiple awards.

The fair value of share options is calculated using a binomial option-pricing model, taking into account the relevant terms and conditions. The binomial option-pricing model is used to estimate the fair value of the Company's share options because it better reflects the possibility of exercise before the end of the options' life. The binomial option-pricing model also integrates possible variations in model inputs, such as risk-free interest rates and other inputs, which may change over the life of the options. The amount recognized as an expense is adjusted each period to reflect actual and estimated future levels of vesting.

The implied volatility for traded options on Elan's shares with remaining maturities of at least one year was used to determine the expected volatility assumption required in the binomial model. The risk-free interest rate assumption is based upon observed interest rates appropriate for the term of the stock option awards. The dividend yield assumption is based on the history and expectation of dividend payouts.

As share-based compensation expense recognized in the "Carve-out" Combined 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 historical experience and estimated future turnover.

The fair value of options granted during the year ended December 31, 2012 was estimated using the binomial option-pricing model with the following weighted-average assumptions:

| | Year Ended December 31, 2012 | |
|------------------------------|------------------------------------|---|
| Expected volatility | 60.1 | % |
| Risk-free interest rate | 0.9 | % |
| Expected dividend yield | — | % |
| Expected life ⁽¹⁾ | 4.9 - 6.8 | |
| Weighted average fair value | \$6.66 | |

The expected life of options granted, as derived from the output of the binomial model, ranged from 4.9 to 6.8 ⁽¹⁾ years in 2012. The contractual life of the options, which is not more than 10 years from the date of grant, was used as an input into the binomial model.

10. Income Taxes

Subsequent to the Separation and Distribution from Elan, the Company began to file its own 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. Prior to the separation from Elan, income taxes as presented in the Consolidated Financial Statements represented current and deferred income taxes of Elan attributed to the Company in a manner that is systematic, rational and consistent with the asset and liability method prescribed by the accounting guidance for income taxes. The Company's income tax provision prior to the separation from Elan was prepared under the "separate return method." The separate return method applies the accounting guidance for income taxes to the standalone financial statements as if Prothena were a separate taxpayer and a standalone enterprise. 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, | | |
|--|-------------------------|--------------|--------------|
| | 2014 | 2013 | 2012 |
| Ireland | \$ (9,714 |) \$ (42,523 |) \$ (35,898 |
| U.S. | 3,375 | 1,942 | (5,507 |
| Loss before provision for income taxes | \$ (6,339 |) \$ (40,581 |) \$ (41,405 |

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

| | Year Ended December 31, | | |
|----------------------------------|-------------------------|-----------|----------|
| | 2014 | 2013 | 2012 |
| Current: | | | |
| U.S. Federal | \$ 1,855 | \$ 958 | \$ 26 |
| U.S. State | 1 | (5 |) — |
| Ireland | — | — | — |
| Total current provision | \$ 1,856 | \$ 953 | \$ 26 |
| Deferred: | | | |
| U.S. Federal | \$ (1,045 |) \$ (538 |) \$ (20 |
| U.S. State | — | — | — |
| Ireland | — | — | — |
| Total deferred benefit | (1,045 |) (538 |) \$ (20 |
| Total provision for income taxes | \$ 811 | \$ 415 | \$ 6 |

Excess tax benefits associated with share-based compensation deductions are credited to shareholders' equity. The reductions in income taxes payable resulting from share-based compensation deductions that were credited to stockholder's equity were approximately \$0.2 million, nil and nil, for the years ended December 31, 2014, 2013 and 2012, respectively.

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 and due to U.S. income taxed at different rates. Following is a reconciliation between income taxes computed at the Irish statutory tax rate and the provision for income taxes for each of the fiscal periods presented (in thousands):

| | Year Ended December 31, | | |
|--|-------------------------|------------|------------|
| | 2014 | 2013 | 2012 |
| Taxes at the Irish statutory tax rate of 12.5% | \$(792) | \$(5,073) | \$(5,176) |
| Income tax at rates other than applicable statutory rate | 705 | (3,169) | 4 |
| Change in valuation allowance | 2,444 | 10,365 | 5,176 |
| Share-based payments | 74 | 164 | — |
| Tax credits | (1,643) | (1,921) | — |
| Other | 23 | 49 | 2 |
| Provision for income taxes | \$811 | \$415 | \$6 |

Deferred income taxes reflect the net tax effect of temporary differences between the carrying amount of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the Company's net deferred tax assets as of December 31, 2014 and 2013 are as follows (in thousands):

| | December 31 | |
|---------------------------|-------------|-----------|
| | 2014 | 2013 |
| Deferred tax assets: | | |
| Net operating losses | \$16,322 | \$15,457 |
| Tax credits | 1,139 | 1,310 |
| Accruals | 1,016 | 1,149 |
| Share-based compensation | 2,225 | 779 |
| Gross deferred tax assets | 20,702 | 18,695 |
| Valuation allowance | (18,815) | (17,798) |
| Net deferred tax assets | 1,887 | 897 |
| Deferred tax liability | — | — |
| Net deferred tax assets | \$1,887 | \$897 |

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, state tax credit carryforwards 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 \$18.8 million against its deferred tax assets as of December 31, 2014 in relation to deferred tax assets arising from tax credits and net operating losses. The net increase of \$1.0 million in the valuation allowance during the year ended December 31, 2014 was primarily due to share-based compensation.

As of December 31, 2014, certain of the Company's Irish subsidiaries had trading loss carryovers of \$100.8 million and non-trading loss carryovers of \$5.7 million, each of which can be carried forward indefinitely but are limited to the same trade/trades. In addition, as of December 31, 2014, the Company had state net operating loss carryforwards of approximately \$34.1 million available to reduce future taxable income for the Company's U.S. subsidiary, if any. If not utilized, the state net operating loss carryforward begins expiring in 2032.

The Company also has California research and development credit carryforwards of \$1.1 million at December 31, 2014. The California tax credits can be carried forward indefinitely.

Cumulative unremitted earnings of the Company's U.S. subsidiary total approximately \$4.1 million at December 31, 2014. The Company's U.S. subsidiary's cash balance at December 31, 2014 is committed for its working capital needs. No taxes have been provided for the unremitted earnings as any tax basis differences relating to investments in this overseas subsidiary are considered to be permanent in duration. Unremitted earnings may be subject to U.S. withholding taxes (potentially at 5%) 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. tax withheld and as of December 31, 2014 the Company's net operating losses in Ireland are sufficient to offset any potential dividend income received from its U.S. subsidiary.

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

| | 2014 | 2013 |
|---|--------|--------|
| Gross Unrecognized Tax Benefits at January 1 | \$ 480 | \$ — |
| Additions for tax positions taken in the current year | 253 | 480 |
| Reductions for tax positions taken in the prior year | (350 |) — |
| Gross Unrecognized Tax Benefits at December 31 | \$ 383 | \$ 480 |

If recognized, none of our unrecognized tax benefits as of December 31, 2014 would reduce our annual effective tax rate but would result in a corresponding adjustment to our deferred tax valuation allowance. As of December 31, 2014, we have not recorded a liability for potential interest or penalties. We also do not expect our unrecognized tax benefits to change significantly over the next 12 months.

The tax years 2012 to 2014 remain subject to examination by the U.S. taxing authorities and the tax years 2010 to 2014 remain subject to examination by the Irish taxing authorities.

11. Employee Retirement Plan

Prothena 401K Retirement Plan

In December 2012 (effective January 1, 2013), the Company established a qualified retirement plan under section 401(k) of the Internal Revenue Code ("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 a discretionary matching and/or profit sharing contribution as determined solely by the Company. The Company did not record any expense in the year ended December 31, 2012 as no contributions, matching or profit sharing contributions were made under the 401(k) plan. The Company recorded total expense for matching contributions of \$0.4 million and \$0.3 million for the years ended December 31, 2014 and 2013, respectively.

Elan Pharmaceuticals 401(k) Retirement Savings Plan

Elan maintained a 401(k) retirement savings plan for its employees based in the U.S., including employees that directly and indirectly provided service to the Prothena Business prior to the Separation and Distribution. The Prothena Business recorded total expense for matching contributions of \$0.1 million for the year ended December 31, 2012.

12. Related Parties

Prior to December 21, 2012, the Prothena Business operated as part of Elan and not as a separate stand-alone entity. Effective December 20, 2012, the Prothena Business separated from Elan. In connection with the separation, a wholly owned subsidiary of Elan acquired an 18% interest in the Company (as calculated immediately following the separation). Elan was subsequently acquired by Perrigo, in December 2013, and such 3,182,253 ordinary shares were held by ESOL, an indirect wholly owned subsidiary of Perrigo, as of December 31, 2013.

February 2014 Offering

In February 2014, ESOL sold 3,182,253 ordinary shares of Prothena at a price to the public of \$26.00 per ordinary share, before the underwriting discount. As a result, ESOL and Perrigo no longer owned any ordinary shares of Prothena as of such sale.

The Company did not receive any of the proceeds from the offering, and the total number of the Company's ordinary shares outstanding did not change as a result of this offering. The Company paid the expenses associated with the sale of these ordinary shares (other than the underwriting discount, fees and disbursements of counsel for the selling shareholder) pursuant to a Subscription and Registration Rights Agreement dated November 8, 2012 by and among the Company, Elan and ESOL.

Agreements with Elan

As described elsewhere in these Consolidated Financial Statements, the results of operations of the Prothena business for the time period prior to the separation include transactions with Elan. The related party revenue recognized by the Company for the years ended December 31, 2014 and 2013 consisted of fees arising from R&D services provided to

Elan. Additionally, the results of operations for the time period prior to the separation include certain costs allocated from Elan to the Company for centralized support services.

The Company entered into certain agreements with Elan, including the Transitional Services Agreement and the R&D Services Agreement.

Transitional Services Agreement

In December 2012, as amended in March 2013, the Company entered into a Transitional Services Agreement (“TSA”) with Elan under which Elan provided to the Company, and the Company provided to Elan, specified services to help ensure an orderly transition following the Separation and Distribution. The services provided by Elan under the Transitional Services Agreement included chemistry, manufacturing and controls/quality assurance, information technology services, facilities services, company secretarial services, finance services, legal services, compliance services and human resources services.

The payment terms of the agreement generally provided that the Company would pay Elan for the time spent by each Elan employee providing the services, which will be calculated by the portion of the employee’s time dedicated to the provision of the

services, plus 40%. Similarly, Elan would pay the Company for the time spent by each of the Company's employee providing services to Elan, which would be an agreed percentage of the employee's time, based on the cost of providing those services plus 40% and including, as applicable, any fees for any services from Elan or the Company provided by third party providers and invoiced to the recipient at cost.

TSA expenses recognized during the years ended December 31, 2014, 2013 and 2012, respectively, were \$nil, \$0.5 million (of which \$0.1 million was included in R&D expenses and \$0.4 million was included in G&A expenses) and \$nil, respectively. The TSA expired on December 31, 2013.

R&D Services Agreement

In December 2012, as amended in March 2013, the Company entered into a Research and Development Services Agreement ("RDSA") with Elan pursuant to which the Company provided certain R&D services to Elan. Either party was entitled to terminate the RDSA at any time by notice in writing to the other party if there has been an uncured material breach by the other party or if the other party becomes insolvent or if the other party is in breach of any of its confidentiality obligations under the agreement. This RDSA expired in December 2014 at the end of its two-year term.

The services provided for under the RDSA included support for the ELND005 program (which include the provision of expert advice and opinion in the areas of nonclinical safety/toxicology and pharmacology, regulatory support for nonclinical sections of pertinent documents, conducting and interpreting externally conducted nonclinical studies, and support in respect of the identification and maintenance of nonclinical expert advisors as required). These services were substantially similar to research services performed by the Company for Elan prior to the separation and distribution.

The payment terms of the RDSA provided that Elan would pay the Company: (i) a fixed charge of \$500,000 per year based on a charge for two of the Company's employees providing the services at a rate of \$250,000 each per annum, (ii) if the \$500,000 fixed charge has been paid in any year, a variable charge of \$250,000 per year for any additional employee that provides services for such year (calculated pro rata based on the number of days the employee provides services in such year), (iii) research costs including direct overheads, and (iv) a mark-up of 10% applied to the fixed charge, variable charge (if any) and research costs such that the total payment reflects a cost-plus standard. Revenue recognized by the Company included fees arising from R&D services provided to Elan of \$534,000, \$676,000, and \$2.7 million for the years ended December 31, 2014, 2013 and 2012, respectively.

13. 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, 2014. 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, 2014 | | | | |
| Revenues | \$ 32,234 | \$ 15,121 | \$ 1,486 | \$ 2,013 |
| Operating expenses | \$ 14,215 | \$ 13,552 | \$ 14,618 | \$ 15,118 |
| Net income (loss) | \$ 17,852 | \$ 1,290 | \$ (13,182) | \$ (13,110) |
| Net income (loss) per share - basic | \$ 0.82 | \$ 0.06 | \$ (0.48) | \$ (0.48) |
| Net income (loss) per share - diluted | \$ 0.78 | \$ 0.06 | \$ (0.48) | \$ (0.48) |
| Year Ended December 31, 2013 | | | | |
| Revenues | \$ 171 | \$ 167 | \$ 171 | \$ 167 |
| Operating expenses | \$ 9,138 | \$ 11,359 | \$ 9,737 | \$ 10,869 |
| Net loss | \$ (8,951) | \$ (11,302) | \$ (9,689) | \$ (11,054) |
| Net loss per share - basic and diluted | \$ (0.51) | \$ (0.64) | \$ (0.55) | \$ (0.52) |

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, 2014, 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.

Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. 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, 2014, 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, 2014, our internal control over financial reporting was effective.

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.

Attestation Report on Internal Control over Financial Reporting

This Form 10-K does not include an attestation report of our independent registered public accounting firm due to the deferral allowed under the Jumpstart Our Business Startups Act for emerging growth companies.

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, 2014 that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

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, 2015 (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 12, 2015.

| Name | Age | Position(s) | Since |
|-----------------------|-----|---|-------|
| Dale B. Schenk, Ph.D. | 57 | President and Chief Executive Officer, Director | 2012 |
| A. W. Homan | 55 | Chief Legal Officer | 2014 |
| Gene G. Kinney, Ph.D. | 46 | Chief Scientific Officer and Head of Research and Development | 2012 |
| Martin Koller, M.D. | 64 | Chief Medical Officer | 2013 |
| Tran B. Nguyen | 41 | Chief Financial Officer | 2013 |
| Tara Nickerson, Ph.D. | 42 | Chief Business Officer | 2014 |
| Karin L. Walker | 51 | Chief Accounting Officer, Controller and Head of Accounting | 2013 |

Dale B. Schenk, Ph.D., is our President and Chief Executive Officer, as well as a member of our Board of Directors, positions he has held since 2012. Prior to that, from 2008 to 2012, Dr. Schenk was Executive Vice President and Chief Scientific Officer of Elan Corporation, plc (a pharmaceutical company), where he provided the leadership and scientific direction for Elan's research and development programs. From 1996 to 2008, Dr. Schenk held various other positions with Elan. He was a founding scientist of Athena Neurosciences, Inc., which was acquired by Elan in 1996. Dr. Schenk has pioneered the immunotherapeutic approach for the treatment of amyloidosis, as exemplified for Alzheimer's disease. His work in this area, as well as in early detection, testing and other pathways to the disease, has led to the most advanced potential treatment approaches for Alzheimer's disease. Dr. Schenk earned his BA and PhD in Pharmacology and Physiology from the University of California, San Diego.

A. W. Homan has served as our Chief Legal Officer since 2014. Prior to joining Prothena, Mr. Homan 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. He 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, Mr. Homan 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.

Gene G. Kinney, Ph.D., has served as our Chief Scientific Officer and Head of Research and Development since 2012. Prior to that, he was Senior Vice President of Pharmacological Sciences (a position he held from 2011 to 2012), and Vice President, Pharmacology (a position he held from 2009 to 2011) for Elan Pharmaceuticals, Inc; while in those

positions, Dr. Kinney 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. Dr. Kinney earned his BA from Bloomsburg University and his MA and PhD from Florida Atlantic University.

Martin Koller, M.D., has served as our Chief Medical Officer since 2013. Dr. Koller is a board-certified neurologist with 25 years of pharmaceutical industry experience in drug development from Phases 1-4, and has been involved with a number of Investigational New Drugs and New Drug Applications in several indications (including Alzheimer's disease, multiple sclerosis, cervical dystonia, pain, anti-epileptics, migraine, stroke, anxiety and depression). Prior to joining Prothena, Dr. Koller served as Chief Medical Officer of Sonexa Therapeutics, Inc. (a pharmaceutical company), a position he held from 2009 to 2013. From 2007 to 2009, he was an independent consultant to various small and medium sized pharmaceutical and biotechnology companies. From 2002 to 2007, Dr. Koller was Vice President of Clinical Development at Elan Pharmaceuticals, Inc., overseeing a national, and then international, drug development group. He also held positions at Athena Neurosciences, Inc., Syntex Corporation and Wyeth Pharmaceuticals, Inc. Dr. Koller earned his BA from Franklin and Marshall College, his MD from the University of Maryland at Baltimore and his MPH with an emphasis in epidemiology from the University of Texas at Houston.

Tran B. Nguyen has served as our Chief Financial Officer since 2013. Mr. Nguyen has over 15 years of finance experience in the healthcare, banking and private equity industries. Prior to joining Prothena, Mr. Nguyen was Vice President, Chief Financial Officer (from 2010 to 2011) and then Senior Vice President, Chief Financial Officer of Somaxon Pharmaceuticals, Inc., from 2011 until its sale in 2013. He was Vice President, Chief Financial Officer and Investor Relations at Metabasis Therapeutics, Inc. (a biopharmaceutical company), from 2009 until its sale in 2010. From 2007 to 2009, Mr. Nguyen 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 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.

Tara Nickerson, Ph.D., has served as our Chief Business Officer since 2014. Prior to that, she was our Head of Corporate and Business Development and Secretary, positions she held since 2012. Dr. Nickerson previously held various positions with Elan Pharmaceuticals, Inc., including Vice President and Head of Business Development (during 2012), Senior Director of Corporate Strategy and Strategic Alliances (from 2007 to 2012) and Director, Corporate Strategy and Strategic Alliances (from 2005 to 2007). During her tenure at Elan, she was responsible for opportunity evaluation, diligence, negotiations and contracting for Elan external opportunities, and established a broad network of collaborations for Elan with academic investigators, not-for-profit disease-focused foundations and industry collaborators. Dr. Nickerson was previously a Senior Scientist at Axys Pharmaceuticals, where she led preclinical programs developing novel small molecule based therapeutics for oncology. Dr. Nickerson earned her BSc and PhD in Experimental Medicine from McGill University and her MBA from the University of California, Berkeley's Haas School of Business.

Karin L. Walker has served as our Controller, Chief Accounting Officer and Head of Accounting since 2013. Prior to joining Prothena, Ms. Walker 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, she was Vice President, Finance and Corporate Controller at Amyris Inc. (a biotechnology company). From 2006 to 2009, Ms. Walker was Vice President, Finance and Corporate Controller for CV Therapeutics, Inc. (a biopharmaceutical company). She also held senior financial leadership positions at Knight Ridder Digital, Accellion, Niku Corporation, Financial Engines, Inc. and NeoMagic Corporation. Ms. Walker earned her BS in business from the California State Polytechnic University, San Luis Obispo, and is a certified public accountant.

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. That Code of Conduct is available on the Company's website at <http://ir.prothena.com>. The Company 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, Alexandra House, The Sweepstakes, Ballsbridge, Dublin 4, 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

• Election 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:

• 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:

• Certain Transactions with Related Persons

• 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:

• Ratification of Appointment of Independent Registered Public Accounting Firm - Fees Paid to KPMG

• 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.

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 12, 2015

Prothena Corporation plc
(Registrant)

/s/ Dale B. Schenk
Dale B. Schenk
President and Chief Executive Officer

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

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose individual signature appears below hereby authorizes and appoints Dale B. Schenk 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/Dale B. Schenk Dale B. Schenk, Ph.D. | President and Chief Executive Officer (Principal Executive Officer) and Director | March 12, 2015 |
| /s/Tran B. Nguyen Tran B. Nguyen | Chief Financial Officer (Principal Financial Officer) | March 12, 2015 |
| /s/Karin L. Walker Karin L. Walker | Controller, Chief Accounting Officer and Head of Accounting (Principal Accounting Officer) | March 12, 2015 |
| /s/Lars G. Ekman Lars G. Ekman, M.D., Ph.D. | Chairman of the Board | March 12, 2015 |
| /s/Richard T. Collier Richard T. Collier | Director | March 12, 2015 |
| /s/Shane M. Cooke Shane M. Cooke | Director | March 12, 2015 |
| /s/Christopher S. Henney Christopher S. Henney, D.Sc., Ph.D. | Director | March 12, 2015 |
| /s/Dennis J. Selkoe Dennis J. Selkoe, M.D. | Director | March 12, 2015 |

EXHIBIT INDEX

| Exhibit No. | Description | Previously Filed | | | Filed Herewith |
|-------------|--|------------------|------------|-------------|----------------|
| | | Form | File No. | Filing Date | |
| 2.1 | Demerger Agreement, dated as of November 8, 2012, between Elan Corporation, plc and Prothena Corporation plc | 10/A | 001-35676 | 11/30/2012 | 2.1 |
| 2.2(a) | Amended and Restated Intellectual Property License and Contribution Agreement, dated as of December 20, 2012, by and among Neotope Biosciences Limited, Elan Pharma International Limited, and Elan Pharmaceuticals, Inc. | 8-K | 001-35676 | 12/21/2012 | 2.1 |
| 2.2(b) | Amendment Number One to the Amended and Restated Intellectual Property License and Contribution Agreement, effective as of December 20, 2012, among Neotope Biosciences Limited, Elan Pharma International Limited, Elan Pharmaceuticals, LLC, Elan Corporation, plc, and Crimagua Limited | S-1/A | 333-191218 | 9/30/2013 | 2.2(b) |
| 2.3 | Intellectual Property License and Conveyance Agreement, dated as of December 20, 2012, among Neotope Biosciences Limited, Elan Pharma International Limited and Elan Pharmaceuticals, Inc. | 8-K | 001-35676 | 12/21/2012 | 2.2 |
| 2.4 | Asset Purchase Agreement, dated as of December 20, 2012, between Elan Pharmaceuticals, Inc. and Prothena Biosciences Inc | 8-K | 001-35676 | 12/21/2012 | 2.3 |
| 3.1 | Amended and Restated Memorandum and Articles of Association of Prothena Corporation plc | 10-K | 001-35676 | 3/29/2013 | 3.1 |
| 4.1 | Reference is made to Exhibit 3.1 | | | | |
| 10.1(a) | Tax Matters Agreement, dated as of December 20, 2012, between Elan Corporation, plc and Prothena Corporation plc | 8-K | 001-35676 | 12/21/2012 | 10.1 |
| 10.1(b) | Amendment No. 1 to Tax Matters Agreement, dated as of June 25, 2013, between Elan Corporation, plc and Prothena Corporation plc | 10-Q | 001-35676 | 8/13/2013 | 10.2 |
| 10.2 | Subscription and Registration Rights Agreement, dated as of November 8, 2012, among Prothena | 10/A | 001-35676 | 11/30/2012 | 10.3 |

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Corporation plc, Elan Corporation, plc and Elan
Science One Limited

10.3† License, Development, and Commercialization
Agreement, dated as of December 11, 2013, among
Neotope Biosciences Limited and Prothena 10-K/A 001-35676 6/6/2014 10.4
Biosciences Inc with F. Hoffmann-La Roche Ltd.
and Hoffmann-La Roche Inc.

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| Exhibit No. | Description | Previously Filed | | | Filed Herewith |
|-------------|--|------------------|------------|-------------|----------------|
| | | Form | File No. | Filing Date | |
| 10.4† | Master Process Development and Clinical Supply Agreement, dated June 23, 2010, as amended August 1, 2011, among Elan Pharma International Limited, Neotope Biosciences limited and Boehringer Ingelheim Pharma GmbH & Co. KG | 10-Q | 001-35676 | 8/13/2013 | 10.3 |
| 10.5 | Research and Development Services Agreement, dated as of December 20, 2012, between Elan Corporation, plc and Prothena Corporation plc | 8-K | 001-35676 | 12/21/2012 | 10.3 |
| 10.6# | Form of Deed of Indemnification between Prothena Corporation plc and its Directors and Officers | 8-K | 001-35676 | 12/11/2014 | 10.1 |
| 10.7(a) | Lease Agreement, dated as of March 18, 2010, between Are-San Francisco No. 33, LLC and Elan Pharmaceuticals, Inc. | 10/A | 001-35676 | 11/30/2012 | 10.6 |
| 10.7(b) | First Amendment to Lease, dated as of November 18, 2011, between Are-San Francisco No. 33, LLC and Elan Pharmaceuticals, Inc. | 10/A | 001-35676 | 11/30/2012 | 10.7 |
| 10.7(c) | Second Amendment to Lease, dated as of June 1, 2012, between Are-San Francisco No. 33, LLC and Elan Pharmaceuticals, Inc. | 10/A | 001-35676 | 11/30/2012 | 10.8 |
| 10.7(d) | Third Amendment to Lease, dated as of October 3, 2012, between Are-San Francisco No. 33, LLC and Elan Pharmaceuticals, Inc. | 10/A | 001-35676 | 11/30/2012 | 10.9 |
| 10.7(e) | Assignment of Tenant's Interest in Lease and Assumption of Lease Obligations, dated as of December 2, 2012, between Elan Pharmaceuticals, Inc. and Prothena Biosciences Inc | 10/A | 001-35676 | 11/30/2012 | 10.10 |
| 10.7(f) | Fourth Amendment to Lease, dated as of November 30, 2013, between ARE-San Francisco No. 33, LLC and Prothena Biosciences, Inc | 8-K | 001-35676 | 12/5/2013 | 10.1 |
| 10.8# | Prothena Corporation plc Amended and Restated 2012 Long Term Incentive Plan | S-8 | 333-196572 | 6/6/2014 | 99.1 |
| 10.9# | Form of Option Award Agreement between Prothena Corporation plc and Registrant's Non-Employee Directors (used beginning January | S-8 | 333-196572 | 6/6/2014 | 99.2 |

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29, 2013)

| | | | | |
|--------|--|------|---------------------|-------|
| 10.10# | Form of Option Award Agreement between Prothena Corporation plc and Registrant's Named Executive Officers (used beginning January 29, 2013 until February 4, 2014) | S-8 | 333-196572 6/6/2014 | 99.3 |
| 10.11# | Form of Option Award Agreement between Prothena Corporation plc and Registrant's Named Executive Officers (used beginning February 4, 2014) | | | X |
| 10.12# | Prothena Biosciences Inc Amended and Restated Severance Plan | 10-K | 001-35676 3/29/2013 | 10.12 |

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| Exhibit No. | Description | Previously Filed | | | Filed Herewith |
|-------------|--|------------------|-----------|-------------|----------------|
| | | Form | File No. | Filing Date | |
| 10.13# | Prothena Corporation plc Incentive Compensation Plan | 8-K | 001-35676 | 12/21/2012 | 10.6 |
| 10.14 | License Agreement, dated as of December 31, 2008, between the University of Tennessee Research Foundation and Elan Pharmaceuticals, Inc. | 10/A | 001-35676 | 11/30/2012 | 10.14 |
| 10.15# | Employment Agreement, dated January 22, 2013, between Prothena Biosciences Inc and Dale B. Schenk | 8-K | 001-35676 | 1/25/2013 | 10.1 |
| 10.16# | Offer letter, dated March 20, 2013, between Prothena Biosciences Inc and Tran B. Nguyen | 8-K | 001-35676 | 3/28/2013 | 10.1 |
| 10.17# | Offer letter, dated December 22, 2012, between Prothena Biosciences Inc and Gene G. Kinney | 10-K | 001-35676 | 3/29/2013 | 10.18 |
| 10.18# | Offer letter, dated March 19, 2013, between Prothena Biosciences Inc and Martin Koller | 8-K | 001-35676 | 3/28/2013 | 10.2 |
| 10.19# | Offer letter, dated December 14, 2012, between Prothena Biosciences Inc and Tara Nickerson | 10-K | 001-35676 | 3/29/2013 | 10.2 |
| 10.20# | Promotion letter, dated February 5, 2014, between Prothena Biosciences Inc and Tara Nickerson | 8-K | 001-35676 | 3/3/2014 | 10.1 |
| 10.21# | Offer letter, dated April 19, 2013, between Prothena Biosciences Inc and Karin L. Walker | 8-K | 001-35676 | 5/22/2013 | 10.1 |
| 10.22# | Offer letter, dated April 11, 2014, between Prothena Biosciences Inc and A. W. Homan | 10-Q | 001-35676 | 8/5/2014 | 10.5 |
| 21.1 | List of Subsidiaries | | | | X |
| 23.1 | Consent of KPMG LLP, independent registered public accounting firm | | | | X |
| 24.1 | Power of Attorney (see signature page hereto) | | | | X |
| 31.1 | Certification of Principal Executive Officer pursuant to Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act | | | | X |

of 2002

| | | |
|-------|--|---|
| 31.2 | Certification of Principal Financial Officer pursuant to Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 | X |
| 32.1* | Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 | X |

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| | | Form | File No. | Filing Date | |
| 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.